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**Scientific  
Report**

2019



**LIBR**

Laureate Institute for Brain Research

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**LIBR**

Laureate Institute for Brain Research

Improving Mental Health Through Neuroscience

IMPROVING  
**MENTAL**  
**HEALTH** THROUGH  
**NEUROSCIENCE**

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# LIBR

The Laureate Institute for Brain Research (LIBR) facilities consist of 28,000 square feet of space in a building that is attached to the Laureate Psychiatric Clinic and Hospital. The neuroimaging and laboratory facilities at LIBR are entirely dedicated to research. They include two MRI scanner bays and a control room, two video-teleconferencing-enabled group meeting sites, several medical examination and patient prep rooms, the computing facility and ample office space for the investigators.



#### Details of LIBR facilities:

LIBR occupies 28,000 square feet of newly constructed space designed for neuropsychiatric and neuroscience research on the campus of the Laureate Psychiatric Clinic and Hospital at Saint Francis Hospital.

- 42 offices, including 3 large shared offices for students and volunteers
- 5 conference rooms
- 2 MRI bays and adjoining control rooms
- 3 psychophysiology testing rooms
- 2 behavioral observation rooms
- 2 medical/blood draw rooms
- 1 mock scanner room
- 1 neuropsychological testing room
- 1 transcranial magnetic stimulation (TMS) room
- 2 float rooms





The Laureate Institute for Brain Research (LIBR) continues to grow and have scientific impact. Researchers from LIBR have published over 58 scientific manuscripts in 2019, a 20% increase. We also continue to seek extramural support from governmental agencies. This highly competitive process requires multiple tries and persistence.

Our investigators have applied for eight major grants over the past six months alone. We are being recognized by leaders in the field as a viable and competitive place for neuroscience-based research. Our researchers have been presenting at international conferences as panel participants and are being asked to provide expert opinion for extramural grant applications. Taken together, the institute is growing into a mature, high-level, highly productive brain research institute focused on using neuroscience tools to improve diagnosis, prognosis, and treatment of mental disorders.

**The Tulsa 1000 study**, which aims to build a comprehensive database of individuals with mood and anxiety, substance, and eating related problems, completed enrollment of all 1,000 subjects in 2018 and continued to complete yearly follow-up visits in 2019. Over the past year, our principal investigators, post-doctoral fellows, and collaborators have begun or continued data analyses toward the publication of over 60 research papers using data from the T-1000, with 12 published or accepted for publication thus far. Currently, investigators at LIBR focus on (1) analysis of the oral microbiome to assess the ability to diagnosis individuals based on characteristics of their microbiome, (2) the emerging role of exosomes in mental health disorders, as exosomes can cross the blood-brain barrier and potentially inform brain dysfunction (3) genetic characterization of individuals through augmented polygenic risk scores involving disease onset, severity and persistence, as well as epigenetic characterization of disease progression and; (4) digital phenotyping through the relatively novel field of mobile assessments (via Fitbit tracking) and application-based interventions. These are just a few examples showing that this dataset will be of immense value in understanding the physiological processes that contribute to mood and anxiety disorders. Importantly, the follow up data of the T-1000 will be critical to establish whether these physiological parameters can be used as clinical predictors.



**Martin Paulus, M.D.**  
Scientific Director and President  
LIBR

#### Adolescent Brain Cognitive Development (ABCD)

**Florence Breslin** continues to lead the study and the four-year follow-up visits began in September. LIBR ABCD exceeds expectations for retention with 99.11 percent of follow-up visits complete. Our effort towards excellence gained the attention of Dr. Nora Volkow, National Institute of Drug Abuse (NIDA) director. We were pleased to welcome her for a visit in August. LIBR was awarded a seven-year renewal of the ABCD grant to continue our work with the Tulsa families and received one of the best scores from NIDA. LIBR, unprecedentedly, had an extremely positive grant review. We continue research into the effects of screen media on development and have started to incorporate evaluations into mental health of participants. Our first accepted manuscript on mental health, led by graduate student Danielle DeVille, evaluated the prevalence rates of suicidal ideation in 9 and 10-year-old children as an early risk signal in this population. As suicide rates increase during adolescence, understanding the risk factors will be critical in detection and prevention.

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

The LIBR Center of Biomedical Research Excellence (CoBRE) award focuses on the identification of objective biomarkers for mood and anxiety and the infrastructure established by this grant provides us the opportunity to train young investigators toward independent funding from National Institute of Health and granting agencies. The core services led by **Dr. Jerzy Bodurka**, **Dr. Kent Teague** (OU) and **Dr. Brett McKinney** (TU) include standardized neuroimaging acquisition and processing pipelines, blood biomarker pipelines and statistical analyses. In January, we added Namik Kirlic, Ph.D., as a CoBRE investigator. In May, the External and Internal Advisory Committees met for a full day to review and assess CoBRE progress. The Committees were highly impressed by the unusually high research subject accrual and participation rates, particularly since the target populations are historically difficult to recruit and retain. The Committees provided valuable feedback to help guide the program into the next year. Since recruitment was ahead of schedule throughout the second year and continued on track during the first half of the third year, investigators were able to begin analyzing data sooner than anticipated. Investigators leveraged this success using the data to generate ideas for new grant proposals with each of the original investigators submitting two grant proposals in the first half of this grant year. Finally, as further evidence of our commitment to train and support young investigators, we set aside funds for CoBRE pilot project grants, three of which were awarded to emerging young investigators.

Our principal investigators continue to produce high-impact, scientifically rigorous publications that are aimed at providing the evidence base to make a difference in mental health. Most of these publications focus on the two strategic goals for LIBR: (1) to identify modifiable neuroscience-based targets that improve mental health; and (2) to develop neuroscience-based interventions.



**Jonathan Savitz** published senior author papers in *Jama Psychiatry* and *Molecular Psychiatry*, two of the top journals in psychiatry. In addition, he was invited to join the editorial boards of *Brain, Behavior and Immunity* as well as *Psychoneuroendocrinology*, the two leading journals in his field. His work focuses on determining whether inflammation and—in particular—viruses that can generate inflammatory responses are one reason for the development of depression.



## LETTER FROM THE PRESIDENT



**Jerzy Bodurka's** group further advanced the capacity for non-invasive brain modulation with real-time EEG and fMRI neurofeedback (EEG-rtfMRI-nf) training of the amygdala, which is a promising and effective novel non-pharmacological intervention for major depressive disorder (MDD) and post-traumatic stress disorder (PTSD). Beyond advancing the mechanistic understanding of neurofeedback action, such as the correction of abnormal amygdala response and abnormal amygdala connectivity with prefrontal brain regions and the normalization of frontal EEG asymmetry in the alpha band in MDD and PTSD, it is now possible to accurately link symptom improvements at a specific time and over time with other brain regions recruited during neurofeedback amygdala modulation. They also discovered that neurofeedback-targeted brain modulation of the amygdala influences immune responses in MDD, specifically baseline serum concentrations of the pro-inflammatory cytokine, TNF-alpha, predict an individual's capacity to upregulate the amygdala during rtfMRI-nf training. Results suggest that inflammatory mediators such as the TNF-alpha may constitute a promising treatment response marker for amygdala neurofeedback modulation and could help to better identify treatment responders.



**Justin Feinstein** commenced the first NIH-funded clinical trial on floating: "Investigating Floatation-REST as a novel technique for reducing anxiety and depression." He was invited to present the keynote address at the 20th annual International Mental Health Conference in Australia and gave the keynote address at the International Society for the Advancement of Respiratory Psychophysiology meeting in Switzerland. His research studying carbon dioxide and anxiety was also featured this year on the longest running Science documentary on television, *The Nature of Things*, in a special episode on the Science of Fear.



**Robin Aupperle** has authored or co-authored 13 publications in 2019 (published or currently in press). This includes results from the TU Tough college resilience study, published in the journal *Depression and Anxiety*. Results indicate that a brief, four-session resilience program, delivered during first year orientation courses, was effective at reducing symptoms of depression and stress for college students. This semester, Dr. Aupperle worked with TU to implement this training for incoming students within the colleges of Health Sciences, Engineering and Natural Sciences, and Business. Dr. Aupperle and two others in her laboratory (post-doctoral fellow, Dr. Evan White, and graduate student, Tim McDermott) received travel awards from the Society of Biological Psychiatry (SOBP). In addition, she submitted four grant applications in 2019 as either a principal investigator or mentor.



**Sahib Khalsa** published a primer on interoception in eating disorders for clinicians that provides a clinical summary of the association between the brain and body in eating disorder. He has been able to conclusively show that the practice of meditation is not associated with improved awareness of the heartbeat, suggesting that the long-term effects of meditation may be related to other body systems, such as the breath, or may involve a mechanism independent of interoceptive accuracy. He participated in a conference on interoception organized by the National Institute of Health entitled "The Science of Interoception and its Roles in Nervous System Disorders." The meeting brought the scientific debate on interoception that was started by the LIBR Interoception Summit to a broader audience of animal and human researchers from all over the world. Another special issue on interoception is underway, and both Martin Paulus and Sahib Khalsa are involved.

In collaboration with his lab and a team of researchers at UCLA, Somatomap was developed. It is a novel mobile tool for assessing body image perception. The initial study, piloted in fashion models, identified body image differences between models and non-models. Ongoing studies are examining whether Somatomap provides a unique way of measuring body image disturbance in eating disorders, which could be useful for the remote detection, monitoring and clinical referral of body image concerns as we begin entering the era of digital psychiatry.



**Yoon-Hee Cha** who had been focusing on neuromodulation via transcranial magnetic stimulation received a terrific offer from the University of Minnesota, which also brought her closer to her family and moved to Minneapolis in the summer. She will continue her work on modulating the cerebellum in anxious individuals to begin to identify novel brain targets for neuromodulation of anxiety. She will continue to collaborate with LIBR in the future.



**Jenny Stewart** co-authored ten publications pointing to potential diagnostic/predictive markers in individuals with mood, anxiety, substance use, and eating disorders. A current theme across most of these papers is that individual differences in disorder presentation, symptoms, and/or brain/behavioral function matter. For example, (1) although depressed people have unhealthy diets, the type of appetite change they experience during their current depressive episode is related to what type of inflammation they experience: diet-based (decrease) or blood-based (increase) (Burrows et al., in press); (2) although women with eating disorders show brain and behavioral biases toward/away from food and body-related stimuli, these biases are more consistent when we focus within specific symptom clusters (e.g., anorexia versus bulimia versus binge-eating), and an important symptom of anorexia, perfectionism, has been understudied but may be an important marker of disease progression/severity (Ralph-Nearman, et al., 2019); (3) brain and behavioral markers of methamphetamine and opioid use disorder are not identical, such that methamphetamine use frequency/recency is specifically associated with cardiac problems (Stewart, Khalsa, et al., 2019); and (4) individual differences in frontal lobe function predict treatment success and recovery for people with posttraumatic stress disorder (Butt et al., 2019) and stimulant/opioid use disorders (Stewart, May, Aupperle, et al., 2019; Stewart, May, & Paulus, 2019). Jenny has an additional 15 papers under review, most coauthored with LIBR post-docs, grad students, principal/associate investigators, and staff. Jenny has also had a fun and productive year working with LIBR's ten post-docs on career development, talks/conference presentations, and paper/grant submissions. Last but not least, Jenny is working on the resubmission of her R01 grant application to the National Institute on Drug Abuse entitled "Interoception adaptations during recovery from opioid and stimulant use disorders" (scored a 44, in the 35th percentile, by the grants review panel on her first submission). Jenny is really enjoying her work at LIBR and is committed to staying in Tulsa for the long-haul (she is closing on her first house in early January 2020).





## LETTER FROM THE PRESIDENT

### Associate Investigators

We have created the track of Associate Investigator to provide up-and-coming young research talent a way to grow into the LIBR family of investigators. The idea is that we will see some of these researchers as principal investigators in the near future. We are very excited to have three extremely talented individuals who have been outstandingly productive this year.



**Hamed Ekhtiari** has been working on using neuroscience-based training of individuals with substance-use problems to enhance abstinence. This work is based on translating complex neuroscience constructs into easy-to-understand cartoons. His work has received international attention and his cartoons have been translated into over 15 languages. This approach was recognized by the Oklahoma Center for the Advancement of Science and Technology with a two-year grant to develop this approach as an intervention for individuals with substance-use disorders. He has recently developed a series of brain imaging tasks with drug cues for methamphetamine and opioid users to explore neural correspondence of drug craving. Moreover, he has been working with the LIBR team to use transcranial direct and alternating current stimulation to target these neural targets involved in drug craving to help substance users remain abstinence in long-term.



**Namik Kirlic** has been investigating mindfulness-based interventions in teens who have experienced adverse life events growing up. In 2019, he completed a small pilot grant awarded through Oklahoma State University where he showed that mindfulness can significantly reduce symptoms of depression in these teens. In addition, he was awarded another grant to investigate whether we can use brain training to enhance mindfulness practice and further improve outcomes.

His long-term goals of using sophisticated brain imaging and behavioral intervention focused on trauma-related problems with mental health will have significant impact and will be highly relevant for young people in Oklahoma.



**Ryan Smith** is focused on bringing a computational framework to the questions we are asking at LIBR. In particular, he is using an active inference approach, which provides a way of explaining how individuals act to make the most preferred outcome more likely. He has been very prolific in 2019. He published 13 journal articles, has four under review and five more in preparation. He is working on multiple collaborative projects with researchers at University College London, the Max Planck Center in London, Yale University and McGill University. Ryan mentors a graduate student at the University of Melbourne as part of a collaborative computational modelling project. He has presented his work at four conferences and is preparing to submit a K-Award application to NIH.

The post-doctoral fellow is the quintessential researcher that is bound to make the most discoveries because she/he focuses exclusively on analyzing and publishing research data. LIBR has added five new post-doctoral researchers in 2019 who will focus their efforts on analyzing collected data and publishing the results in scientific journals. We welcomed Leandra Figueroa-Hall, Ph.D., Hiaxia Zhang, Ph.D., Philip Spechler, Ph.D., Evan White, Ph.D., and Adam Teed, Ph.D.

Taken together, 2019 has been a productive year for LIBR. We recognize that the suffering of individuals with psychiatric disorders is current and pressing. Therefore, there is a sense of urgency to push the field to apply neuroscience to identify objective markers for disease and to use these tools for innovative treatments. There is light at the end of the tunnel but we are not there yet.

### LIBR MISSION

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

### SPECIFIC AIMS

Bring to bear a multidisciplinary research program aimed at illuminating the pathophysiology of neuropsychiatric disorders

Develop novel therapeutics, cures and preventions to improve the well-being of persons who suffer from or are at risk for developing neuropsychiatric disorders

Foster collaboration among scientists, clinicians and institutions engaged in research that enhances wellness and alleviates suffering from neuropsychiatric disorders

### 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, neurology, developmental neuroscience, computer science and genetics.

## AREAS OF RESEARCH

The goal for LIBR is to generate impactful research (knowledge) that makes a difference in mental health. That is, the principal product of LIBR is knowledge building. In order for knowledge to be impactful, it needs to change behavior of the stakeholders and, as a consequence, improve the quality of life of the mentally ill. This change in behavior could be applying a new treatment, providing information to the patient that affects their behavior to improve outcomes, changing the strategy of treatment based on novel assessments or providing information about likely outcomes in the future. A critical task in creating impactful knowledge at LIBR is to shorten the gap of time between the acquisition of knowledge and the implementation in clinical practice. This gap of time will be greater if production of knowledge focuses on basic processes underlying the pathophysiology of the disorder as opposed to changing behavior. Therefore, we need to be mindful of creating knowledge that will affect mental health in the short-term as well as the long-term.

### THERE IS A NEED FOR:

- 1** Earlier detection of the development and/or exacerbation of mental health conditions, e.g., early but not late stages of mood disorder may be treatable with an anti-inflammatory agent
- 2** Sensitive and specific tests for severity of mental health conditions, e.g., predicting relapse may allow the clinician to intervene earlier
- 3** Earlier and sensitive detectors of treatment effects of interventions for mental health conditions, e.g., rather than waiting four to six weeks for an antidepressant to show significant effects, early changes may help select treatments that work faster
- 4** Detection of the emergence of side effects
- 5** More effective interventions for anxiety, depression and substance disorders

### BEHAVIORAL PROCESSES

This research theme focuses on identifying the physiological bases for drives and behaviors that contribute to the development, maintenance or recovery from neuropsychiatric dysfunction to improve the assessment and treatment of mental and physical health.

### NEUROIMAGING

This research theme focuses on the existing and emerging tools and techniques in multimodal imaging.

### NEUROMODULATION

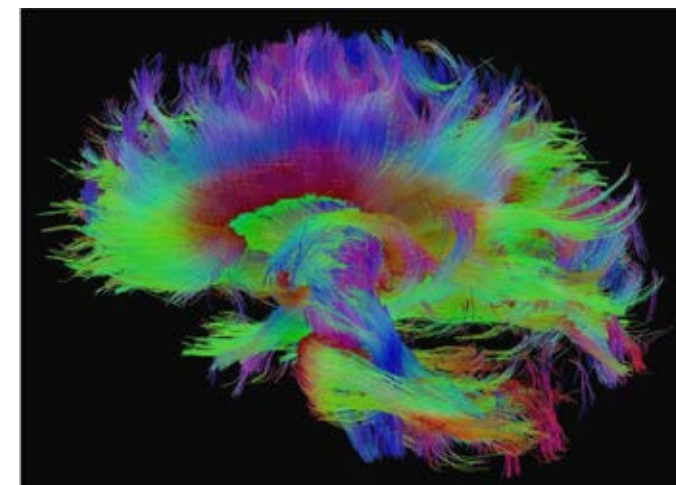
This research theme focuses on real-time feedback modalities and non-invasive brain stimulation to change dysfunctional processes in psychiatric populations.

### PSYCHOPHYSIOLOGY

This research theme focuses on the use of physiological measures to examine the connection between body and brain.

### BIOASSAYS

This research theme focuses on the use of biochemical measures, ranging from inflammatory markers to microbiome assessments to genetics.



### LIBR LEADERSHIP



**Martin Paulus, M.D.**  
Scientific Director and President



**Tom Cooper, MBA**  
Chief Executive Officer



**Colleen McCallum, MBA**  
Chief Operating Officer



**Jerzy Bodurka, Ph.D.**  
Chief Technology Officer

**LIBR BY THE NUMBERS 2019**

**58** journal article publications by LIBR investigators



**3,835** inquiries for study participation

**2,545** participants enrolled across all studies

**10** active grants and clinical trials

**228** participants enrolled in their first MRI study

**1** new externally funded grant

**\$2.6 million** in external grant funding

**9** post-doctoral fellows



**8** distinguished speakers for The William K. Warren Jr. Frontiers in Neuroscience 2019 lecture series

**8** principal investigators

**100+** poster presentations and talks at conferences and universities

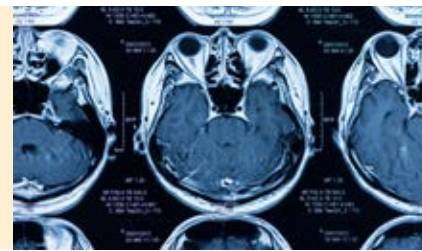
**6** staff scientists

**4** associate adjunct investigators

**60+** collaborative institutions

**8** graduate students

**1,772** Magnetic Resonance Imaging (MRI) scanning sessions



**2019 FUNDING SOURCES**

**ACTIVE AND AWARDED GRANTS**

**National Institute of Drug Abuse (NIDA)**

*Adolescent Brain Cognitive Development (ABCD) Study*  
09/30/2015 – 05/31/2020  
PI: Martin Paulus, M.D.

*3/6 Planning for the HEALthy Early Development Study*  
09/30/2019 – 09/30/2021  
PI: Jerzy Bodurka, Ph.D.

**National Institute of Mental Health (NIMH)**

*Common and Distinct Interoceptive Phenotypes of Anorexia Nervosa and Panic Disorder*  
5/1/2017 – 3/31/2022  
PI: Sahib Khalsa, M.D., Ph.D.

*Approach-Avoidance Conflict: A Multi-Level Predictor of Exposure Therapy Response*  
4/12/2016 – 3/31/2021  
PI: Robin Aupperle, Ph.D.

*Acute modulation of neural circuitry regulating immune function in depression*  
08/01/2018 – 07/31/2020  
PI: Jonathan Savitz, 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  
PI: Martin Paulus, M.D.

*Dyadic Inter-Brain Signaling Project*  
02/01/2017 – 03/31/2021  
PI: Jerzy Bodurka, Ph.D.

**National Center for Complementary & Integrative Health**

*Investigating Flotation-REST as a novel technique for reducing anxiety and depression*  
09/25/2018 – 07/31/2021  
PI: Justin Feinstein, Ph.D.

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

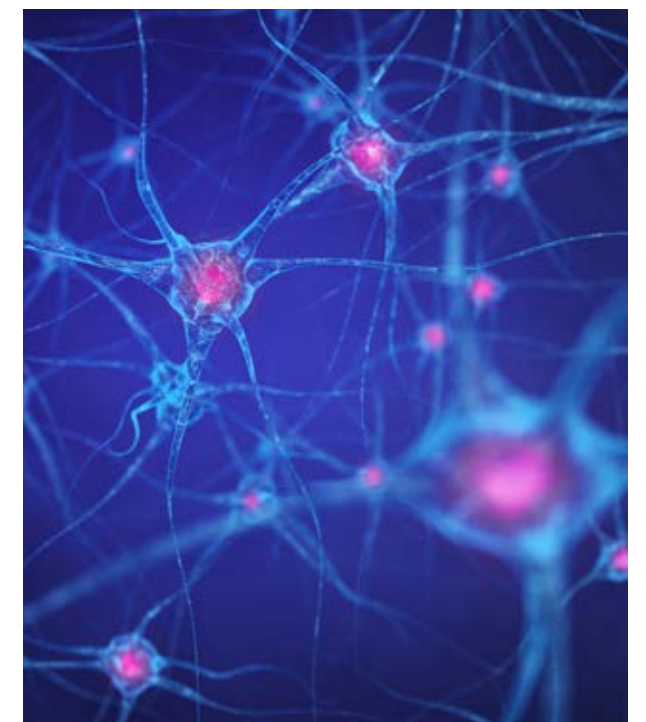
*Examining the Utility of Frontoparietal Synchronization to Modulate Drug Craving to Enhance Self-Control to Cue Induced Cravings in Individuals with Opioid Use Disorder*  
01/15/19 – 01/14/21  
PI: Hamed Ekhtiari, M.D., Ph.D.

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

*Neurocognitive Empowerment for Addiction Treatment (NEAT): A Randomized Controlled Trial for Opioid Addiction*  
07/01/18 – 07/17/21  
PI: Hamed Ekhtiari, M.D., Ph.D.

**2019 DONORS**

- Marie Elise Howard Fund
- John J. King, Jr.
- Saxifrage Summit Partnership, LTD c/o John J. King, Jr.
- Christopher W. King
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- Judith King
- J. Falcon, LTC c/o Judith King
- Margaret King Kelley
- Overall Five, LTD c/o Margaret King Kelley
- Constance King Cowett
- DWK Legacy, LTD c/o Constance King Cowett
- Natalie Bryant
- W. Kelly Vandever Revocable Trust
- William K. Warren, Jr., LLC
- Stephen K. Warren, Trust A
- The William K. Warren Foundation
- Jean M. Warren Fund





# T-1000 STUDY

## Tulsa 1000 Study

The Tulsa 1000 (T-1000) study, the largest study at LIBR, began in January 2015 and completed baseline enrollment of all 1,000 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 will continue throughout 2020. 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, 12 papers have been published by the T-1000 project authors and their collaborators. An additional five were under review at the end of 2019. Data analysis of the T-1000 variables is ongoing, with over 60 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, and how processing of body signals differs in individuals with opioid and stimulant use disorders.

The Tulsa 1000 investigators include the following contributors: Robin Aupperle, Ph.D., Jerzy Bodurka, Ph.D., Justin Feinstein, 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.

# ABCD STUDY



The Adolescent Brain Cognitive Development (ABCD) study is continuing strong starting the fourth year of annual assessments in September. Through the hard work of our ABCD team, the LIBR site has a 99.11% retention rate.

During 2019, the ABCD grant had to go through an NIH renewal requiring a new grant submission as well as progress during the first five years. LIBR was excited to receive the best score of 18 on our renewal and will receive funding for the ABCD for the next seven years.

Our ABCD team is working on data analysis, with several papers on screen media and mental health being submitted during 2019. Our latest submission, "Prevalence and family-related correlates of suicidal ideation, suicide attempts, and self-injury in children aged 9-10," has been accepted to JAMA Open Network.

The LIBR ABCD team has also been working hard on ensuring we are sharing our results with the ABCD collaborators and Tulsa community with our annual update and party, as well as reports on local and national media. We also had the opportunity to showcase our ABCD work on a documentary, "Screen generation: a sick generation?" with Arte television, expected in 2020.

## 2019 AWARDS

### BART FORD, PH.D., CANDIDATE AWARDED TRAVEL AND RESEARCH PRESENTATION AWARDS

Congratulations to Bart Ford, graduate student at The University of Tulsa, in the Savitz Lab, for receiving the Michael Irwin Diversity and Equity Award for the 2019 Psychoneuroimmunology Research Society (PNIRS) Conference in Berlin, Germany. He presented his work on "Reduced immunity to measles and rubella, but not polio in adults with major depressive disorder: a follow up study."

At the University of Tulsa's Student Research Colloquium, Bart Ford was awarded first place for his oral presentation on "T-cell subsets associated with cytomegalovirus and family history of mood disorder." As well, he was awarded third place for his poster presentation on the same topic at the University of Oklahoma Research Forum in the Biomedical category.



### GEOFFREY BURNSTOCK AWARD PRESENTED TO DR. SAHIB KHALSA

Dr. Sahib Khalsa received the Geoffrey Burnstock Award from the International Society of Autonomic Neuroscience. This was the only award given at the meeting,

which is held every two years, and was based on outstanding presentation of research at the meeting. The talk was titled: "Association between bilateral cardiac sympathetic denervation and mental health." A total of four awards were distributed at the meeting; all other recipients were animal researchers conducting basic neuroscience.

### GRINDLEY GRANT AWARDED TO DR. CHRISTINA RALPH-NEARMAN

Dr. Christina Ralph-Nearman, a postdoctoral scholar in the Khalsa lab, received a Grindley Grant from the Experimental Psychology Society in January 2019 to attend the annual meeting.

### UNIVERSITY OF TULSA UNDERGRADUATE RESEARCH AWARD GIVEN TO MEGAN SINIK

Megan Sinik, an undergraduate research volunteer from The University of Tulsa in the Khalsa lab, received an honorable mention at The University of Tulsa's annual undergraduate research colloquium, for her talk titled: "Relationship between psychotropic medication use and suffocation fear."

### "RISING STAR" AWARD RECEIVED BY RACHEL LAPIDUS

Rachel Lapidus from the Khalsa Lab, and graduate student at The University of Tulsa, received the "Rising Star" award from the University of California-San Diego (UCSD) Eating Disorders Center. This was a highly competitive application with only one award given. She presented a poster on: "Augmented Interoceptive Exposure Training For Food-Related Fear in Anorexia Nervosa: a Proof-of-Concept Study."

### SOCIETY OF BIOLOGICAL PSYCHIATRY TRAVEL FELLOWSHIP AWARDS

Dr. Robin Aupperle, Dr. Evan White and graduate student Tim McDermott (The University of Tulsa) each received a Society of Biological Psychiatry Travel Fellowship Award to attend the 74th annual scientific conference "Innovations in Clinical Neuroscience: Tools, Techniques and Transformative Frameworks" in Chicago, Illinois, on May 16-18, 2019.

### GRADUATE STUDENT TRAVEL AWARD RECEIVED BY KELLY COSGROVE

Kelly Cosgrove, graduate student at The University of Tulsa, in the Aupperle Lab at LIBR, received a travel award to attend the 2019 Society for Research in Child Development biennial meeting.

### UNIVERSITY OF WASHINGTON FELLOWSHIP AWARDED TO DR. EVAN WHITE

Post-doctoral research associate, Evan White, in the Aupperle Lab, was awarded the Indigenous Substance Abuse, Medicines and Addictions Research Training Fellowship from the Indigenous Wellness Research Institute at the University of Washington.

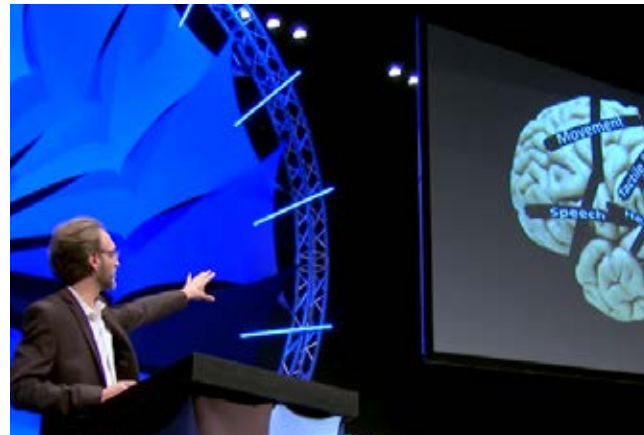
## FLOAT CLINIC AND RESEARCH CENTER (FCRC)

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 promoting mental health and healing in patients who suffer from anxiety and other forms of mental illness.

Floatation therapy allows the nervous system to naturally enter a relaxed physiological state by reducing stimulation from the external environment. In a world of 24/7 connectivity, the float experience helps an individual disconnect from this constant stream of stimulation. All visual, auditory, thermal, tactile and proprioceptive input is minimized in our specially designed circular pools. Moreover, each pool is saturated with 2,000 pounds of Epsom salt, allowing individuals to effortlessly float in a bed of water that is denser than the Dead Sea.



The FCRC is directed by Dr. Justin Feinstein and is now in its fifth year of operation. Based on initial studies, the float environment appears to rapidly reduce levels of stress throughout the nervous system, allowing one's brain and body to enter a deep state of relaxation. In 2018, the FCRC published the first float study to measure blood pressure during the float itself, documenting significant reductions in blood pressure (10 to 15 points). The FCRC also developed other wireless and waterproof sensors to measure neural and physiological changes during the float itself, including heart rate, respiration, movement and frontal EEG brain waves. The lab has also completed the first brain imaging study examining the effects of floating on the brain.



*Dr. Feinstein delivers keynote address on his research about floating at the 20th International Mental Health Conference in Australia on August 1, 2019.*

Building from this base of knowledge, the FCRC has completed its first set of clinical studies examining the effects of floatation therapy in individuals who have been chronically suffering from high levels of anxiety and stress, including patients with PTSD, panic disorder, generalized anxiety disorder, major depression and anorexia nervosa. Across two different trials that were published in 2018, an open label trial and a randomized controlled trial, the initial data showed very promising short-term effects in these patient populations, with a single float session able to provide significant reductions in stress and anxiety, improving both mood and well-being. Current studies are tracking the time course of these effects as well as studying whether there is evidence for long-term benefit following repeated practice.

In 2019, the FCRC commenced the first NIH-funded clinical trial on floating entitled, "Investigating Floatation-REST as a novel technique for reducing anxiety and depression." The trial is funded from an R34 grant from the National Center for Complementary and Integrative Health. This unique program of research is just beginning, so please stay tuned as we learn more about how floatation therapy works, and how it can help those who suffer from anxiety, PTSD, depression, anorexia nervosa, and other forms of mental illness.

## EEG-FMRI FACILITY: 2019

Established in July 2009 and in research operation since June 2010, the MRI and EEG facility provides advanced, state-of-art structural, diffusion and perfusion MRI, functional MRI (fMRI), and electroencephalography (EEG) neuroimaging capabilities to non-invasively measure, quantify, modulate, and study normal and abnormal human brain structure and functions.



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

Both recently upgraded MRI scanners are fully dedicated to research and provide state-of-the-art advanced capacity for the latest ultra-fast and accelerated imaging and visualizing human brain structure. The scanners also measure and monitor brain activity. LIBR's main research approach to study brain function is a combination of simultaneous EEG and fMRI, which provides a unique capacity to capture and measure brain activity at high spatial and temporal resolution.

Each MRI scanner is also equipped with 128-channel high density EEG, wide arrays of MRI phased array coils for imaging brain and spinal cord. In addition, a custom-made real-time MRI system allowing for the management of large amounts of neuroimaging data, real-time fMRI (rtfMRI), real-time integration of physiological data (respiration, pulse oximetry or ECG waveforms) and EEG data simultaneously acquired with fMRI, and neurofeedback (rtfMRI-nf) experiments to modulate and influence brain activity during subject scanning. Both scanners are



also synchronized and integrated with other imaging and stimulation modalities to conduct multimodal simultaneous EEG and fMRI, simultaneous transcranial direct or alternating

current stimulation (tDCS/tACS) during fMRI, hyperscanning experiments where two or more subjects' EEG and/or fMRI responses and their interactions are measured simultaneously. This advanced combination and customization of state-of-the-art MRI, RF coils, and EEG and brain stimulation technologies along with custom-developed software solutions and a wide range of auxiliary computerized equipment offer unique potential for conducting advanced brain research.



In the state of Oklahoma, the LIBR MRI-EEG facility is the only facility that provides this unique technology and know-how to conduct advanced non-invasive neuroscience research for studying the human brain, and brain development in health and disease.

The MRI facility was created and is overseen by Jerzy Bodurka, Ph.D., an expert in MRI/EEG-fMRI/real-time fMRI. It is also staffed by three staff scientists: Vadim Zotev, Ph.D. (physics), an expert in MRI, simultaneous EEG and fMRI, and fMRI data analysis; Qingfei Luo, Ph.D. (physics) an expert in EEG and fMRI, and quantitative MRI (arterial spin labeling); and Masaya Misaki, Ph.D. (computational neuroscience), an expert in structural MRI image, real-time fMRI processing as well as fMRI decoding and multivariate multimodal fMRI/EEG data analysis. Other staff include four MRI technologists (Julie Owen, Bill Alden, Julie DiCarlo and Greg Hammond), and a computer programmer support (Jared Smith).





# BRAIN AWARENESS FOR ADDICTION RECOVERY INITIATIVE (BARI)



## LIBR'S BRAIN AWARENESS MATERIALS IN 12 LANGUAGES ON FIVE CONTINENTS

Brain Awareness for Addiction Recovery Initiative (BARI) started at LIBR to help people who suffer from substance use disorders and their families have a better understanding about how the brain could be affected by drug addiction and how they can help the brain in the process of recovery. Drs. Hamed Ekhtiari, Martin Paulus and Robin Aupperle developed a cartoon, neuroscience-informed psychoeducation (NIPE) package for BARI. NIPE incorporates neuroscience content that targets negative valence (e.g., anxiety and loss), positive valence (e.g., reward), cognitive systems (e.g., attention, executive control, and working memory), social processes (e.g., affiliation), and arousal/modulatory systems (e.g., sleep-wake). NIPE uses cartoons and affiliated text to promote insight and metacognitive awareness, and increase motivation for brain recovery. Some of the NIPE messages are organized in three posters in two different versions for male and female audiences. NIPE posters are translated and culturally adopted by local scientific authorities in 12 languages on five continents so far.

NIPE materials are organized into a structured psychoeducation package for four sessions called "Brain Healing First Aid." NIPE materials are also incorporated into a larger brain training/rehabilitation program for substance use disorders in 14 sessions (Neurocognitive Empowerment for Addiction Treatment (NEAT) or, simply, Brain Gym for Recovery). In a trial funded by Oklahoma Center for Advancement of Science and Technology (OCAST), NEAT is being implemented to promote the recovery process in Tulsa. Furthermore, BARI plans to develop new brain awareness activities/materials to promote brain recovery for other psychiatric disorders, such as mood and anxiety disorders.



# COBRE GRANT

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

In 2017, LIBR was awarded an \$11.3 million CoBRE grant from the National Institutes of Health (NIH) to help researchers predict and treat mood and anxiety disorders, resulting in the establishment of NeuroMAP, which includes collaborative efforts from the University of Tulsa and the University of Oklahoma.

NeuroMAP provides scientific, operational and educational infrastructure for innovative, neuroscience-based research using individual differences on several biological levels together with sophisticated statistical approaches to generate clinically meaningful predictions of risk and outcomes for mood, anxiety and eating disorders.

NeuroMAP Includes:

- A research core of established biomedical research scientists with expertise in mental health, imaging, research laboratories, relevant peer-reviewed funding, and demonstrated leadership and mentoring experience.



Martin Paulus, M.D. Jerzy Bodurka, Ph.D. Brett McKinney, Ph.D. Kent Teague, Ph.D.

- A dedicated mentor and development plan for junior investigators to transition into independently funded investigators.
- Research projects supervised by a single junior investigator that stand alone but share a common scientific focus.

### Individual Research Projects:

- *Predicting Response to Exposure Therapy Using a Carbon Dioxide Challenge in Patients with High Levels of Anxiety Sensitivity*
- *Response to Inflammatory Challenge in Major Depressive Disorder*
- *Neural Basis of Interoceptive Dysfunction and Anxiety in Anorexia Nervosa*
- *NA-MindREaL: Augmented Mindfulness Training for Resilience in Early Life*



Justin Feinstein, Ph.D. Sahib Khalsa, M.D., Ph.D. Namik Kirlic, Ph.D. Jonathan Savitz, Ph.D.

### Progress

The External and Internal Advisory Committees met for a full day review and assessment of NeuroMAP's progress. The committees provided valuable feedback to help guide the program into the next year.

Namik Kirlic, Ph.D., was added as investigator, replacing Yoon-Hee Cha, M.D., who left LIBR.

The investigators leveraged last year's success in surpassing enrollment targets to continue projects and begin analyzing data that was used to generate ideas for new grant submissions to help secure independent funding. Each of the original investigators had two grant proposals submitted in the first half of this grant year.

As part of the CoBRE grant's commitment to training and development of investigators, a variety of educational opportunities were offered.



### Internal Advisory Committee

#### Beverly Greenwood-Van Meerveld, Ph.D.

Internal Advisory Committee Chair  
The University of Oklahoma  
Health Sciences Center

**Darrin Akins, Ph.D.**  
The University of Oklahoma  
Health Sciences Center

**Gerard Clancy, M.D.**  
The University of Tulsa

**Judith James, M.D., Ph.D.**  
Oklahoma Medical Research Foundation

**James Sluss, Ph.D.**  
The University of Oklahoma

**Jennifer Hays-Grudo, Ph.D.**  
Oklahoma State University

### External Advisory Committee

#### Charles Nemeroff, M.D., Ph.D.

External Advisory Committee Chair  
The University of Texas  
Dell Medical School

**Mary Phillips, Ph.D.**  
University of Pittsburgh

**Stephen Higgins, Ph.D.**  
The University of Vermont

**Leanne Williams, Ph.D.**  
Stanford University

## CLINICAL COLLABORATORS

LIBR works closely with several clinical entities in Tulsa to recruit new participants to LIBR research studies.



### Family and Children's Services (FCS)

Family and Children's Services is devoted to helping families in crisis, and serving people struggling with mental illness, addiction and homelessness. They are committed to the families and individuals of the Tulsa area, helping over 110,000 individuals each year, or one in six Tulsans. As part of LIBR's collaboration, a LIBR assessment team member is stationed at FCS and regularly recruits individuals to participate in LIBR studies. LIBR has continued our research partnership with the Family and Children's Services program Women in Recovery. The intensive outpatient program is an alternative for women facing long prison sentences for non-violent, drug-related offenses. This award-winning program is dedicated to changing the lives of women in Oklahoma and giving them the tools to become positive, contributing members of the community.



### 12 & 12, Inc.

12 & 12 is an award-winning leader in the Tulsa community for addiction treatment and recovery services. Last year, they served over 1,600 clients in Oklahoma. Through LIBR's established collaboration with 12 & 12's Clinical Director, Richard Turnham, individuals with substance use-related problems are recruited to participate in LIBR studies of addiction.



### Laureate Psychiatric Clinic and Hospital

LIBR has continued to work closely with our neighbors at the Laureate Psychiatric Clinic and Hospital. Through a "universal consent" process, LIBR is able to reach out to Laureate patients to inquire about their interest in participating in research. LIBR has extended the partnership to include monthly informational sessions on research studies with participants in the Intensive Outpatient Programs to recruit individuals with substance use and mental health disorders in the Tulsa area.



## 2019 WKW SPEAKERS



**January 8**

Carol Tamminga, M.D.

*Is it Psychosis or Schizophrenia?*



**August 27**

Nora Volkow, M.D.

*Drug Addiction as a Disease of the Human Brain*



**March 5**

Walter Kaye, M.D.

*Is Anorexia Nervosa an Eating Disorder?*



**September 4**

Richard Davidson, Ph.D.

*Cultivating Well-Being: Perspectives From Affective and Contemplative Neuroscience*



**April 2**

Carlos Zarate, M.D.

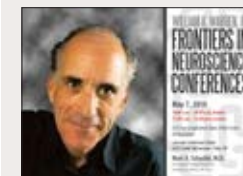
*Deconstructing the Neurobiology of Mood Disorders using Rapid Acting Antidepressant and Anti-suicidal Ideation Interventions as a Bridge to Novel Therapeutics*



**October 1**

Read Montague, Ph.D.

*Tilting Back to Neurobiology: Computational Psychiatry in an Invasive Setting*



**May 7**

Marc Schuckit, M.D.

*A 35-year Longitudinal Study of Risk Factors for Alcoholism*



**November 19**

Peter Kalivas, Ph.D.

*Using the Neuroscience of Willpower to Treat Addiction*



## 2019 VISITING SCIENTISTS AND DISTINGUISHED GUESTS

### LIBR welcomed several visiting scientists to our institute in 2019.

January 3	Xaixia Zheng	<i>Resting State BOLD Signal and its Potential for Machine Learning-aided Clinical Decisions</i>
January 29	Philip Spechler	<i>Predicting Risky Behaviors in Adolescence Using Brain, Behavioral and Genetic Features</i>
April 23	Stacey Daughters	<i>Treating Substance Use Disorder from a Neurobehavioral Translational Perspective</i>
May 13	Stefan Ehrlich	<i>To Eat or Not to Eat: Value-based Decision Making in Anorexia Nervosa</i>
June 4	Laura Huckins	<i>Beyond GWAS: Translating Psychiatric Disease Risk Loci into Multi-Omic Mechanism</i>
June 26	Albert Powers	<i>Hallucinations, Inference, and the Psychosis Spectrum</i>
August 6	Shmuel Lissek	<i>Pavlovian and Instrumental Generalization of Aversive Conditioning as Markers of Clinical Anxiety and Affiliated Traits</i>
August 28	Vincent Clark	<i>Combining Brain Imaging and Stimulation to Improve Treatments for Brain and Mental Illness</i>
September 16	Philipp Homan	<i>Individual Differences and the Challenge of Precision Medicine in Psychiatry</i>
October 22	Lindsay Squeglia	<i>Medication and Cognitive Intervention Trials for Adolescent Substance Use Disorders</i>
November 20	Konrad Kording	<i>Machine Learning and Causal Inference</i>
December 3	Thomas Wolfers	<i>Individual Differences vs. The Average Patient</i>
December 13	Quentin Huys	<i>Applying Computational Methods to Predicting and Understanding Relapses After Antidepressant Discontinuation</i>

# IN THE NEWS 2019

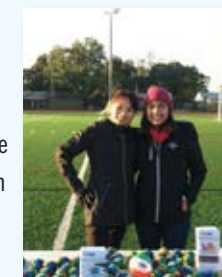
## LIBR Celebrates 10th Anniversary

LIBR celebrated our 10th anniversary in 2019 with a catered luncheon and awards ceremony for our staff. Dr. Jerzy Bodurka was presented with the LIBR Pioneer Award for his research excellence and dedication to MRI facilities as LIBR's Chief Technology Officer and Director of the MRI-EEG Facility.



Dr. Feinstein gave the keynote address at the International Society for the Advancement of Respiratory Psychophysiology meeting in Switzerland on October 5, 2019 entitled, "Searching for the source of suffocation false alarms in the human brain." Dr. Feinstein's research studying carbon dioxide and anxiety was also featured this year on the longest-running science documentary on television, *The Nature of Things*, in a special episode on the Science of Fear.

LIBR's assessment team braved the chilly weather to greet runners and spectators as a sponsor of the Trojan Tough 5k event for Jenks East Intermediate. They enjoyed meeting everyone who stopped by the LIBR booth for information on research studies, a quick snack, and one of our favorite squishy stress-relief brains.



## A Q&A with Dr. Martin Paulus – *Tulsa Lifestyle*

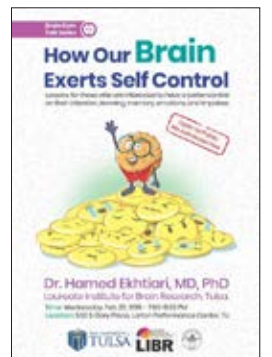
The January 2019 issue of *Tulsa Lifestyle* included an interview with Dr. Martin Paulus where he answered questions about ways to stay mentally healthy in the new year, current research studies at LIBR and turning neuroscience-based methods into practical living.

## People to Watch: Dr. Martin Paulus is helping to put Tulsa on the map for brain research

Dr. Paulus was featured in a series on "People To Watch" in the *Tulsa World*. "I think we are seeing things really come together," Paulus said. "We're in a really good place. The institute is beginning to get well known. It's putting Tulsa on the map (for brain research), and that's significant."

The *Tulsa World's* Let's Talk: Mental Health Forum at The University of Tulsa in May 2019 included a panel of experts and special guests who discussed issues connected to the mental health of Oklahomans, including progress, reform, funding and current trends. The panel included TU President Gerard Clancy, a psychiatrist; Terri White, commissioner of the Oklahoma Department of Mental Health and Substance Abuse Services; and Dr. Martin Paulus, scientific director and president of the Laureate Institute for Brain Research.

Dr. Hamed Ekhtiari presented a talk at the TU Lorton Performance Center on February 20, 2019 to discuss "How Our Brain Exerts Self Control." The talk covered lessons in having better control of attention, learning, memory emotions and impulses.



Amber Selvidge, Director of Regulatory and Compliance and Grants Administrator, represented LIBR at the annual Association of Independent Research Institutes meeting in Washington, D.C. She had the opportunity to connect with the Oklahoma Medical Research Foundation (OMRF) and members of Congress while advocating for continued research funding.



# INTHE NEWS 2019

In August 2019, LIBR enthusiastically welcomed world-renowned addiction researcher, Dr. Nora Volkow, Director of the National Institute on Drug Abuse at the National Institutes of Health to discuss progress, priorities and challenges in drug use and addiction research.

Dr. Volkow was instrumental in establishing the Adolescent Brain Cognitive Development (ABCD) study, the largest long-term study of brain development and child health in the country. LIBR is one of 21 sites participating in this landmark research endeavor.



## Study Suggests Not all Screen Time is Created Equal

Oklahoma Magazine and Tulsa Kids published articles on findings from the Adolescent Brain Cognitive Development (ABCD) study. "Whether social media and excessive screen time create mental illness is murky. Many factors contribute to poor mental health, and researchers at the Laureate Institute for Brain Research in Tulsa aim to find answers."



"Screens. They're the bane of every parent's existence, or at least a significant point of contention. Regulating the use of computers, phones and video games can seem like, and often is, a constant battle. In addition, parents worry that all this digital consumption could have a negative impact on their child's health and well-being. Fortunately for those of us raising kids in a digital world, scientists at Tulsa's Laureate Institute for Brain Research (LIBR) have been hard at work investigating these very issues. Preliminary data is in, and the initial findings might surprise you."

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One-in-three college students experience significant depression or anxiety that interferes with their life. Dr. Robin Aupperle and collaborators at The University of Tulsa developed a brief, four-session program aiming to enhance resilience to college stress. They tested the potential benefit of this program for first-year college students at The University of Tulsa who volunteered for the study. Students who received resilience training (compared to those who did not) reported lower levels of depression and stress over the first semester of college. Results indicate that students may benefit from colleges and universities adopting widespread implementation of resilience-skills training.

Dr. Martin Paulus and his co-authors were honored with the "Best Environmental Epidemiology Paper Award" from the International Society for Environmental Epidemiology (ISEE). The paper, "Empirical Evidence of Mental Health Risks Posed by Climate Change," published in PNAS, was recognized for making an outstanding contribution to the knowledge of environmental epidemiology and was selected because of its quality, originality, importance and expected impact.



## LIBR sponsors 2019 Cannabis Conference

The Laureate Institute for Brain Research (LIBR) sponsored a conference "Cannabis: What We Have Learned Through Scientific Research" on January 17, 2019, at the Lorton Performance Center on The University of Tulsa campus.

A panel of academic experts from around the country discussed their research findings related to public health and cannabis use. The conference consisted of opening remarks and introductions, plenary talks, panelist sessions and moderated discussions throughout the day.

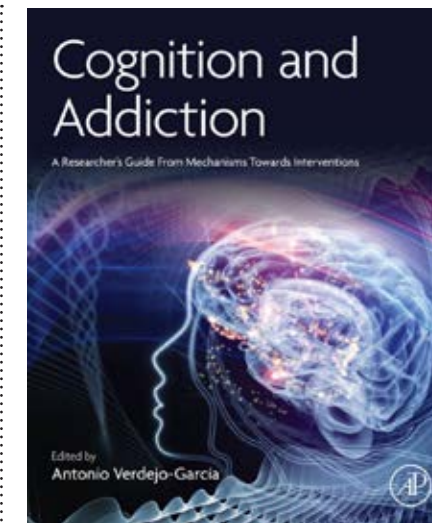
### DISTINGUISHED SPEAKERS

- Jason Beaman, D.O.**  
Chair, Department of Psychiatry and Behavioral Sciences, OSU CHS
- Gerard Clancy, M.D.**  
President, University of Tulsa
- Sarah W. Feldstein Ewing, Ph.D.**  
Oregon Health & Science University, Director, Adolescent Behavioral Health Clinic
- Francesca Filbey, Ph.D.**  
University of Texas at Dallas, School of Behavioral and Brain Science
- Scott Grantham, M.D.**  
Medical Director, Laureate Psychiatric Clinic and Hospital
- Kent Hutchinson, Ph.D.**  
University of Colorado Boulder, The Center for Health and Addiction: Neuroscience, Genes, and Environment
- Martin Paulus, M.D.**  
Scientific Director, Laureate Institute for Brain Research
- Susan Tapert, Ph.D.**  
University of California at San Diego, Department of Psychiatry
- Terri White, M.S.W.**  
Commissioner, Office of Mental Health and Substance Abuse



LIBR was honored to have several researchers present at the 2019 Zarrow Mental Health Symposium, celebrating 25 years of excellence and innovation in mental health. "Resilience. Recovery. Rethink Mental Health." examined the human capacity to thrive amid adversity. "The Symposium brought together 800+ participants from across the region to explore the latest in mental healthcare and treatment.

- LIBR PRESENTED AT THE FOLLOWING SESSIONS:**
- Inflamed Body, Inflamed Mind**  
Jonathan Savitz, Ph.D.; Kaiping Burrows, Ph.D.; and Bart Ford, B.S., CG (ASCP)
  - Adolescent Adversity from the ABCD Study**  
Janna Colaizzi, Ph.D.; and Florence Breslin, M.S.



LIBR investigators, Drs. Martin Paulus, Robin Aupperle, Hamed Ekhtiari and Ryan Smith contributed two chapters to the textbook "Cognition and Addiction" by Elsevier. The textbook provides an excellent overview of the potential contributions of brain science in addiction medicine.

Chapter 4: Decision-making deficits in substance use disorders: cognitive functions, assessment paradigms and level of evidence

Chapter 29: Clinical translation and implementation neuroscience for novel cognitive interventions in addiction medicine





**Robin Aupperle, Ph.D.**  
Principal Investigator  
Laureate Institute for Brain Research  
Assistant Professor  
University of Tulsa  
Email: [raupperle@laureateinstitute.org](mailto:raupperle@laureateinstitute.org)  
Phone: 918-502-5744

**Dr. Aupperle's 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 how this may relate to the development and maintenance of anxiety, depression and trauma-related symptoms.
- 2** How knowledge from neuroscientific research may be used to enhance treatment and prevention efforts.

**In regards to the former, she has conducted research related to neuropsychological correlates of trauma and post-traumatic stress disorder (PTSD) and has developed translational exploratory and decision-making tasks to better understand behavioral, physiological, and neural correlates of anxiety and depression. In regards to the latter, she has been involved in research investigating behavioral and neural mechanisms of current pharmacologic and behavioral treatments for anxiety, depression and trauma-related disorders. She is also actively involved in identifying strategies to optimize psychological well-being for college students and examining novel interventions for trauma-related and substance-use disorders.**



## SCIENTIFIC BACKGROUND

**Dr. Aupperle** was born and raised in rural Oklahoma and obtained her bachelor's degree in psychology from Oklahoma State University. She received her master's and doctoral education in clinical health psychology at the University of Kansas, under the mentorship of Cary Savage, Ph.D., and Douglas Denney, Ph.D. Her graduate research and clinical education focused on neuropsychology, neuroimaging and anxiety disorders. She then continued out west to complete a clinical internship at the VA San Diego Healthcare System, during which her training focused on clinical neuropsychology, cognitive rehabilitation and treatment of post-traumatic stress disorder (PTSD).

Dr. Aupperle remained in San Diego to complete a postdoctoral fellowship under the mentorship of Drs. Martin Paulus and Murray Stein, conducting research related to neural substrates of anxiety disorders and PTSD, with a particular emphasis on decision-making processes and treatment. She moved to Kansas City to join the University of Missouri – Kansas City (UMKC) Department of Psychology as Assistant Professor in August, 2011. In August, 2014, Dr. Aupperle joined the Laureate Institute for Brain Research (LIBR) in Tulsa, Oklahoma, as Assistant Professor.

## SELECTED PUBLICATIONS

- Clausen, A.N., et al. "Computer-based Executive Function Training for Combat Veterans with PTSD: A Pilot Clinical Trial Assessing Feasibility and Predictors of Dropout." *Frontiers in Psychiatry* 10 (2019): 62.
- Akeman, E., Kirlic, N., Clausen, A.N., Cosgrove, K.T., McDermott, T.J., Cromer, L.D., Paulus, M.P., Yeh, H.W., Aupperle, R.L. (in press). A Pragmatic Clinical Trial Examining the Impact of a Resilience Program on College Student Mental Health. *Depression and Anxiety*. doi: 10.1002/da.22969
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- \*McDermott, T.J., Kirlic, N., Aupperle, R.L. (2018). Roadmap for optimizing the clinical utility of emotional stress paradigms in human neuroimaging research. *Neurobiology of Stress*, 8, pp.134-146. doi: 10.1016/j.ynstr.2018.05.001
- Clausen, A.N., Francisco, A.J., Thelen, J., Bruce, J., Martin, L.E., McDowd, J., Simmons, W.K., Aupperle, R.L. (2017). PTSD and cognitive symptoms relate to inhibition-related prefrontal activation and functional connectivity. *Depression and Anxiety*, 34(5): 427-436.
- Chrysikou, L., Gorey, C., Aupperle, R.L. (2017). Anodal transcranial direct current stimulation over right dorsolateral prefrontal cortex alters decision making during approach-avoidance conflict. *Social Cognitive and Affective Neuroscience*, 12(3):468-475.
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- Aupperle, R.L., Allard, C.B., Grimes, E.M., Simmons, A.N., Flagan, T., Cissell, C.H., Thorp, S.R., Norman, S.B., Paulus, M.P., Stein, M.B. (2012). Dorsolateral prefrontal cortex activation during emotional anticipation and neuropsychological performance in posttraumatic stress disorder. *Archives of General Psychiatry*, 69(4), 360-371. doi:10.1001/archgenpsychiatry.2011.153
- Aupperle, R.L., Melrose, J., Stein, M.B., Paulus, M.P. (2012). Executive function and PTSD: Disengaging from trauma. *Neuropharmacology*, 62(2):686-94. doi: 10.1016/j.neuropharm.2011.02.008

## LAB MEMBERS

- Elisabeth Akeman**  
Research Assistant
- Alyssa Clinard**  
Research Volunteer
- Kelly Cosgrove**  
Graduate Student,  
University of Tulsa
- Danille DeVille**  
Graduate Student,  
University of Tulsa
- Timothy McDermott**  
Graduate Student,  
University of Tulsa
- Jessica Santiago**  
Research Therapist
- James Touthang**  
Data Analyst
- Evan White**  
Postdoctoral Scholar

## RESEARCH COLLABORATORS

- Jim Abelson, M.D., Ph.D.**  
University of Michigan
- Michelle Craske, Ph.D.**  
University of California- Los Angeles
- Amy Jak, Ph.D.**  
University of California- San Diego
- Arpi Minassian, Ph.D.**  
University of California- San Diego
- Amanda Morris, Ph.D.**  
Oklahoma State University
- Murray Stein, Ph.D.**  
University of California- San Diego
- Kate Wolitzky-Taylor, Ph.D.**  
University of California- Los Angeles
- Charles Taylor, Ph.D.**  
University of California- San Diego
- Jared Young, Ph.D.**  
University of California- San Diego



**Jerzy Bodurka, Ph.D.**

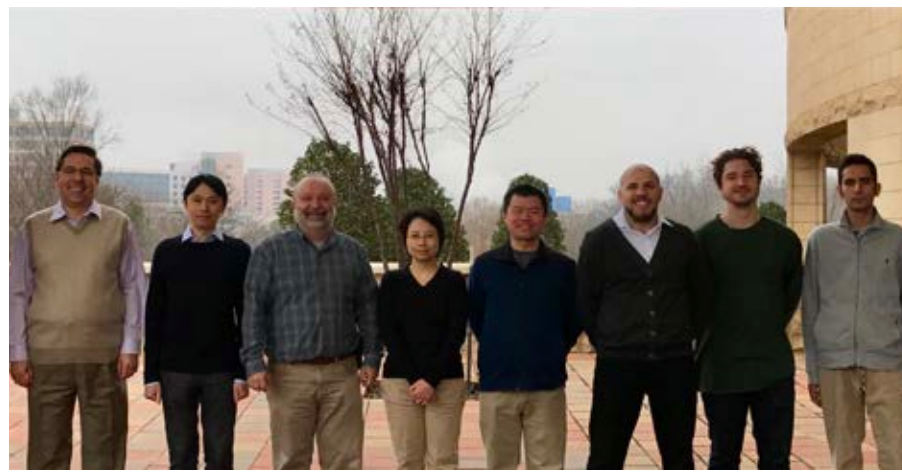
Chief Technology Officer  
Director MRI-EEG Facility  
Laureate Institute for Brain Research

Associate Professor  
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The University of Oklahoma

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Phone: 918-502-5101

**Dr. Bodurka's research focuses on three main areas:**

- 1 Non-invasive, multimodal neuroimaging method development and applications for studying brain function including: structural and functional MRI (fMRI), real-time fMRI with neurofeedback, multimodal simultaneous electroencephalography (EEG) and fMRI brain imaging, real-time integration of fMRI and EEG data, simultaneous EEG and fMRI neurofeedback, EEG and fMRI hyperscanning.**
- 2 Novel non-invasive brain neuromodulation and neuroenhancement approaches to better understand brain emotion regulation and social interactions in major depressive disorder (MDD) and post-traumatic stress disorder (PTSD). Dr Bodurka's research has shown that the use of real-time fMRI neurofeedback during recall of positive emotions in patients with depression can normalize the neural activity of the amygdala and result in significant depression symptom relief.**
- 3 Translational approaches to discover and research novel therapeutic strategies to improve treatments by training and recovering healthy function of brain networks, and to improve psychotherapy by determining the neural features of socially interacting individuals in MDD and PTSD.**



**SCIENTIFIC BACKGROUND**

**Dr. Bodurka** has broad expertise in Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI) physics. He received his doctorate degree in physics from the University of Nicolaus Copernicus in Torun, Poland, and completed part of his postdoctoral training in NMR at the Department of Chemistry at Free University of Berlin, Germany. As a postdoctoral fellow at Medical College of Wisconsin, he received firm training in MRI technology and functional MRI (fMRI). As a staff scientist at the functional MRI Facility of the National Institute for Mental Health (NIMH) and the National Institute of Neurological Disorders and Stroke (NINDS) and National Institutes of Health (NIH), he was responsible for providing a state-of-the-art imaging environment for conducting advanced MRI and fMRI research. In 2007, for his development of a Scalable Multi-Channel MRI Data Acquisition System, he received NIH's Director Award for Advancements in MRI Parallel Imaging Technology. The advancements in MRI receiver and multi-element coils technologies allowed for major improvements in MRI signal-to-noise ratio, and pushed spatial and temporal limits for both functional and anatomical imaging. He has also developed an advanced real-time software set-up allowing for conducting real-time fMRI with neurofeedback.

In 2009, Dr. Bodurka joined the newly established Laureate Institute for Brain Research (LIBR) to create a state-of-the-art MRI/fMRI/EEG neuroimaging facility and to establish multimodal brain neuroimaging program with the overall purpose of advancing clinical research focused on mental disorders, with a broad research goal of advancing our understanding and characterization of brain abnormalities due to mental illness.

**LAB AND MRI-EEG FACILITY RESEARCH STAFF**

**Obada Al Zoubi, M.S., Ph.D.**  
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**SELECTED PUBLICATIONS**

Misaki, M., Phillips, R., Zotev, V., Wong, C.K., Wurfel, B.E., Krueger, F., Feldner, M., Bodurka, J. (2019) Brain activity mediators of PTSD symptoms reduction during real-time fMRI amygdala neurofeedback emotional training. *Neuroimage Clinical*, 102047.

Mayeli, M., Phillips, R., Zotev, V., Tsuchiyagaito, A., Al Zoubi, O., Phillips, R., Smith, J., Stewart, J.L., Refai, H., Paulus, M.P., Bodurka, J. (2019) Self-regulation of ventromedial prefrontal cortex activation using real-time fMRI neurofeedback- Influence of default mode network. *Human Brain Mapping* <https://doi.org/10.1002/hbm.24805>

Al Zoubi, O., Mayeli, A., Tsuchiyagaito, A., Misaki, M., Zotev, V., Refai, H., Paulus, M.P., Bodurka, J., Tulsa 1000 Investigators (2019) EEG microstates temporal dynamics differentiate individuals with mood and anxiety disorders from healthy subjects. *Frontiers Human Neuroscience* 26:13:56.

Misaki, M., Phillips, R., Zotev, V., Wong, C.K., Wurfel, B.E., Krueger, F., Feldner, M., Bodurka, J. (2018) Real-time fMRI amygdala neurofeedback positive emotional training normalized resting-state functional connectivity in combat veterans with and without PTSD: a connectome-wide investigation. *Neuroimage Clinical*, 20:543-555.

Le, T.T., Savitz, J., Suzuki, H., Misaki, M., Teague, T.K., White, B.C., Marino, J.H., Wiley, G., Gaffney, P.M., Drevets, W.C., McKinney, B.A., Bodurka, J. (2018) Identification and replication of RNA-Seq gene network modules associated with depression severity. *Translational Psychiatry* 2018 8(1):180.

Zotev, V., Misaki, M., Phillips, R., Wong, C.K., Bodurka, J. (2018) Real-time fMRI neurofeedback of the mediodorsal and anterior thalamus enhances correlation between thalamic BOLD activity and alpha EEG rhythm. *Human Brain Mapping* 39(2): 1024-1042.

**RESEARCH COLLABORATORS**

**Peter Bandettini, Ph.D.**  
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**Matthew Feldner, Ph.D.**  
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**Frank Krueger, Ph.D.**  
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Industry Collaborators

**INDUSTRY COLLABORATORS**

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**Yoon-Hee Cha, M.D.**

Principal Investigator  
Laureate Institute for Brain Research

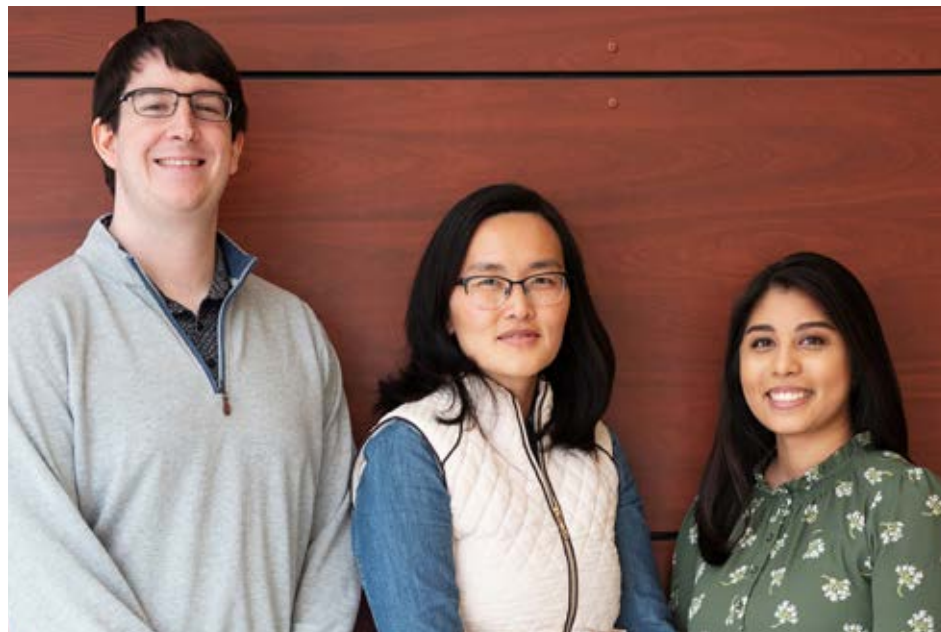
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**Dr. Cha's main research interests include:**

- 1** Exploring the role of the cerebellum in regulating cerebral networks, especially as it pertains to anxiety and depression.
- 2** Understanding the connection between motion perception disorders, anxiety and migraine headaches.
- 3** Using functional neuroimaging and EEG to guide neuromodulation treatment.
- 4** Developing neuromodulation tools that can be accessible to more patients.



**SCIENTIFIC BACKGROUND**

**Dr. Yoon-Hee Cha** is a neurologist with subspecialty training in neurotology. She completed her premedical studies at Stanford University graduating with a degree in biology with honors in 1995. She earned her medical degree from Mayo Medical School in 2001, which included a year of research at the National Institutes of Health through the Howard-Hughes-NIH Research Scholars Program from 1998-1999. In 2002, she completed a preliminary year in internal medicine at the Brigham and Women's Hospital in Boston, Massachusetts, before going on to complete her neurology residency training at the University of California – San Francisco in 2005—she was also chief resident from 2004-2005. From 2005-2007, she was the neurotology fellow at the University of California – Los Angeles (UCLA), where she trained with Dr. Robert W. Baloh. She worked with Dr. Baloh on the genetics of episodic ataxia and vestibular migraine. At UCLA, she developed her interest in understanding the neurological basis of motion perception, which led to her current work using functional MRI, EEG and neuromodulation techniques such as transcranial magnetic stimulation and transcranial electrical stimulation to probe the biological basis of and treat disorders of motion perception. She joined LIBR in August 2012. Her current work focuses on a group of patients with a disorder of motion entrainment called mal de débarquement syndrome (MdDS) as well as disorders of spatial processing related to anxiety and migraine. Her work has expanded to include studies that explore the role of the cerebellum in mood and anxiety disorders, particularly in its role in fear conditioning and fear extinction. In conjunction with other LIBR investigators, she is studying how vestibular and cerebellar networks can be targeted to modulate cerebral function.

**LAB MEMBERS**

**B. Chipper Doudican**  
Research Assistant

**Diamond Urbano**  
Research Assistant  
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**SELECTED PUBLICATIONS**

Mucci, V., Cha, Y.H., Wuyts, F.L., Van Ombergen, A. Perspective: SteppingStones to Unraveling the Pathophysiology of Mal de Debarquement Syndrome with Neuroimaging. *Frontiers Neurology*, 2018 Feb 12;9:42. doi: 10.3389/fneur.2018.00042. PMID: 29483889,PMCID: PMC5816028 (openaccess)

Cha, Y.H., Cui, Y.Y., Baloh, R.W. Comprehensive clinical profile of mal de débarquement syndrome. *Frontiers Neurology*, 2018 May 7;9:261doi:10.3389/fneur.2018.00261 (open access)

Li, C., Yuan, H., Shou, G., Cha, Y.H., Sunderam, S., Besio, W., Ding, L. Cortical Statistical Correlation Tomography of EEG RestingState Networks, 2018 *Frontiers in Neuroscience, Neural Technology*, 2018, May 30, *Frontiers in Neuroscience*

Cha, Y.H., Shou, G., Gleghorn, D., Doudican, B., Yuan, H., Ding, L. Electrophysiological Signatures of Intrinsic Functional Connectivity Related to rTMS Treatment for Mal de Debarquement Syndrome. 2018, Aug 18. *Brain Topography*

Yuan, H., Shou, G., Urbano, D., Ding, L., Cha, Y.H. (2017). Resting state functional connectivity signature of treatment effects of rTMS in Mal de Debarquement Syndrome. *Brain Connectivity*, Epub Oct 1

Cha, Y.H., Urbano, D., Pariseau, N. (2016). Randomized single blind sham controlled trial of adjunctive home-based tDCS after rTMS for Mal de Debarquement Syndrome: safety, efficacy, and participant satisfaction assessment. *Brain Stimulation*, 9(4):537-44

Cha, Y.H., Deblieck, C., Wu, A. (2016). Double-blind sham-controlled cross-over trial of repetitive transcranial magnetic stimulation for Mal de Debarquement Syndrome. *Otol Neurotology*, 37(6):805-12

Cha, Y.H. (2015). Mal de Debarquement Syndrome: New insights. *Ann N Y Acad Sci.*, 1343:63-68

Cha, Y.H., Chakrapani, S. (2015). Voxel based morphometry alterations in Mal de Debarquement Syndrome. *PLoSOne*. 10(8):e0135021

**RESEARCH COLLABORATORS**

- Walter Besio, Ph.D.**  
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**Hamed Ekhtiari, M.D., Ph.D.**  
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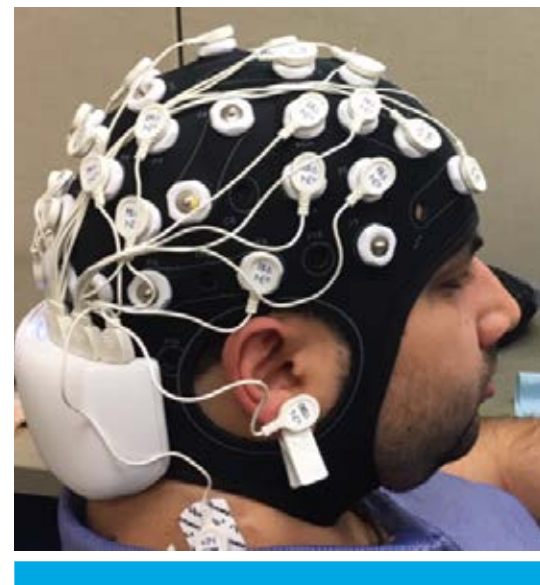
**Dr Ekhtiari's main research interests include:**

**Using neuroimaging/neurocognitive markers among people with substance-use disorders to inform development, predict outcome and monitor efficacy of:**

- 1 non-invasive transcranial electrical/magnetic stimulation (TES/TMS); and**
- 2 neurocognitive interventions.**

**ONGOING RESEARCH PROJECTS IN 2019:**

- Clinical Trial (ClinicalTrials.gov Identifier: NCT03382379): Transcranial Direct Current Stimulation to Modulate Top-down Regulation for Drug Craving in Methamphetamine-use Disorder (Recruitment Completed, In the Analysis Phase)
- Clinical Trial (ClinicalTrials.gov Identifier: NCT03907644): Frontoparietal Synchronization to Modulate Drug Craving in Opioid-use Disorder (Recruiting) (NARSAD Young Investigator Award)
- Clinical Trial (ClinicalTrials.gov Identifier: NCT03922646) Neurocognitive Empowerment for Addiction Treatment (NEAT) in Opioid-use Disorder and Amphetamine-use Disorder (Recruiting) (OCAST-funded)
- Analysis Study Development of fMRI Drug Cue Reactivity Measures as Intervention Development Tools for Substance-use Disorders
- Pilot Technical Study Feasibility Testing for Closed-loop Online fMRI tACS Neurofeedback to Individually Maximize Connectivity within Executive Control Network with Active Searching for Optimized Stimulation Parameters



**SCIENTIFIC BACKGROUND**

**Dr. Ekhtiari** went to Tehran University of Medical Sciences (TUMS), the most-distinguished medical school in Iran, as a medical student after passing the highly competitive national university entrance exam with a rank of 11 out of over 350,000 participants. Facing daily challenges of people with substance use disorder (SUD) in Tehran, he became interested in the neuroscience of cognitive disorders associated with SUDs. He received his first small grant as a medical student in this field in 2000, and published his first paper on the “role of prefrontal cortex in risky decision making” in 2001. He graduated from medical school with honors in 2004 with a dissertation on risky decision-making and impulsivity. Immediately, he started work at the Iranian National Center for Addiction Studies (INCAS) in 2004 in one of the least affluent neighborhood in Tehran and launched a neurocognitive lab there in 2005. He also started a research program at Institute for Cognitive Science Studies (ICSS) in Tehran in 2010 called the Translational Neuroscience Program. He enrolled in a Ph.D. program in neuroimaging at TUMS in 2011 and did his thesis project on the neural basis of response inhibition using fMRI. Then, He moved to the U.S. for a postdoctoral position with Dr. Martin Paulus at the Laureate Institute for Brain Research (LIBR). He was promoted to associate investigator position at LIBR in January 2018.



Dr. Ekhtiari started to work in the field of transcranial brain stimulation with an awarded short-term fellowship at Harvard University in 2009. Afterwards, during contribution in different studies using fMRI and brain stimulation, he realized many potentials in this field for understanding causal mechanisms involved in SUD to design therapeutic interventions. In 2014, he published one of the first pieces of evidence on the potential hopes for modulation of drug craving among methamphetamine users with transcranial direct current stimulation (tDCS). His joint review paper on non-invasive brain stimulation and its challenges was published in the Neuron in 2015. In early 2018, he published his preliminary results for the first combined tDCS fMRI study among people with SUD. He completed his first randomized controlled clinical trial in methamphetamine users at LIBR as a PI with tDCS fMRI in January 2019 (NCT03382379). In late 2018, he received the NARSAD young investigator award on “examining the utility of fronto-parietal synchronization (FPS) to enhance self-control to cue induced cravings in individuals with opioid use disorders.” He hopes to extend his activities with transcranial electrical and magnetic stimulation (TES/TMS) technologies using fMRI as a biomarker for prediction and monitoring among people with mental health disorders.

Dr. Ekhtiari has also focused intently on the development of cognitive training and rehabilitation programs for people with SUDs. He has recently written a chapter for the world-renowned textbook Neuropsychological Rehabilitation: The International Handbook on brain rehabilitation for psychiatric disorders with specific sections focused on SUDs. In 2014, he conducted his first clinical trial of neurocognitive rehabilitation for people with SUDs, using a package termed “NEuroCOgnitive Rehabilitation for Disease of Addiction” (NECOREDA) in a collaboration with Mehmet Sofuoglu, Yale University. Results from this study were published in 2017. Based on his background in the field, in collaboration with Drs. Robin Aupperle and Martin Paulus, he recently developed a new package with more in-depth neuroscience informed interventions called “Neurocognitive Empowerment for Addiction Treatment” (NEAT). In July 2018, he received a three-year grant from Oklahoma Center for Advancement of Science and Technology (OCAST) to run a randomized clinical trial among people with opioid-use disorder with NEAT as PI. Dr. Ekhtiari has already recruited half of the subjects for this trial by the end of 2019. He is planning to extend the idea of brain rehabilitation in drug addiction based on the experiences in this trial.

**SELECTED PUBLICATIONS**

Rezapour, T., Aupperle, R.L., Paulus, M.P., Ekhtiari, H. (2020). Clinical translation and implementation neuroscience for novel cognitive interventions in addiction medicine *Cognition and Addiction* (pp. 393-404): Academic Press.

Ekhtiari, H., Kuplicki, R., Pruthi, A., Paulus, M.P. (2019). LIBR Methamphetamine and Opioid Cue Database (LIBR MOCD): Development and Validation. *bioRxiv*, 731331.

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Soltaninejad, Z., Nejati, V., Ekhtiari, H. (2019). Effect of anodal and cathodal transcranial direct current stimulation on DLPFC on modulation of inhibitory control in ADHD. *Journal of Attention Disorders*, 23(4), 325-332.

Verdejo-García, A., Lorenzetti, V., Manning, V., Piercy, H., Bruno, R., Hester, R., ... Ekhtiari, H. (2019). A Roadmap for Integrating Neuroscience into Addiction Treatment: A Consensus of the Neuroscience Interest Group of the International Society of Addiction Medicine. *Front Psychiatry*, 10, 877.

Ekhtiari, H., Kuplicki, R., Yeh, H. W., Paulus, M.P. (2019). Physical characteristics not psychological state or trait characteristics predict motion during resting state fMRI. *Sci Rep*, 9 (1), 419. doi:10.1038/s41598-018-36699-0

Shahbabaie, A., Ebrahimipour, M., Hariri, A., Nitsche, M.A., Hatami, J., Fatemizadeh, E., ... Ekhtiari, H. (2018). Transcranial DC stimulation modifies functional connectivity of large-scale brain networks in abstinent methamphetamine users. *Brain and Behavior*. e00922. doi.org/10.1002/brb3.922doi:10.1016/bs.pbr.2015.10.001

**RESEARCH COLLABORATORS**

- |   |   |
|---|---|
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| <b>Felipe Fregni, M.D., Ph.D.</b><br>Harvard University   | <b>Vincent Walsh, Ph.D.</b><br>University College London<br>United Kingdom                                      |
| <b>Irene Jillson, Ph.D.</b><br>Georgetown University  | <b>Hedy Kober</b><br>Yale University  |
| <b>Kaveh Ashenayei, Ph.D.</b><br>University of Tulsa  | <b>Hugh Garavan</b><br>University of Vermont  |
| <b>Marom Bikson, Ph.D.</b><br>City University of New York   |   |
| <b>Mehmet Sofuoglu, M.D.</b><br>Yale University   |   |
| <b>Tara Rezapour, Ph.D.</b><br>Institute for Cognitive Science Studies<br>India                         |   |
| <b>Michael Nitsche, M.D.</b><br>Dortmund University   |   |





**Justin Feinstein, Ph.D.**

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**Dr. Feinstein's three main research areas are to:**

- 1** Develop floatation as a tool for reducing stress and enhancing well-being in individuals who suffer from anxiety.
- 2** Use functional neuroimaging and the lesion method to help determine the causal source of anxiety in the human brain.
- 3** Study how the brain dynamically maps the internal world of our body, determine how these maps are dysregulated in conditions of anxiety, and whether floatation therapy can help regulate these disturbances, allowing patients to reshape their internal experience.



**SCIENTIFIC BACKGROUND**

**Dr. Justin Feinstein** joined the faculty of the Laureate Institute for Brain Research in December of 2013 after completing his Ph.D. in clinical neuropsychology at the University of Iowa, and his postdoctoral fellowship at the California Institute of Technology. He earned his undergraduate degree in cognitive neuroscience at the University of California – San Diego. His clinical internship occurred at the San Diego VA hospital and focused on the treatment of veterans with PTSD using Prolonged Exposure therapy.



Dr. Feinstein's research utilizes the lesion method and functional neuroimaging to explore how the human brain produces primal states of emotion, with an emphasis on the neuroscience of fear and treatments that alleviate anxiety. His laboratory is interested in understanding the intimate connection between the body and the brain, and developing new technologies to help bring this connection to the forefront of awareness. To this end, he is exploring several new approaches that can selectively enhance "interoceptive awareness," in order to help patients with anxiety establish a healthier balance between their body and brain.

**LAB MEMBERS**

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- M.S. Flux**  
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- McKenna Pierson**  
Ph.D. Graduate Student –  
University of Tulsa

**SELECTED PUBLICATIONS**

Feinstein, J.S., Khalsa, S.S., Yeh, H., Al Zoubi, O., Arevian, A.C., Wohlrab, C., Pantino, M.K., Cartmell, L.J., Simmons, W.K., Stein, M.B., Paulus, M.P. (2018). The elicitation of relaxation and interoceptive awareness using floatation therapy in individuals with high anxiety sensitivity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 3, 555-562.

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Feinstein, J.S., Khalsa, S.S., Salomons, T.V., Prkachin, K.M., Frey-Law, L.A., Lee, J.E., Tranel, D., Rudrauf, D. (2016). Preserved emotional awareness of pain in a patient with extensive bilateral damage to the insula, anterior cingulate, and amygdala. *Brain Structure and Function*, 221:1499-1511.

Khalsa, S.S., Feinstein, J.S., Wi, L., Feusner, J.D., Adolphs, R., Hurlmann, R. (2016). Panic anxiety in humans with bilateral amygdala lesions: Pharmacological induction via cardiorespiratory interoceptive pathways. *Journal of Neuroscience*, 36(12):3559-3566.

Guzman-Velez, E., Feinstein, J.S., Tranel, D. (2014). Feelings without memory in Alzheimer Disease. *Cognitive and Behavioral Neurology*, 27(3):117-29.

Feinstein, J.S., Buzza, C., Hurlmann, R., Follmer, R.L., Dahdaleh, N.S., Coryell, W.H., Welsh, M.J., Tranel, D., Wemmie, J.A. (2013). Fear and panic in humans with bilateral amygdala damage. *Nature Neuroscience*, 16:270-272.

Feinstein, J.S., Adolphs, R., Damasio, A., Tranel, D. (2011). The human amygdala and the induction and experience of fear. *Current Biology*, 21, 34-38.

Feinstein, J.S., Duff, M.C., Tranel, D. (2010). Sustained experience of emotion after loss of memory in patients with amnesia. *Proceedings of the National Academy of Sciences*, 107:7674-7679.

Khalsa, S.S., Rudrauf, D., Feinstein, J.S., Tranel, D. (2009). The pathways of interoceptive awareness. *Nature Neuroscience*, 12:1494-1496.

**RESEARCH COLLABORATORS**

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- Jason Beaman, M.D.**  
Oklahoma State University
- Paul Davenport, Ph.D.**  
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- Christopher Lowry, Ph.D.**  
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- Victoria Risbrough, Ph.D.**  
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- David Rudrauf, Ph.D.**  
University of Geneva, Switzerland
- Murray Stein, M.D.**  
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**Sahib Khalsa, M.D., Ph.D.**

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**Dr. Khalsa’s laboratory studies the heart-brain connection.**

**His research explores three main questions:**

- 1** How do we perceive our heartbeat?
- 2** Is there dysfunctional cross talk between the heart and brain in psychiatric and cardiovascular illnesses?
- 3** How can we develop new treatments that re-establish a functional dialogue between the body and brain?



**SCIENTIFIC BACKGROUND**

**Dr. Khalsa** received a bachelor’s degree in psychology from The State University of New York – Stony Brook in 2002. He graduated from the medical scientist training program at the University of Iowa, receiving M.D. and Ph.D. degrees in neuroscience in 2009. He completed his residency training in psychiatry at University of California – Los Angeles (UCLA) in 2013, serving as the program chief resident and chief resident in the UCLA Anxiety Disorders Clinic, subsequently joining the department as a faculty member in the Division of Adult Psychiatry at UCLA, and becoming an assistant professor in residence. In 2015, Dr. Khalsa joined LIBR as the Director of Clinical Studies, and as assistant professor (tenure track) at the University of Tulsa.



Dr. Khalsa’s research investigates how people perceive their heartbeat and overall body image, how the human brain maps cardiac sensation, and whether there is dysfunctional cross talk between the heart and brain in psychiatric and cardiovascular illnesses. To address these questions, his studies have examined the effects of aging, focal brain injury, cardiac dysfunction and meditation practice on awareness of the heartbeat. Current projects examine the neural basis of heart-brain communication in anorexia nervosa and anxiety disorders, the effect of a novel drug on targeting brain function, the utility of a new mobile measure of body image perception in eating disorders, and the potential impact of floatation therapy on body image disturbance and anxiety in anorexia nervosa. These studies aim to ultimately answer the question: “How can we develop new tests and treatments that re-establish a functional dialogue between the body and brain?”

Dr. Khalsa’s clinical expertise focuses on the assessment and treatment of anxiety disorders. Dr. Khalsa previously served as associate director of the UCLA Anxiety Disorders Clinic, supervising resident physicians in the treatment of anxiety disorders, and was an attending psychiatrist in the UCLA OCD Intensive Outpatient Program. As founding Director of the Healthy Hearts Behavioral Medicine Program, an interdisciplinary endeavor started with the UCLA Cardiac Arrhythmia Center, he specialized in treating anxiety and mood disorders in individuals with cardiac arrhythmias. Current clinical activities include conducting case conferences with the Laureate Psychiatric Hospital and Clinic and psychoeducation groups with inpatients from the Laureate Eating Disorders Program.

**LAB MEMBERS**

- Katie Baker**  
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Research Volunteer  
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- Megan Sinik**  
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University of Tulsa
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- Valerie Upshaw, R.N., B.S.N.**  
Clinical Research Coordinator

**SELECTED PUBLICATIONS IN 2019:**

Paulus, M.P., Feinstein, J.S., Khalsa, S.S. An active inference approach to interoceptive psychopathology. *Ann. Rev. of Clinical Psychology* 2019 15: 97-122.

Khalsa, S.S. Interoception in eating disorders: a clinical primer. *Psychiatric Times* 2019 36(9): 31-37.

Khalsa, S.S., Rudrauf, D., Hassanpour, M.S., Davidson, R.J., Tranel, D. The practice of meditation is not associated with improved interoceptive awareness of the heartbeat. *Psychophysiology* (in press). doi: 10.1111/psyp.13479.

Murphy, J., Brewer, R., Plans, D., Khalsa, S.S., Catmur, C., Bird, G. Testing the independence of self-reported interoceptive accuracy and attention. *Quarterly Journal of Experimental Psychology* (in press) doi: 10.1177/1747021819879826.

Samad, M., Ralph-Nearman, C., Helleman, G., Khalsa, S.S., Shams, L., Feusner, J.D. Disturbed eating and body dysmorphic symptoms in a nonclinical sample are separable constructs each with bimodal distributions. *Assessment* (in press). doi: 10.1177/1073191119879241.

Stewart, J.L., Khalsa, S.S., Kuplicki, R., Puhl, M., T1000 Investigators, Paulus, M.P. Interoceptive attention in opioid and stimulant use disorder. *Addiction Biology* (in press) doi: 10.1111/adb.12831.

Ralph-Nearman, C., Arevian, A.C., Puhl, M., Kumar, R., Villaroman, D., Suthana, N., Feusner, J.D., Khalsa, S.S. Somatomap: A novel mobile tool to assess body image perception, piloted with fashion models and non-models. *JMIR Mental Health* 2019 6(10): e14115. doi: 10.2196/14115.

**RESEARCH COLLABORATORS**

- Olujimi Ajjola, M.D., Ph.D.**  
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- Armen Arevian, M.D., Ph.D.**  
University of California – Los Angeles
- Karl-Jürgen Bär, M.D.**  
University of Jena
- Jamie Feusner, M.D.**  
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- Rene Hurlmann, M.D., Ph.D.**  
University of Bonn
- Mike Keller, Ph.D.**  
University of Tulsa
- Richard Lane, M.D., Ph.D.**  
University of Arizona
- Scott Moseman, M.D.**  
Medical Director  
Laureate Eating Disorders Program
- David Rudrauf, Ph.D.**  
University of Geneva, Switzerland
- Kalyanam Shivkumar, M.D., Ph.D.**  
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**Namik Kirlic, Ph.D.**  
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**Dr. Kirlic's laboratory focuses on improving our understanding of the broad consequences of early life adversity, and which preventative interventions may mitigate the risk for psychiatric and medical illness in this population. His research explores these questions:**

- 1 Can we identify adaptive versus maladaptive patterns of responses to early life adversity, and establish whether these predict resilience or vulnerability, respectively, over time?**
- 2 By using novel preventative interventions, can we target the neurobiological and psychosocial systems disrupted by early life adversity, thereby improving short- and long-term outcomes?**

*Dr. Kirlic's research is currently funded by LIBR and the National Institute for General Medical Sciences (NIGMS).*



## SCIENTIFIC BACKGROUND

**Dr. Kirlic** was born and raised in southeastern Europe. In 2005, he earned his B.A. in psychology from Middlebury College in Vermont. There, under mentorship of Dr. Adela Langrock, he wrote his senior thesis on the cumulative effects of perceived war- and post-war stress on current psychological functioning. Following his undergraduate studies, he spent two years in the laboratory of Drs. Hans Breiter and Anne Blood at Massachusetts General Hospital, managing studies on addiction and movement disorder, and learning neuroimaging methods and technology.

He moved to Tulsa, Oklahoma, in 2010 to pursue a Ph.D. in clinical psychology at the University of Tulsa and LIBR. Under mentorship of Drs. Elana Newman and Ruben Alvarez, Dr. Kirlic focused on individual differences in neural responses to predictable and unpredictable threats, effects of prenatal drug exposure and postnatal adversity on biological stress responses in children, and effectiveness of interventions for youth survivors of natural disasters and war. His clinical practice in graduate school, as well as during his clinical residency at the University of New Mexico Hospitals and New Mexico VA, centered on the assessment and evidence-based treatment of mood, anxiety, and emotion dysregulation disorders.

Dr. Kirlic returned to Tulsa for his postdoctoral fellowship at LIBR in 2016. Under mentorship of Dr. Robin Aupperle, he trained in the use of translational behavioral and neuroimaging methods to identify reliable predictors of resilience and treatment responses. Additionally, he had an active role in the delivery of the related evidence-based interventions.

In January 2019, Dr. Kirlic became an Associate Investigator at LIBR. His current research focuses on consequences of early life adversity, preventative interventions, and multi-system responses during aversive conditions.

## LAB MEMBERS

**Zsofia Cohen, BS**  
 Lab Manager  
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 Graduate Student Volunteer

## SELECTED PUBLICATIONS IN 2019:

Kirlic, N., Cohen, Z.P., Singh, M.K. (invited review). Is There an Ace Up Our Sleeve? A Review of Interventions and Strategies for Addressing Behavioral and Neurobiological Effects of Adverse Childhood Experiences for Youth. *Adversity and Resilience Science: Journal of Research and Practice*.

Kirlic, N., Aupperle, R.L., Rhudy, J.L., Misaki, M., Kuplicki, R., Sutton, A., Alvarez, R.P. (2019). Latent variable analysis of negative affect and its contributions to neural responses during shock anticipation. *Neuropsychopharmacology*, 0, 1-8.

McDermott, T.J., Kirlic, N., Aupperle, R.L. (2018). Roadmap for optimizing the clinical utility of emotional stress paradigms in human neuroimaging research. *Neurobiology of Stress*, 8, 134-146.

Kirlic, N., Young, J., Aupperle, R.L. (2017). Animal-to-human translational paradigms relevant for approach-avoidance conflict decision. *Behaviour Research and Therapy*, 96, 14-29.

Alvarez, R.P., Kirlic, N., Misaki, M., Bodurka, J., Rhudy, J.L., Paulus, M.P., Drevets, W.C. (2015). Increased anterior insula activity in anxious individuals is linked to diminished perceived control. *Translational Psychiatry*, 5, e591, 1-9.

Newman, E., Pfefferbaum, B., Kirlic, N., Tett, R., Nelson, S., Liles, B. (2014). Meta-analytic review of psychological interventions for children survivors of natural and man-made disasters. *Current Psychiatry Reports*, 16(462) 1-10.

Kirlic, N., Newman, E., LaGasse, L., Derauf, C., Shah, R., Smith, L.M., Arria, A., Huestis, M.A., Haning, W., Strauss, A., Della Grotta, S., Dansereau, L.M., Abar, B., Neal, C., Lester, B.M. (2013). Cortisol reactivity in two-year-old children prenatally exposed to methamphetamine. *Journal of Studies on Alcohol and Drugs*, 74(3), 447-451.

## RESEARCH COLLABORATORS

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 Stanford University  
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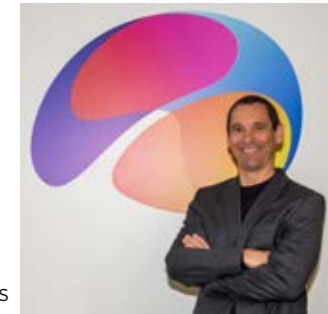
**Dr. Paulus' research focuses on three main areas:**

- 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 toward precision psychiatry**
- 3 To develop prevention strategies for psychiatric disorders**



## SCIENTIFIC BACKGROUND

**Dr. Paulus** studied medicine at the Johannes Gutenberg University in Mainz from 1979-1985. He received a postdoctoral fellowship from the Deutsche Forschungsgemeinschaft (German Research Foundation) in 1986 to study the effects of calcium antagonists on animal models of mania at the University of California – San Diego (UCSD). In 1993, Dr. Paulus left UCSD to resume his medical training and completed his internship at the Long Island Jewish Medical Center/Zucker Hillside Hospital in Long Island, New York. In 1994, he rejoined the department of psychiatry at UCSD as a psychiatric resident. Dr. Paulus completed his residency in psychiatry in 1997. At that time, he joined the department of psychiatry at UCSD as an assistant professor and became a staff psychiatrist at the Veterans Affairs San Diego Health Care System (VASDHS). In May 2014, Dr. Paulus joined the Laureate Institute for Brain Research (LIBR) in Tulsa, Oklahoma, as the scientific director and president.



Dr. Paulus has published over 350 peer-reviewed publications (some in top tier journals like *Science*, *Nature Reviews Neuroscience*, *PNAS*, *JAMA Psychiatry*, *Lancet Psychiatry*, *Biological Psychiatry*, *Neuropsychopharmacology*, and *the American Journal of Psychiatry*). Dr. Paulus received the UCSD Lew Judd Young Investigator Award, the NAMI Young Investigator Award, and the NIMH Outstanding Resident Award. He is the deputy editor of *JAMA Psychiatry* and is on several editorial boards of top-tier psychiatric journals. He has served on numerous NIH and International Study Sections. LIBR focuses on using neuroscience approaches to develop better assessments for diagnosis or prognosis of mental health problems, and to develop neuroscience-based novel interventions. Dr. Paulus' research focuses on pragmatic academic psychiatry, i.e., how to use neuroscience-based measurements to identify modifiable treatment targets and to generate predictions that can be useful for clinicians. Moreover, Dr. Paulus is interested in whether computational approaches can be useful to better develop explanatory basis for psychiatric disorders that can be submitted to rigorous scientific examination.

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Researcher

## SELECTED PUBLICATIONS

- Steele, J.D., M.P., Paulus. Pragmatic neuroscience for clinical psychiatry. *Br J Psychiatry*, 2019. p. 1-5.
- Paulus, M.P., W.K., Thompson. The Challenges and Opportunities of Small Effects: The New Normal in Academic Psychiatry. *JAMA Psychiatry*, 2019.
- Paulus, M.P., J.S., Feinstein, S.S., Khalsa. An Active Inference Approach to Interoceptive Psychopathology. *Annu Rev Clin Psychol*, 2019. 15: p. 97-122.
- Harle, K.M., A.J., Yu, M.P., Paulus. Bayesian computational markers of relapse in methamphetamine dependence. *Neuroimage Clin*, 2019. 22: p. 101794.
- Ford, B.N., R.H., Yolken, R.L., Aupperle, T.K., Teague, M.R., Irwin, M.P., Paulus, J., Savitz. Association of Early-Life Stress With Cytomegalovirus Infection in Adults With Major Depressive Disorder. *JAMA Psychiatry*, 2019.
- Akeman, E., N., Kirlic, A.N., Clausen, K.T., Cosgrove, T.J., McDermott, L.D., Cromer, M.P., Paulus, H.W., Yeh, R.L., Aupperle. A pragmatic clinical trial examining the impact of a resilience program on college student mental health. *Depress Anxiety*, 2019.

## RESEARCH COLLABORATORS

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- Hugh Garavan Ph.D.**  
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- Rita Z. Goldstein, Ph.D.**  
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- Paul Davenport, Ph.D.**  
University of Florida
- Greg Fonzo, Ph.D.**  
Stanford University
- Walter Kaye, M.D.**  
University of California- San Diego
- Alan N Simmons, Ph.D.**  
University of California- San Diego
- Rajita Sinha, Ph.D.**  
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- Lindsay M. Squeglia, Ph.D.**  
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- Douglas Steele, M.D.**  
University of Dundee; Consultant Psychiatrist, NHS, UK
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- Susan F. Tapert, Ph.D.**  
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- Wesley R. Thompson, Ph.D.**  
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- Angela Yu, Ph.D.**  
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**Jonathan Savitz, Ph.D.**

Principal Investigator  
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**Dr. Savitz’s work focuses on three main areas:**

**1** Just as a cardiac stress test can be used to identify abnormalities of the heart that are not visible at rest, so to can “stressing” the immune system enable us to detect hidden factors that may lead to maladaptive immune responses. We use low-dose endotoxin, part of the cell wall of gram-negative bacteria, to “trick” the immune system into launching a transient inflammatory response. To our knowledge, we are the first group in the world to perform an endotoxin challenge on depressed volunteers. Knowledge gained from this study will help us understand the mechanisms through which an inflammatory stimulus alters brain activity in a way that makes some people vulnerable to developing depression in the setting of inflammation.

**2** Herpesvirus infections in healthy adults were traditionally considered to be harmless but there is emerging evidence that these viruses may not be completely benign. Herpesviruses lie dormant until they are reactivated by physical or psychological stressors. Conceivably, this periodic viral replication may trigger inflammatory responses that lead to depression. We are testing this hypothesis by following volunteers over the course of several months in order to evaluate whether fluctuations in stress and mood co-occur with changes in viral activity. This research may lead to the initiation of a clinical trial to test whether anti-viral agents have therapeutic benefits in depression.

**3** The balance of kynurenine pathway metabolism has been shown to be altered in depression, such that an excess of neurotoxic kynurenines is produced. These metabolites damage neuronal cells and impair synaptic plasticity (changes in the junctions between neurons that allow them to communicate). Real time neurofeedback of the amygdala is a promising treatment for depression that likely works in part by altering the connections between neuronal cells. This study tests whether people with higher levels of neurotoxic kynurenine metabolites will be less likely to respond to neurofeedback. The research may help us develop a blood biomarker to determine who should receive this type of treatment.

**SCIENTIFIC BACKGROUND**

**Dr. Savitz** received an undergraduate degree in psychology and genetics from the University of the Witwatersrand in Johannesburg, South Africa, performed further graduate work in neuropsychology, including a clinical internship, and then completed a Ph.D. on the genetics of bipolar disorder at the University of Cape Town in 2006. He subsequently completed a postdoctoral fellowship at the National Institutes of Health and is currently a principal investigator at the Laureate Institute for Brain Research and an associate professor at the University of Tulsa. Jonathan has trained with two of the most well-known experts in their respective fields: Wayne Drevets (mood disorders, neuroimaging) and Robert Dantzer (psychoneuroimmunology), and has conducted a number of innovative studies that have addressed important gaps in our knowledge regarding the relationship between genes, immunological function and neuroimaging abnormalities in mood disorders. Dr. Savitz has published over 60 first or senior author scientific papers and has been the PI on three NIH grants. He is an associate editor of the journal, *Neuroscience Letters*, and is an editorial board member of *Heliyon and Brain, Behavior and Immunity*. He has served as a reviewer for numerous European and American grant agencies, including the MESH study section of the NIH.



**LAB MEMBERS**

- Nour El-Sabbagh**  
Lab Manager
- Leandra Figueroa-Hall**  
Postdoctoral Associate
- Bart Ford**  
Graduate Student,  
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- Haixia Zheng**  
Postdoctoral Associate

**SELECTED PUBLICATIONS**

Savitz, J. (2019). The Kynurenine Pathway: A Finger in Every Pie. *Molecular Psychiatry*. In press.

Ford, B.N., Yolken, R.H., Aupperle, R.L., Teague, T.K., Irwin, M.R., Paulus, M.P., Savitz, J. (2019). Childhood abuse is associated with cytomegalovirus infection. *JAMA Psychiatry*. 76, 545-547.

Ford, B.N., Yolken, R.H., Dickerson, F.B., Teague, T.K., Irwin, M.R., Paulus, M.P., Savitz, J. (2019). Reduced Immunity to Measles in Adults with Major Depressive Disorder. *Psychological Medicine*. 49, 243-249.

Nitta, M.E., Savitz, J., Nelson, L.D., Teague, T.K., Hoelzle, J.B., McCrea, M.A., Meier, T.B. (2019). Acute elevation of serum inflammatory markers predicts symptom recovery after concussion. *Neurology*. 93, e497-e507.

Savitz, J., Teague, T.K., Misaki, M., Macaluso, M., Wurfel, B.E., Meyer, M., Drevets, D., Yates, W., Gleason, O., Drevets, W.C., Preskorn, S.H. (2018). Treatment of Bipolar Depression with Minocycline and/or Aspirin: An adaptive, 2 X 2 double-blind, randomized, placebo-controlled, phase IIA clinical trial. *Translational Psychiatry*. 8, e27.

Wurfel, B.E., Drevets, W.C., Bliss, S.A., McMillin, J.R., Suzuki, H., Ford, B.N., Morris, H.M., Teague, T.K., Dantzer, R., Savitz, J. (2017). Serum Kynurenine Acid is Reduced in Affective Psychosis. *Translational Psychiatry*. 7, e1115.

Mechawar, N. and Savitz, J. (2016). Neuropathology of Mood Disorders: Do we see the stigmata of inflammation? *Translational Psychiatry*. 6, e946.

Savitz, J., Drevets, W.C., Smith, C.M., Victor, T.A., Wurfel, B.E., Bellgowan, P.S.F., Bodurka, J., Teague, T.K., Dantzer, R. (2015). Putative Neuroprotective and Neurotoxic Kynurenine Pathway Metabolites are Associated with Hippocampal and Amygdalar Volumes in Subjects with Major Depressive Disorder. *Neuropsychopharmacology*. 40, 463-471.

Savitz, J.B., Rauch, S.L., Drevets, W.C. (2013). Clinical Application of Brain Imaging for the Diagnosis of Mood Disorders: The current state of play. *Molecular Psychiatry*. 18, 528-539.

Savitz, J.B., Nugent, A.C., Bogers, W., Roiser, J.P., Bain, E.E., Neumeister, A., Zarate, Jr., C.A., Manji, H.K., Cannon, D.M., Marrett, S., Henn, F., Charney, D.S., Drevets, W.C. (2011). Habenula Volume in Bipolar Disorder and Major Depressive Disorder: A High Resolution MRI Study. *Biological Psychiatry*. 69, 336-343.

Savitz, J., van der Merwe, L., Stein, D.J., Solms, M., Ramesar, R. (2007). Genotype and childhood sexual trauma moderate neurocognitive performance: A possible role for BDNF and ApoE variants. *Biological Psychiatry*. 62, 391-399.

**RESEARCH COLLABORATORS**

- Jin Cho, M.D., Ph.D.**  
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- Robert Dantzer, DVM, Ph.D.**  
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University of Texas
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- Mike Irwin, M.D.**  
University of California – Los Angeles
- Brett McKinney, Ph.D.**  
University of Tulsa
- Kent Teague, Ph.D.**  
University of Oklahoma – Tulsa
- Bob Yolken, M.D.**  
Johns Hopkins University



**Ryan Smith, Ph.D.**

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**Dr. Smith's main research interests include understanding how conscious and unconscious emotion-related processes are realized within the brain, and how these processes may be altered in mood and anxiety disorders. Dr. Smith's primary research methods are neuroimaging and computational modeling. A major focus of his work is characterizing differences between mentally healthy and unhealthy individuals, with the goal of improving diagnosis and treatment selection within psychiatry and clinical psychology.**

**RESEARCH PROGRAM HIGHLIGHTS**

**Main Questions**

**How does the brain generate emotions, and how do we subsequently recognize and become aware of our own emotions? Can these processes be understood in terms of the computational processes performed by the brain? How might these computational processes be affected in psychiatric disorders? Could understanding these mechanisms improve treatment?**

**Approach**

**We employ several methods aimed at providing multiple levels of description in characterizing emotion-related psychological and biological processes, including self-reported experience, behavioral and physiological responses, functional neuroimaging, and computational modeling.**

**Future Directions**

**We aim to establish (1) the role of conscious and unconscious emotional 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.**

**SCIENTIFIC BACKGROUND**

**Dr. Smith** received his bachelor's degree in psychology from Arizona State University in 2010. He subsequently completed three graduate degrees from the University of Arizona between 2011 and 2015: master's degrees in neuroscience and philosophy (with a focus on the philosophy of science and mind), and a Ph.D. in psychology (with a focus in cognitive neuroscience). His graduate work in philosophy focused on the relationship between scientific explanation and understanding, and on the relationship between physical and mental processes. This work was done primarily under the supervision of Jenann Ismael, who is a recognized leader in the philosophy of cognitive science and the philosophy of physics. Dr. Smith's graduate work in neuroscience/psychology focused on the role of the prefrontal cortex in emotion and its pathology in major depression, using both structural and functional neuroimaging as well as measurement of heart-rate variability. This work was done primarily under the supervision of Dr. Richard Lane, who is both a practicing psychiatrist and a recognized pioneer in studying the brain basis of emotion.

Dr. Smith completed a three-year postdoctoral fellowship with Dr. W.D. Scott Killgore in the University of Arizona College of Medicine psychiatry department. During this fellowship, he designed and ran a neuroimaging study focused on understanding the ability to hold emotional information within working memory. He also played a primary role in creating an online emotional intelligence training program designed to minimize the development of emotional disorders in military personnel.

Upon completing this postdoctoral fellowship, Dr. Smith accepted an associate investigator position at LIBR, following completion of a four-month visiting fellowship with Dr. Karl Friston at University College London. This fellowship focused on designing computational models of brain function for use in understanding emotions and mechanisms underlying psychopathology.

Dr. Smith has authored more than 50 publications within peer-reviewed journals and scholarly books, based in part on the work described above. Many of these publications have also made theoretical contributions, proposing neurocognitive and computational models of conscious/unconscious emotion, neurovisceral integration, emotional intelligence, and depression.

**SELECTED PUBLICATIONS**

Smith, R., Allen, J.J., Thayer, J.F., Lane, R.D. (2015). Altered functional connectivity between medial prefrontal cortex and the inferior brainstem in major depression during appraisal of subjective emotional responses: A preliminary study. *Biol Psychol*, 108, 13-24.

Smith, R., Braden, B.B., Chen, K., Ponce, F.A., Lane, R.D., Baxter, L.C. (2015). The neural basis of attaining conscious awareness of sad mood. *Brain Imaging Behav*, 9(3), 574-587.

Smith, R., Lane, R.D. (2015). The neural basis of one's own conscious and unconscious emotional states. *Neurosci Biobehav Rev*, 57, 1-29.

Smith, R., Alkozei, A., Lane, R.D., Killgore, W.D.S. (2016). Unwanted reminders: The effects of emotional memory suppression on subsequent neurocognitive processing. *Conscious Cogn*, 44, 103-113.

Smith, R., Lane, R.D. (2016). Unconscious emotion: A cognitive neuroscientific perspective. *Neurosci Biobehav Rev*, 69, 216-238.

Smith, R., Thayer, J.F., Khalsa, S.S., Lane, R.D. (2017). The hierarchical basis of neurovisceral integration. *Neurosci Biobehav Rev*, 75, 274-296.

Smith, R., Lane, R.D., Parr, T., Friston, K.J. (2019). Neurocomputational mechanisms underlying emotional awareness: Insights afforded by deep active inference and their potential clinical relevance. *Neurosci Biobehav Rev*.

Smith, R., Lane, R.D., Alkozei, A., Bao, J., Smith, C., Sanova, A., Killgore, W.D.S. (2017). Maintaining the feelings of others in working memory is associated with activation of the left anterior insula and left frontal-parietal control network. *Soc Cogn Affect Neurosci*, 12(5), 848-860.

Smith, R., Alkozei, A., Bao, J., Smith, C., Lane, R.D., Killgore, W.D.S. (2017). Resting state functional connectivity correlates of emotional awareness. *Neuroimage*, 159, 99-106.

Smith, R., Alkozei, A., Killgore, W.D.S. (2017). Contributions of self-report and performance-based individual differences measures of social cognitive ability to large-scale neural network functioning. *Brain Imaging Behav*, 11(3), 685-697.

Smith, R., Alkozei, A., Killgore, W.D.S., Lane, R.D. (2018). Nested positive feedback loops in the maintenance of major depression: An integration and extension of previous models. *Brain Behav Immun*, 67, 374-397.

Smith, R., Lane, R.D., Alkozei, A., Bao, J., Smith, C., Sanova, A., Killgore, W.D.S. (2018). The role of medial prefrontal cortex in the working memory maintenance of one's own emotional responses. *Sci Rep*, 8(1), 3460.

Smith, R., Killgore, W.D.S., Alkozei, A., Lane, R.D. (2018). A neurocognitive process model of emotional intelligence. *Biol Psychol*, 139, 131-151.

Smith, R., Killgore, W.D.S., Lane, R.D. (2018). The structure of emotional experience and its relation to trait emotional awareness: A theoretical review. *Emotion*, 18(5), 670-692.

Smith, R., Bajaj, S., Dailey, N.S., Alkozei, A., Smith, C., Sanova, A., Killgore, W.D.S. (2018). Greater cortical thickness within the limbic visceromotor network predicts higher levels of trait emotional awareness. *Conscious Cogn*, 57, 54-61.

Smith, R., Lane, R.D., Sanova, A., Alkozei, A., Smith, C., Killgore, W.D.S. (2018). Common and Unique Neural Systems Underlying the Working Memory Maintenance of Emotional vs. Bodily Reactions to Affective Stimuli: The Moderating Role of Trait Emotional Awareness. *Front Hum Neurosci*, 12, 370.

Smith, R., Sanova, A., Alkozei, A., Lane, R.D., Killgore, W.D.S. (2018). Higher levels of trait emotional awareness are associated with more efficient global information integration throughout the brain: A graph-theoretic analysis of resting state functional connectivity. *Soc Cogn Affect Neurosci*, 13(7), 665-675.

Smith, R., Weihs, K.L., Alkozei, A., Killgore, W.D.S., Lane, R.D. (2019). An Embodied Neurocomputational Framework for Organically Integrating Biopsychosocial Processes: An Application to the Role of Social Support in Health and Disease. *Psychosom Med*, 81(2), 125-145.

**RESEARCH COLLABORATORS**

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Dr. Stewart employs subjective reports (questionnaires and clinical interviews), behavioral methods, electroencephalography (EEG), event-related potential (ERP) and functional magnetic resonance imaging (fMRI) to investigate how brain patterns linked to cognition, emotion and their interaction intersect with individual differences in substance use, depression and anxiety disorders. People who are suffering from drug addictions, depression and/or anxiety often have difficulties processing emotions and making decisions that are evident in patterns of brain activity and behavior.

**Dr. Stewart's primary research areas include:**

- 1 Can we identify brain/behavioral markers of risk for future addiction in young adults who have not yet transitioned to chronic mental health problems?**
- 2 In individuals experiencing chronic addiction, can we identify brain/behavioral markers of short-term and long-term abstinence and recovery?**
- 3 Once viable brain/behavioral markers are identified, these can be used in clinical prevention and early intervention efforts.**

**SCIENTIFIC BACKGROUND**

**Dr. Stewart** earned a B.S. in psychology from University of California – San Diego (UCSD) in 1998, where she worked with Dr. Brett Clementz on EEG and eye-tracking studies of schizophrenia and bipolar disorder. Following further EEG and ERP training with Dr. John Polich at the Scripps Research Institute, Dr. Stewart completed her M.A. (2005) and Ph.D. (2008) in clinical psychology at the University of Illinois at Urbana-Champaign working with Drs. Greg Miller and Wendy Heller. Her graduate work used EEG, ERP and fMRI methods to investigate patterns of functional brain asymmetry as a function of approach- versus withdrawal-related anger expression styles (anger-out versus anger-in), taking patterns of comorbid depression and anxiety into account. In her postdoctoral studies, Dr. Stewart evaluated the viability of brain asymmetry as a biomarker of depression risk with Dr. John Allen at the University of Arizona and investigated potential markers of stimulant addiction risk and relapse with Dr. Martin Paulus at UCSD.

Starting in 2014, Dr. Stewart spent four years as an assistant professor of clinical psychology at the City University of New York (CUNY Queens College/The Graduate Center) where she served as training area coordinator for their APA-accredited clinical program. While at CUNY, she supervised undergraduate and graduate students on EEG/ERP data collection/analysis for studies evaluating biomarkers of depression risk and heavy marijuana use in college students. She taught courses on psychopathology, introduction to clinical psychology, multivariate statistics, clinical interviewing and neuropsychological assessment.

In the past decade, Dr. Stewart has assisted in mentoring and training undergraduates, graduate students, postdoctoral researchers and visiting scientists on clinical assessment measures as well as EEG, ERP and fMRI methodology, data collection/analysis, manuscript writing, talks, poster presentations and grant applications. She is enthusiastic about science and hopes to empower students with the tools to become successful researchers. Dr. Stewart joined LIBR in July 2018.

**SELECTED PUBLICATIONS (2016-Present)**

Butt, M., Espinal, E., Aupperle, R.L., Nikulina, V., Stewart, J.L. (2019). The electrical aftermath: Brain signals of posttraumatic stress disorder filtered through a clinical lens. *Frontiers in Psychiatry*, 10, 368 (online publication). doi: 10.3389/fpsy.2019.00368

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**RESEARCH COLLABORATORS**

- John J.B. Allen, Ph.D.**  
University of Arizona
- Robin L. Aupperle, Ph.D.**  
Laureate Institute for Brain Research
- April C. May, M.A.**  
University of California- San Diego
- Martin P. Paulus, M.D.**  
Laureate Institute for Brain Research



**ONGOING STUDIES**

**Ongoing Studies**

If you are interested in participating in any of the studies below, or would like to be considered for future studies, please call our assessment team at 918-502-5100 or email [info@laureateinstitute.org](mailto:info@laureateinstitute.org).



**LIBR**  
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## FLOAT STUDY

**Do these statements describe you?**

- I feel anxious, stressed, and tense all the time
- When under stress, I am easily irritated or upset
- I feel that anxiety and stress interfere with my ability to function in life and at work
- I always feel like something bad is going to happen to me and that my life is in danger
  - When my heart beats rapidly, I sometimes worry I might be having a heart attack
  - When my stomach feels upset, I worry that I might be seriously ill
  - When I feel like I am not getting enough air, I get scared I might suffocate

**FLOAT CHAIR**      **FLOAT BED**

**FLOAT POOL**

If you said "yes" to most of the items above, then you may qualify for a new research study at the Laureate Institute for Brain Research (LIBR) that involves weekly float therapy over a two-month period.

The study will provide up to \$250 in compensation and aims to understand the effect of three different float experiences on both physical and mental health.

**Call 918-502-5100 or Email [info@libr.net](mailto:info@libr.net)**

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**Affected by depression?**  
We want to help.

**JOIN OUR THERAPY STUDY**  
**CALL 918-344-8611**

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

**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.

**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.

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.

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.

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## 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.

**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.

**WE NEED YOU**  
Participation is always **voluntary** and your information is kept **confidential**.

**Qualified teen research volunteers must be:**

- Ages 13-17, male or female
- Free of psychiatric symptoms OR
- Currently experiencing symptoms of anxiety or depression
- Accompanied by a parent or legal guardian

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**.

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.

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

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**LIBR**  
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## 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 18-55
- 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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## VOLUNTEER for LIBR ADDICTION STUDIES

Neuroscience-based Core Assessments for People with Substance Use Disorders (NeuroCAPS)

**ABOUT OUR RESEARCH**  
LIBR is a scientific research institute that focuses on discovering brain-based techniques to improve mental health. LIBR is unique in a number of different ways. First, it challenges its scientists to think outside the box to come up with game-changing research findings that improve mental health care. Second, it closely works with different addiction treatment programs in Oklahoma to develop new treatments for drug addiction. Third, it has one of the best brain imaging facilities in the country to study the living brain.

**PARTICIPATION**  
LIBR addiction studies include participation in a series of visits involving:

- psychiatric assessments
- behavioral testing
- brain imaging scans and tasks
- blood marker testing

All study assessments and procedures will be provided free of charge to you. You will be paid for your time spent participating in the LIBR addiction studies.

**WE NEED YOU**  
**Qualified volunteers will:**

- Be ages 18-55, male or female
- Have problems with substance use
- Be planning to start or already in a treatment program

Joining this research study helps us move toward our goal of personalizing substance use treatment.

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

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## Volunteer for Brain Gym for Recovery Project

Neurocognitive Empowerment for Addiction Treatment (NEAT) Project

**WHY BRAIN GYM FOR RECOVERY?**

- Drug addiction is not only associated with increased mental health symptoms, such as anxiety and depression, but also with brain (cortical and subcortical) deficits.
- Cognitive deficits in memory, attention, decision-making, and inhibitory control disrupt normal daily functioning and attempts for abstinence, and are associated with worse long-term recovery outcomes.
- Current treatment programs for addiction are mainly focused on abstinence, with the assumption that these brain deficits will subsequently heal. However, these deficits are found to persist even after a long-term abstinence and are thought to contribute to relapse, decrease quality of life, and lack of reintegration into society.
- Brain rehabilitation programs focused on compensatory strategies and training exercises for brain deficits have consistently been found to improve functioning and long-term outcomes for different clinical populations.
- However, there has been a relative lack of research focused on identifying interventions targeting brain deficits in the context of addiction.

**BRAIN GYM PARTICIPATION**  
Brain Gym is composed of 14 sessions of 2 hours classes with goal:

- (1) cartoons, brain awareness games and real-life scenarios to ensure it is interactive and engaging.
- (2) Focus on the role of brain deficits in recovery from addiction and co-occurring mental health disorders, and
- (3) Incorporation of scientific findings specific to addiction to the brain training and exercise strategies.

Participants will be followed for six months to explore the efficacy of the Brain Gym on cognitive performance, and functional and structural brain changes using magnetic resonance imaging (MRI).

This research study has the potential to identify a novel intervention that can be integrated into addiction treatment programs in Oklahoma and nation-wide to more effectively support recovery from addiction.

You will be paid for your time spent participating in the Brain Gym study.

**WE NEED YOU**  
**Qualified research volunteers will:**

- Be ages 18-55, male or female
- Have problems with substance use
- Currently in a recovery treatment program

Joining this research study provides you with an opportunity to contribute to an exciting time in mental health research, one that is moving toward personalized care for the millions of people worldwide who suffer from addiction at a brain disease.

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

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**Curious about anxiety?**  
JOIN OUR STUDY

**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.

**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

**For more information, please call LIBR at: 918-344-8611**

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ONGOING STUDIES, CONTINUED



**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**  
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**LIBR**  
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Improving Mental Health Through Neuroscience

- Postdoctoral positions available
- Projects include behavioral and pharmacological clinical trials, EEG-fMRI studies, computational modeling of multilevel data sets
- Interested? Contact [careers@laureateinstitute.org](mailto:careers@laureateinstitute.org)



**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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**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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2019 PUBLICATIONS

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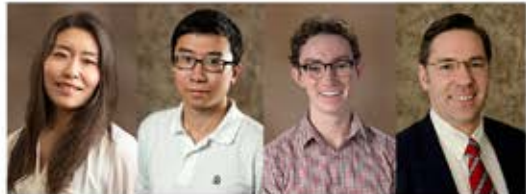
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