NRC newsletter

go.uth.edu/UTHealthNRC | News & Featured Research of the Neuroscience Research Center | Volume 28, Number 2, 2024

Bridging Large Network Activity with the Mesoscale of Electrophysiology

John P. Seymour, PhD

Seymour

Abstract: Electrophysiology is still a powerful and burgeoning neuroscience tool despite its age and the competition from many disruptive technologies such as optogenetics, calcium imaging, and optical voltage indicators. This article discusses our recent development of depth arrays with mesoscale spatiotemporal dynamics in rodents and humans. Mesoscale tools are a critical component in the push toward intrinsic network mapping. However, further advances will be required in power harvesting, microelectronics miniaturization, and source localization software if we are to democratize whole-brain recording and stimulation hardware.

In today's global "chip war," we can imagine government engineers peering deep inside their competitor's billion-transistor chip to tease apart technology advances from the other side. This challenge is most straightforward to unravel in the von Neumann world of serialized transistors, but modern neural network computation requires seeing recurrent network connections among large-scale nodes. Since information transfer in modern chips is increasingly parallel and dynamic, destructive testing will only tell the probing spies so much. Neuroscientists have a more formidable problem when interfacing with the brain, the ultimate parallel computer. Excitingly, mapping a microcircuit in each brain subregion has improved as our recording microelectrode channel count has scaled in the last two decades. An important example is the development of IMEC's Neuropixel probe, a recording device manufactured in an advanced European foundry, which can track more than 1,000 single neurons (Steinmetz et al., *Science* 372:6539, 2021). The sparsity and locality of single cells are ideal for studying local computation, but this does not address the grand challenge of understanding brain-wide network dynamics. Our laboratory in UTHealth Houston's Department of Neurosurgery is working to contribute to this grand challenge by first addressing the mesoscale gap – the large resolution loss when shifting from microscale to macroscale electrodes.

Continued on Page 3; Seymour

Adapting and Optimizing Brain Stimulation Techniques for the Treatment of Cocaine Use Disorder

Heather E. Webber, PhD

Webber

Abstract: Cocaine use and related overdose deaths are on the rise in the United States. Despite considerable effort, there are still no FDA-approved medications for treating adults with a cocaine use disorder. Non-invasive brain stimulation techniques hold considerable promise in this regard, but more controlled research to iron out stimulation parameters and indicators of change are needed.

Cocaine-related overdose deaths have increased nearly 50% in recent years. Unlike the opioid crisis, the cocaine crisis is worsened due to limited treatment options. Decades of research on monoaminergic medications have failed to yield U.S. Food and Drug Administration (FDA)-approved medications for the treatment of cocaine use disorder (CUD). Although effective behavioral treatments exist, success rates are low and relapse rates are high, suggesting there is an urgent need to identify new treatment methods.

Neuroscience-informed CUD treatments hold promise, as neuroadaptation of the dopamine reward system and its prefrontal targets is central to the maintenance of CUD. Administration of cocaine leads to an increase in the neurotransmitter dopamine in the nucleus accumbens by blocking the reuptake of monoamines. With repeated use, more of the drug is needed to achieve the same amount of physiological and subjective effects. This adaptation leads to a lack of pleasure in everyday rewarding activities (like eating or socializing), accompanied by an increased focus on obtaining and using cocaine. Years of research indicate that CUD is associated with changes in basic reward and prefrontal functioning, such as emotional control, inhibition, decision-making, and the processing of motivationally salient stimuli.

Transcranial magnetic stimulation (TMS) is a promising method that can directly modulate the reward system and downstream prefrontal areas. By passing an electrical current through an insu-

Continued on Page 5; Webber

Director's Column

From the Director, John H. Byrne, PhD

Summer is traditionally associated with relaxation and leisure, but for us at the UTHealth Houston Neuroscience Research Center, it marks our busiest season. As the academic year comes to an end, we begin to plan our upcoming events for the next year. In this issue's column, I am delighted to fill you in on our recent developments and programming.

The underlying theme this year was essentially the title of our Neurobiology of Disease course, "Neuromodulation and Brain-Computer Interfaces." Much of our programing fell under the umbrella of this timely topic. Advances in this ever-growing field are further highlighted in this issue by our two course directors, who consider the advantages and limitations of both invasive and non-invasive recording and stimulating techniques. **John Seymour, PhD**, Associate Professor in the Department of Neurosurgery and Adjunct Associate Professor at Rice University's Department of Electrical & Computer Engineering, utilizes more invasive techniques in his research. Dr. Seymour's article discusses his group's development of depth arrays with mesoscale spatiotemporal dynamics, which are used in both rodents and humans, and how bridging these mesoscale data with large network activity is a critical component of network mapping. **Heather Webber, PhD**, Assistant Professor in the Faillace Department of Psychiatry and Behavioral Sciences, employs non-invasive techniques in her research. Dr. Webber's article discusses her group's work to utilize and optimize brain stimulation techniques for the treatment of cocaine use disorder. I hope you enjoy reading about their cutting-edge research, as they are both greatly advancing our understanding of neural circuitry and neuromodulation.

The NRC is honored and delighted to host Gregoire Courtine, PhD, Professor at the École Polytechnique Fédérale de Lausanne, for our annual Distinguished Lecturer Series. This event brings internationally renowned scientists to our campus to deliver a lecture on their eminent work. Using a combination of electrical stimulation, neuroprosthetics, and rehabilitation protocols, Dr. Courtine's group develops innovative technologies and therapies aimed at reactivating spinal cord circuits and facilitating motor function recovery. In addition to better understanding the neural mechanisms underlying the control of locomotion, his research offers great hope for improving the quality of life for individuals with severe injuries or neurological disorders, and represents a significant advancement in the field of neurorehabilitation. Please check our website for more information about his upcoming visit.

This fall, our graduate level course, "Current Topics in the Neurobiology of Disease," is expanding in breadth, highlighting collaborations between the McWilliams School of Biomedical Informatics (SBMI) and McGovern Medical School. The course topic, "Artificial Intelligence and the Brain," will be directed by **Amy Franklin, PhD**, Associate Professor in the Department of Clinical and Health Informatics and Associate Dean for Student, Faculty, and Community Affairs at the SBMI. The series of lectures will present a survey of Artificial Intelligence (AI) tools utilized in clinical and research applications with a focus on Alzheimer's disease, depression, stroke, epilepsy, addiction, and movement disorders. Each topic will be explored by both a faculty member from the SBMI and a faculty member from the medical school, highlighting existing and future collaborations within UTHealth Houston. The course lectures, which are open to all students, postdoctoral fellows, residents, researchers and faculty, will be posted to our website and listed on the Neurofax calendar of events.

In addition to our NRC program updates, I am delighted to share that **Nitin Tandon, MD**, NRC Executive Committee member and former chair *ad interim* of the Department of Neurosurgery, has taken on a new role as the first vice president for strategy and development at UTHealth Houston Neurosciences. The new chair of the Vivian L. Smith Department of Neurosurgery, **Jacques Morcos, MD**, has joined us from the University of Miami Health System. Along with **Louise McCullough, MD, PhD**, chair of the Department of Neurology, Dr. Morcos will serve as co-director of UTHealth Houston Neurosciences. Dr. Morcos is a renowned neurosurgeon, specializing in radiosurgery and cerebrovascular and skull base lesions, and is currently president of the American Association of Neurological Surgeons and president-elect of the World Federation of Skull Base Societies. We will hear more about his plans for the future of the Department of Neurosurgery in our next issue. Congratulations to both Drs. Morcos and Tandon on their new roles at UTHealth Houston.

Looking ahead, please keep an eye out for communication regarding our annual Neuroscience Poster Session. This event will be held on Saturday, December 7th at the UTHealth Houston Cooley University Life Center. Participating institutions include UTHealth Houston, Baylor College of Medicine, and Rice University.

We look forward to seeing you at one of our many upcoming events in the fall. Until then, I hope your summer is filled with the ever-elusive balance of productivity and relaxation.

Continued From Page 1; Seymour

Field potential measurements are readily accessible at some distance from the neural source and are commonly measured using electroencephalography (EEG), magnetoencephalography (MEG), stereoelectroencephalography (SEEG), and electrocorticography (ECoG). The noninvasive EEG, MEG and the subdural ECoG offer impressive spatial coverage but without depth. SEEG provides improved resolution at depth but not nearly enough to parse out neural activity at the mesoscale range (0.1-5 mm) required in many neuroscience applications (**Fig. 1**). A significant challenge with field potentials at any scale is to parse the enormous number of source contributions, often called the "cocktail party" problem. The voltage at any point in the brain is a superposition of voltage from all of the neural sources within a range of that point. Superposition is why the "ideal" microelectrode, often described as an ultra-fine wire and electrode contact, turns out to be far less ideal in field potential recordings.

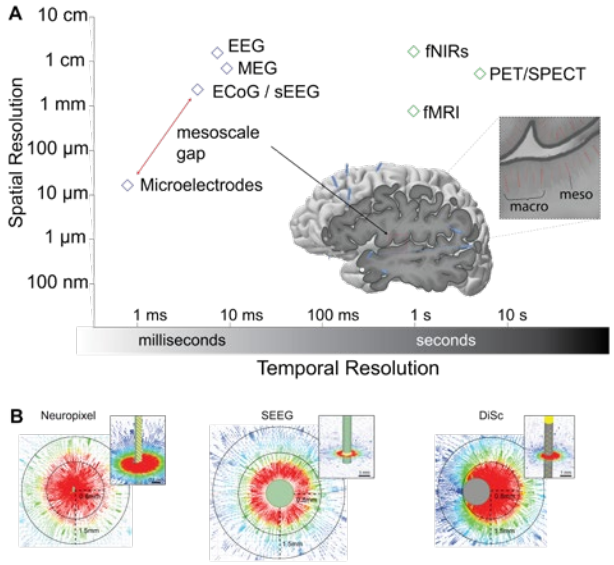


Figure 1. The mesoscale gap in electrophysiology. (A) While macroscale electrodes are excellent for spanning multiple brain regions, mesoscale information, such as cortical column circuits, will be aggregated. Conversely, microelectrodes provide single-cell resolution with a recording range of only ~70 µm. (B) We demonstrate the directional sensitivity maps of microelectrodes arrayed onto a standard 0.8mm diameter depth array and contrast this with two other state-of-the-art electrodes, the Neuropixel and an SEEG. Unlike the microelectrode on the Neuropixel (or any narrow thin-film device) and the ring on an SEEG, DiSc has excellent amplification and directionality at the mesoscale.

Our laboratory mission is to improve mesoscale recordings, and we foresee this will contribute to the democratization of network-wide electrophysiology for the neuroscience community. The clinical success of SEEG inspired this effort. It is now used worldwide as a minimally invasive alternative to ECoG because of its lower risk to the subject and its ability to target deep and even multiple regions of interest. The apparent limitation of SEEG contacts is their size, but this sensitivity turns out to be far more interesting and controllable than reducing contact dimensions. The sensitivity of a microelectrode and SEEG ring contact are surprisingly similar for population activity (**Fig. 1B**). Neither design offers any preferred direction at the mesoscale, so field potentials become massively redundant. The microelectrode can only reach up to ~70 microns and thus has many practical limits to solving the mesoscale and network challenges. The key realization for us has been that the sensitivity of the microelectrode is highly controllable by the insulating body itself and that the SEEG insulation body at 0.8 mm diameter is highly effective at amplifying the local field potential in one direction while shielding the many other field potential sources. This directionality gives the user a rich view of the local field potential (LFP) including a multi-dimensional current source density plot. The same diameter microelectrode that is used for single unit recordings now has a vastly improved mesoscale sensitivity. It can also be averaged together to provide customizable "montages" of the meso- to macro-scale views of neural activity. Put another way, the combination of microelectrodes on a mesoscale cylinder offers directional and scalable information, something we call a DiSc (directional and scalable) depth array.

Neurosurgeons have been particularly excited by the potential of such a device, given the rich clinical evidence demonstrating an unequivocal advantage of the 0.8 mm diameter depth array over subdural grids (Engel, *Curr. Opin. Neurol*. 31:192, 2018). Translation has been a major focus for us, but it is reasonable to wonder if this technology will be useful in the small brains of rodents. Using the classic whisker stimulation experiment, we contrasted the performance of this recording array against that of the tetrode and another SEEG at various contact sizes. Despite the large cortical column diameter of a rat barrel and the known lateral excitation between barrels, we found that the DiSc array provides excellent amplification, directionality, and discrimination between whisker stimuli relative to all other electrode types tested (**Fig. 2**) (Abrego et al., *J. Neural Eng*. 20:016041, 2023).

Surgical techniques in rodents using large depth arrays continue toward a low-cost, rapid stereotactic procedure with increasing brain region coverage. As in humans, eliminating the craniotomy is expected to reduce pain and surgical complications and accelerate the procedure. Access to the brain should be minimal, and we have found 1 mm skull openings prevent the rat brain from dimpling during insertion. Also, knowing the local vascular map of the subject to avoid large surface vessels will improve outcomes. Not everyone has access to contrast-based MRI as in humans, but in these experiments, we simply thinned the skull and imaged blood vessels using a 540 nm filter. Future work in our lab will also adapt this surgery for mice, especially by developing a stereotactic procedure that expands the device tract with a rapid succession of guidewire diameters.

A possible limitation in translating DiSc to large animal and human applications may be a lack of spatial diversity in activity sources. As an analogy, acoustic shielding around a generic microphone can provide a highly directional acoustic sensitivity map, but this may not be enough for large amplitude sources. In field potentials, large amplitude comes from large volumes of synchronous inputs, and volume can especially overwhelm the sensitivity of this

Continued on Page 4; Seymour

Continued From Page 3; Seymour

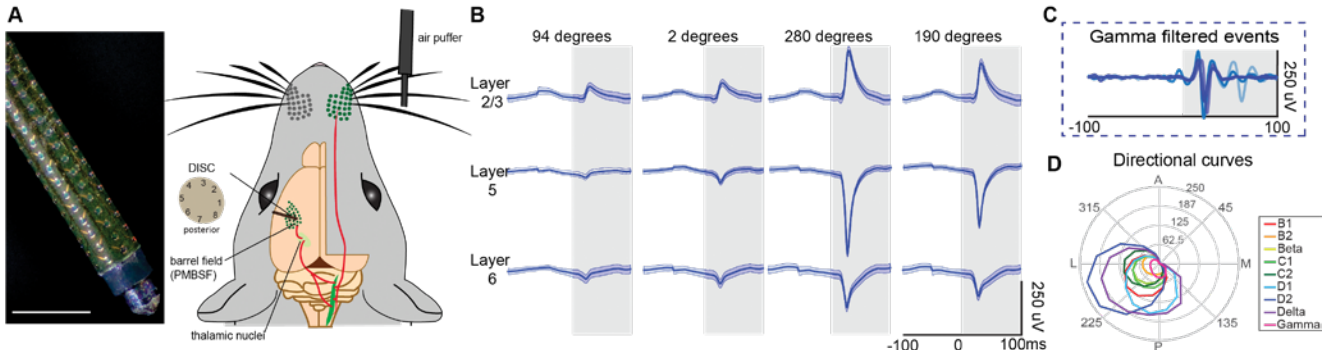


Figure 2. Mesoscale and multi-scale demonstration in rat whisker barrel recording. (A) DiSc device and experimental design. Scale = 1 mm. (B) Example of a trial averaged LFP demonstrating directionality (columns are unique angles) during a specific whisker (D2) stimulus. (C) Example of single trial gamma band response of whisker D2 at 280 degrees. Five individual trials represented with different colors. (D) Polar plot or directional curve calculated using the LFP-band evoked response across eight electrodes for each whisker. Minimum value has been subtracted for contrast.

sized device. Thus, we were excited when we first demonstrated DiSc in several human resection surgeries, where several large amplitude sources have a direction-specific peak amplitude (even for single events). We hope this approach may be helpful for epilepsy or tumor resection surgeries where directionality near an eloquent brain region may provide clinical guidance in resection or ablation.

DiSc is multiscale, but no minimally invasive implant can provide network-wide information, which is critical in cracking the parallel recurrence problem. DiSc is a multi-region tool that must be linked to other depth arrays, electrodes, or imaging methods. We foresee EEG or fMRI as two critical options to connect micro- and meso-scale spatiotemporal dynamics with the intrinsic network-level context required by neuroscience. Our lab is working on miniaturized electronic packaging so that neuroscientists can easily integrate EEG, for example, as an option. The goal is to employ network-wide recording with stereotactic mesoscale recording and stimulation in a small, lightweight wireless system. Conventional wireless radiofrequency transmission typically consumes substantial power and is currently only practical in larger animals. Integrating recent advances in power harvesting will be critical to making chronic, large-scale recording and stimulation systems practical, and doing so at the network scale in a mouse would be a breakthrough for network neuroscience. Our lab is excited to develop packaging solutions to integrate our novel depth arrays with large-scale EEG, low-noise amplifiers, power harvesting, and microcontrollers.

Software is another major component required for future parallel network investigation. Source localization is an inverse model for electrophysiology that can provide access to what would otherwise be overwhelming datasets for most neuroscience labs. It enables the neuroscientists to "image" the source activity and perform brain-wide analyses like fMRI. Fortunately, our fMRI data is not a pattern of squiggly lines attached to RF antenna labels, so we hope the field can move from electrode space to source space. Along with collaborators at UTHealth Houston and the University of Southern California who developed the popular open-source source imaging software Brainstorm, we are adapting this software to practically address the mesoscale gap from mouse to man.

Electrode design is currently far from simple or optimal. Electrode sensitivity maps are a function of anatomy and lead body insulation, and the signal amplitude is a function of the unique information structure of a given brain region. If designed well, the hardware should have a manageable number of well-planned electrode contacts and be delivered in a simple and minimally invasive surgery. Spatial coverage must strive to be as broad and diverse as allowable with mesoscale information from critical regions of interest. Source space software must also be computationally tractable and multiscale. However, progress is happening in each of these dimensions, so we are excited to help electrode and system design mature alongside network neuroscience.

About the Author

John Seymour, PhD *is an associate professor in the UTHealth Houston McGovern Medical School Department of Neurosurgery. Dr. Seymour received a Bachelor of Science degree with Honors in Engineering Physics from the Ohio State University and completed his PhD in Biomedical Engineering at the University of Michigan. After graduating, he joined NeuroNexus as a Principal Scientist before returning to the University of Michigan as an Assistant Research Scientist. In 2019, he joined UTHealth Houston in his current role. He is also presently an Adjunct Associate Professor in the Department of Electrical and Computer Engineering at Rice University. Dr. Seymour's research focuses on the advancement of neurotechnology for improved treatment of neurological disease.*

Continued From Page 1; Webber

lated coil, TMS generates a magnetic field that can pass unimpeded through the skull. This magnetic field can facilitate or impede the firing of neurons directly under the coil. Repetitive TMS can produce longer lasting effects by facilitating long-term potentiation or depression of synaptic connections, depending on the stimulation pattern and frequency. TMS was originally approved by the FDA in 2008 for the treatment of depression and is now approved for a variety of other disorders. Considering the overlap of neural circuits affected in depression and CUD, TMS may hold promise for modifying reward functioning in addiction populations.

Although some studies have shown initial evidence that TMS might be useful for treating CUD, inconsistent results indicate that there is room for optimization. Unfortunately, the parameter space is wide. Brain area to target, stimulation pattern, stimulation intensity, stimulation frequency, number of pulses, number of sessions, and time between sessions are among the many potential parameters that need to be assessed. To this end, our group is testing different stimulation sites and patterns, as well as identifying optimal outcome measures, to assess TMS effects on CUD.

The majority of TMS studies in cocaine users have aimed to apply excitatory stimulation to dorsolateral prefrontal cortex to bolster reward functioning, based on the evidence from the depression field (for a review, see Bolloini et al., *Subst. Abuse Rehabil.* 9:11, 2018). However, dorsomedial prefrontal cortex is also implicated in CUD, has more direct connections to other affected areas (including the anterior cingulate cortex), and might be a more direct site for stimulation. Yet, no studies have compared dorsolateral and dorsomedial prefrontal cortex in a sample of individuals with CUD.

In terms of the type of stimulation, intermittent theta burst stimulation (iTBS), is a pattern of stimulation that is thought to mimic endogenous theta rhythms, enhancing the long-term potentiation effects of TMS. iTBS uses trains of short, high-frequency bursts and can be administered within three minutes, which is much shorter than the 15-20 minute 10-15 Hz stimulation TMS protocols. This protocol lowers the time burden on the participant and may be more tolerable, depending on the location of the stimulation. Further, as iTBS sessions are so short, multiple sessions can be administered within a day, increasing the "dose" a patient can receive when visiting a clinic. iTBS has been shown to have similar effectiveness as the standard protocol for the treatment of depression (Blumberger et al., *Lancet* 391:1683, 2018). An extremely limited number of studies have tested iTBS for the treatment of CUD, but preliminary evidence shows promise for using this stimulation pattern.

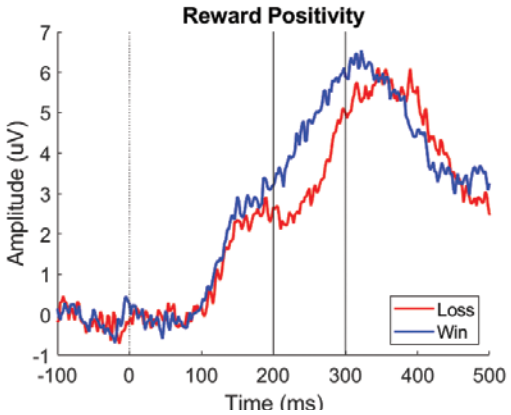


Figure 1. The reward positivity component in a sample (n = 16) of adults with cocaine use disorder. Winning money typically elicits a more positive waveform compared to losing money.

Finally, the identification of biomarkers that can assess TMS effects is critical. The majority of studies have relied on self-reported measures of craving as the primary outcome. Although informative, subjective measures can be limited by ineffective reporting due to lack of insight, altered cognitive functioning, and shame with reporting drug use. An electroencephalogram (EEG) measures the electrical activity of groups of neurons firing in the brain. EEG can measure

Continued on Page 10; Webber

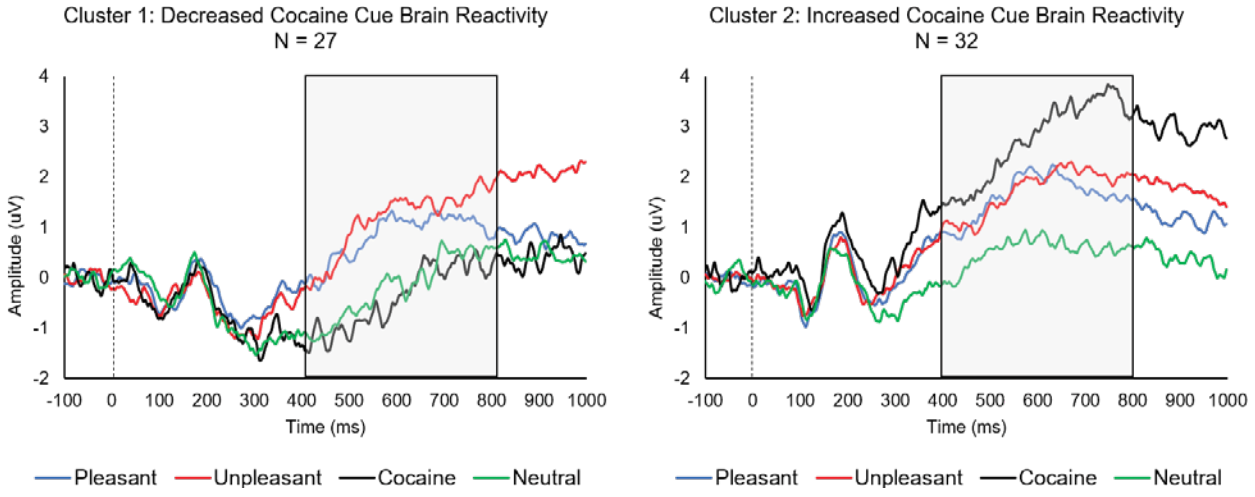


Figure 2. The late positive potential component in a sample of (n = 59) adults with cocaine use disorder. Participants were grouped by cluster analysis of the late positive potential response to viewing emotional (pleasant and unpleasant), cocaine, and neutral images. While all participants have a cocaine use disorder, one group displayed a blunted response to cocaine imagines, while the other displayed an enhanced response to cocaine images that is even greater than other emotional images.

grants & awards

McGovern Medical School received funding from The University of Texas (UT) System STARs (Science and Technology Acquisition and Retention) funding to support faculty members and purchase state-of-the-art research equipment. NRC faculty member recipients include **Jung Hwan Kim, PhD**, associate professor of neurosurgery, **Sunil Krishnan, MD**, professor of neurosurgery, **Rodrigo F. Morales, PhD**, professor of neurology, **Long Jun Wu, PhD**, professor and Founding Director of the Institute of Molecular Medicine-Center for Neuroimmunology and Glial Biology, and **Xiaoqin Wu, PhD**, assistant professor of integrative biology and pharmacology..

The Trauma Research and Combat Casualty Collaborative (TRC4), an initiative of the UT System, funded traumatic injury research projects for several NRC faculty members. **Charles S. Cox, Jr., MD**, professor of pediatric surgery, received funding for a project aimed at unraveling how genes affect brain swelling after traumatic injury. **Pramod Dash, PhD**, professor and chair of neurobiology and anatomy, received support for a project aimed at understanding the impact of traumatic brain injuries in senior citizens and potential links to neurodegenerative disorders. **David E. Meyer, MD**, assistant professor of surgery, received funding for a project which aims to determine the most effective strategy for blood pressure management after spinal cord injuries.

Sushanth R. Aroor, MD, assistant professor of neurology, Deepa Dongarwar, Data Scientist, **Amanda Jagolino-Cole, MD**, associate professor of neurology, **Sunil A. Sheth, MD**, associate professor of neurology, along with Dileep R. Yavagal, MD (University of Miami Miller School of Medicine) and Kaiz S. Asif, MD (University of Illinois Chicago) received the 3rd Place Prize (of 44 submissions) in the American Heart Association/American Stroke Association Stroke Data Challenge. The data challenge links social determinants of health from Institute for Health Metrics and Evaluation to clinical outcomes from the Get With the Guidelines Stroke registry. The group was a finalist for a project on large vessel occlusion stroke in rural populations.

Michael Beierlein, PhD, associate professor of neurobiology and anatomy, was selected as the recipient of the 2024 John P. McGovern Award for Outstanding Teaching by students from the MD Anderson Cancer Center UTHealth Houston Graduate School of Biomedical Sciences. The award recognizes excellence in teaching based on several criteria: the knowledge of the subject, interest in and enthusiasm for teaching and understanding of students, responsiveness to student questions, encouragement of independent thinking, and accessibility to students.

Asia Bright, PhD, assistant professor of psychiatry and behavioral sciences and director of the Office of Professionalism, was named as the winner of the John P. and Kathrine G. McGovern Distinguished Faculty Award in Professionalism Education by McGovern Medical School at UTHealth Houston Office of Professionalism.

Ying Chen, MD, assistant professor of ophthalmology & visual science, received the 2023 Marvin Quickert Thesis Award from the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS). The project was titled, "Combined orbital adipose tissue and activated platelet rich plasma fibrin membrane promotes conjunctival regeneration."

Deniz Dishman, PhD, assistant professor in the Department of Research at the School of Nursing, received a grant from the American Association of Nurse Anesthesiology Foundation for her study, "Calculating objective measures of pain after stroke (COMPAS)." The project will utilize a new technology to measure pain objectivity, rather than using self-reported scales in stroke patients, who often have hindered speech following a stroke. Co-investigators include **Charles Green, PhD**, associate professor of pediatrics, and **Sean Savitz, MD**, the Frank M. Yatsu Chair in Neurology and director of the Institute for Stroke and Cerebrovascular Disease.

Erin Furr-Stimming, MD, professor of neurology, has received several honors and recognitions. The Texas Neurological Society honored her with the 2024 Lifetime Achievement Award, a peer-recognition award honoring members in the state for outstanding service to patients and their specialty. She also received the Huntington Study Group (HSG) Outstanding Investigator award, which recognizes an accomplished leader in Huntington's Disease (HD) research who is providing significant contributions toward understanding HD and developing applications that may lead to a breakthrough in biomedical, behavioral, or clinical HD research. In addition, Dr. Furr-Stimming received the American Academy of Neurology 2024 A.B. Baker Teacher Recognition Award recognizing her contributions to improving neurology now and in the future, as well as the Lamar High School 2024 Distinguished Alumni which honors those who attended Lamar High School and have accomplished much in their respected careers. Furthermore, she received the Houstonia Magazine Top Doctor 2023 award and the Texas Monthly Top Doctor of 2023.

Vijayasree V. Giridharan, PhD, MPharm, assistant professor of psychiatry and behavioral sciences, was awarded a three-year grant from the American Heart Association Transformational Project Award to study the long-term neurobehavioral effects of COVID-19 in older individuals, and identify effective solutions after recovering from the virus.

Bhavani R. Iyer, OD, associate professor of ophthalmology & visual science, received a grant from the Houston Delta Gamma Foundation, an award given to promote and encourage services to the visually impaired population of Houston.

Eunhee Kim, PhD, assistant professor of neurosurgery, received an R01 grant from the NIH/NINDS (National Institutes of Health/National Institute of Neurological Disorders and Stroke) to determine the role of endothelial-to-mesenchymal transition in mutant KRAS-induced brain arteriovenous malformations.

David A. Lee, MD, MBA, clinical professor of ophthalmology & visual science, received the American Academy of Ophthalmology's Life Achievement Honor Award, symbolizing his longstanding commitment to advancing the profession and positively impacting patients' eye health.

Rodrigo F. Morales, PhD, professor of neurology, received three grants from the United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS). (1) The project, "Estimation of infectivity titers in environmental samples exposed to CWD (chronic wasting disease) prions," will evaluate the infectivity titers of relevant environmental samples previously identified to contain CWD prions using in vitro assays. (2) The project, "Identification and characterization of CWD contaminated meats," will measure the CWD prion infectivity titers in contaminated meats using in vitro and in vivo assays and

develop new screening techniques for these products. (3) The project, "Feral swine as spreaders of CWD prion," aims to identify the presence of prions in feces and intestinal tissues from wild hogs living in CWD endemic areas using prion replication assays.

In addition to these grants, Dr. Morales received Pilot Project Funds from the UTHealth Houston McGovern Medical School for a project titled, "Aβ seeding activity in eyes from Alzheimer's disease (AD) patients." This project will preliminarily analyze the seeding activity of disease-associated Aβ in the eyes of AD patients using in vitro and in vivo assays. He also received an Alzheimer's Association grant titled, "Cross-seeding between bacterial and mammalian amyloids." This study will explore whether specific bacterial components (bacterial amyloids) accelerate AD/Parkinson's disease phenotypes by "cross-seeding" the misfolding of Aβ, tau, or α-synuclein.

Mya C. Schiess, MD, professor of neurology and director of Movement Disorders & Neurodegenerative Diseases, received the 2023 President's Scholar Award for Excellence in Clinical Service, a top honor from UTHealth Houston President Giuseppe N. Colasurdo, MD, Alkek-Williams Distinguished Chair.

Andrey Tsvetkov, PhD, associate professor of neurology, along with Sung Yun Jung, PhD, (Baylor College of Medicine) received grant funding from the National Institutes of Health (NIH) National Institute on Aging (NIA) for a project titled, "Contribution of HUWE1 to sex differences in aging and Alzheimer's disease."

PI **Consuelo Walss-Bass, PhD**, professor of psychiatry and behavioral sciences, along with Co-PIs **Joy Schmitz, PhD**, professor of psychiatry and behavioral sciences, and Preethi Gunaratne, PhD (University of Houston), received a grant from Wellcome Leap for a project titled, "Identifying miRNA signatures of opioid misuse risk in trauma patients." The project will identify a miRNA signature associated with risk for opioid misuse in patients following exposure to opiate medication after trauma surgery. Success of this project will provide the go signal for a subsequent implementation study to optimize the use of this screening tool for identification of patients at risk for opioid misuse, and its potential to inform targeted interventions to prevent opioid misuse and opioid use disorder after traumatic injury.

Jiajie Zhang, PhD, dean of McWilliams School of Biomedical Informatics, and Leslie Beckman, director of the Office of Postdoctoral Affairs, received the UTHealth Houston President's Award for Leadership at the 2023 STAR Awards banquet. This award recognizes exceptional leaders in three categories: classified staff, management/administrative professional, and faculty.

Graduate & Medical Students, Postdoctoral Fellows & Residents

The Dee S. and Patricia Osborne Endowed Scholarship in the Neurosciences was awarded at the 29th Annual Neuroscience Poster Session to Heather Tsong (1st Place; lab of **Andrea Stavoe, PhD**, assistant professor of neurobiology and anatomy), Stephen Farmer (2nd Place; lab of **Sheng Zhang, PhD**, associate professor at the IMM-Center for Metabolic and Degenerative Diseases), and Pavula Bender (3rd Place; lab of **Vasanthi Jayaraman, PhD**, professor of biochemistry and molecular biology). All students are part of The University of Texas MD Anderson Cancer Center UTHealth Houston Graduate School of Biomedical Sciences.

Suelyn Koerich, PhD, a postdoctoral fellow in the lab of **Claudio Soto, PhD**, professor of neurology, received third place prize at the 29th Annual Neuroscience Poster Session. The poster was titled, "Plasma exchange reduces Aβ plasma levels and amyloid plaques in the brain of Alzheimer's disease transgenic mice."

UTHealthLeads, a one-year student fellowship program to develop future leaders in health care, awarded several students of NRC faculty members. Stephen Farmer, a PhD student in the lab of **Sheng Zhang, PhD**, is studying neurodegenerative diseases using fruit flies and molecular modeling. Heather Tsong, a PhD student under **Andrea Stavoe, PhD**, is currently working to understand mechanisms of neuronal health during aging and disease.

Andrea Boscutti, MD, postdoctoral research fellow in the Department of Psychiatry and Behavioral Sciences working with **Jair C. Soares, MD, PhD**, and Keiko Kunitoki, MD, MPH, a first-year psychiatry research track resident, were recently awarded a Travel Fellowship Award from the Society of Biological Psychiatry (SOBP). This award recognizes excellence in scholarly activity and allows for the opportunity to attend the annual meeting and participate in special programming.

Thiago Macedo e Cordeiro, MD, a postdoctoral fellow working with **Erin Furr-Stimming, MD**, and **Antonio Teixeira, MD, PhD**, professor of psychiatry and behavioral sciences, recently received a grant from the Human Biology Project of the Huntington's Disease Society of America to study the use of transcranial direct current stimulation (tDCS) to potentially alleviate symptoms of HD.

Jared Lim, a medical student in the lab of **David A. Lee, MD, MBA,** received an award from the Dean's Office for the 2024 MS-1 Summer Research Program, allowing him to perform research and gain valuable training between the first and second year of medical school.

Shafeeque C. Mohammed Ali, PhD, a postdoctoral fellow in the Department of Neurosurgery, received the Travel Award from the Postdoctoral Association in collaboration with the UTHealth Houston Office of Postdoctoral Affairs.

Antonio Pagán, PhD, a postdoctoral fellow working with **Katherine A. Loveland, PhD**, director of the UTHealth Houston C.L.A.S.S. (Changing Lives through Autism Spectrum Services) Clinic, recently received three awards, a Local Impact Grant from Autism Speaks, the UTHealth Houston TL1 Postdoctoral Research Fellowship, and the UTHealth Houston Career Development and Research Excellence (CaDRE) Program in Psychiatry Training grant, to develop and pilot test a military-culture adapted Launching! group program for military and veteran families and military-dependent young adults with autism spectrum disorder (ASD) transitioning to adulthood and their parents.

Dr. Pagán also received two awards, an Autism Speaks Postdoctoral Research Fellowship and a UTHealth Houston Seed Grant, to develop and evaluate the feasibility, acceptability, and satisfaction of the culturally adapted and translated Launching! group program for bilingual, Latino young adults with ASD transitioning to adulthood, and also the !Iniciando! la adultez group program for their Spanish-speaking parents.

Emma Stenz, MD, a recent graduate of McGovern Medical School, was the recipient of the Department of Neurobiology and Anatomy Outstanding Student in Neuroscience Award. She will do her residency in ophthalmology at the University of Washington.

Brain Night for Kids

at The Health Museum

March 14, 2024

Over 450 children and their parents attended Brain Night for Kids. Guests participated in a variety of demonstrations at 18 different stations managed by volunteers from the UTHealth Houston departments of Biochemistry & Molecular Biology, Neurobiology & Anatomy, Pediatrics, Psychiatry & Behavioral Sciences, the Children's Learning Institute, and students from McGovern Medical School.

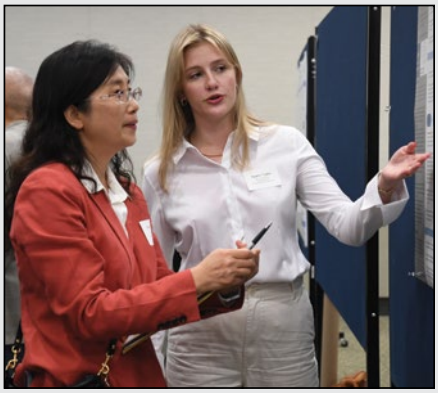
29th Annual Neuroscience Poster Session

Saturday, December 2, 2023
UTHealth Cooley University Life Center

The NRC hosted the 29th Annual Neuroscience Poster Session on Saturday December 2, 2023. Faculty, residents, postdoctoral fellows, graduate and medical students, as well as undergraduate students, from three Texas Medical Center institutions gathered to present and discuss their neuroscience research. The large group included the Departments of BioSciences, Psychological Sciences, and Electrical and Computer Engineering at Rice University, the Department of Neuroscience at Baylor College of Medicine, and the UTHealth Houston Neuroscience Research Center. Seventy-four research posters were presented to faculty judges from each institution and prizes were awarded for the best poster presentations in each category. Congratulations to all of the winners from the 29th Annual Neuroscience Poster Session!

Undergraduate, graduate, and medical students, as well as postdoctoral fellows and research scientists, presented their recent findings at the Poster Session.

Faculty judges from Baylor College of Medicine, Rice University, and UTHealth Houston.



WINNERS

(Left to Right): Aila Teimouri (GS; Rice ECE), Suelyn Koerich, PhD (PD; UTHealth NRC), Sanjana Murali (GS; BCM), Paula Bender (GS; UTHealth NRC), Michael Williamson, PhD (PD; BCM), Takese McKenzie (GS; UTHealth NRC), Heather Tsong (GS; UTHealth NRC), Kevin Jiang (GS; BCM), Victoria Albanese (UG; Rice BioSci), Gabriel Escobedo, Jr. (GS; BCM), Madelyn Castro (GS; Rice Psych), Stephen Farmer (GS; UTHealth NRC), Yan Yu, PhD (PD; BCM), Mikhail Monakhov, PhD (PD; BCM), Peyshyuan Chin (GS; BCM).

GS: Graduate Student; PD: Postdoctoral Fellow; Rice ECE: Rice University Department of Electrical and Computer Engineering; UTHealth NRC: UTHealth Houston Neuroscience Research Center; BCM: Baylor College of Medicine Department of Neuroscience; Rice BioSci: Rice University Department of BioSciences; Rice Psych: Rice University Department of Psychological Sciences

Continued From Page 5; Webber

fluctuations in neuronal firing with millisecond precision and has excellent temporal precision for measuring neurocognitive processes. EEG directly measures the electrical activity of the brain, whereas TMS directly alters the electrical activity of the brain. Assessing the effects of TMS on EEG measures might provide more sensitive and proximal measures of CUD, yet no studies have compared self-report and EEG measures in terms of TMS effects in those with CUD.

Our work has focused on identifying EEG measures of reward functioning deficits that would be good candidates for biomarkers of TMS effects in those with a CUD. One candidate is the EEG component named the "reward positivity." The reward positivity occurs over the frontal central electrodes when a participant wins money (**Fig. 1**), usually in a guessing or gambling-type computer task. It is thought to represent overall reward functioning, or the ability to properly process rewards and losses. The brain source of the reward positivity is estimated to come from the anterior cingulate cortex, a direct target of the dopamine reward system. Prior work has indicated that the reward positivity is altered in those with substance use disorders, indicating lower reward functioning compared to healthy controls. The reward positivity amplitude might serve as a good indicator of TMS-related effects on prefrontal brain activity to receiving non-drug rewards (e.g., money).

Another component that could serve as a biomarker of TMS effects is the "late positive potential." This component occurs in response to motivationally salient stimuli, regardless of valence (such as pleasant and unpleasant emotional images). Our work has shown that the late positive potential (LPP) to drug cues is increased in those with a substance use disorder compared to those without a substance use disorder, with a large effect size (Webber et al., *Neurosci. Biobehav. Rev.* 141:104835, 2022). Our work has also demonstrated individual differences in this response, which could be useful in individualizing TMS treatments for CUD (Webber et al., *Exp. Clin. Psychopharmacol.* 30:514, 2022). In **Figure 2**, one group of participants with CUD displays an increased LPP response to viewing cocaine images compared to other types of emotional images. The other group displays a blunted response to cocaine images. Future work might be able to use baseline LPP amplitudes as a guide for determining what type of stimulation or location for stimulation is needed for that particular patient.

The National Institute on Drug Abuse recently funded our work through a five-year K01 award. This project will assess the acute effects of TMS to the dorsomedial prefrontal cortex, dorsolateral prefrontal cortex, and sham (fake TMS) on EEG measures of reward sensitivity and motivated attention to cocaine cues. Participants with a CUD will complete questionnaires, behavioral tasks, and an EEG before and after receiving three iTBS sessions within one hour. Participants will repeat these study tasks on three separate days, receiving iTBS to a different location each day. These findings will aid in clarifying the best location and stimulation pattern for treating CUD, as well as identifying the optimal EEG biomarker of change to be used in future clinical trials. Ultimately, we hope these results will facilitate the development of brain stimulation therapies for cocaine and other treatment-resistant substance use disorders.

About the Author

Heather E. Webber, PhD *is an assistant professor and cognitive neuroscientist at the Center for Neurobehavioral Research on Addiction at McGovern Medical School at UTHealth Houston. Dr. Webber's research focuses on neurophysiological markers of reward and emotional functioning and how they relate to addiction. The long-term goal of Dr. Webber's work is to leverage these neurophysiological measures to develop brain stimulation therapies and to aid in the individualization of treatment for substance use disorders.*

UTHealth Houston NRC Executive Committee

Ewing-Cobbs

The NRC would like to extend our deepest gratitude and best wishes to UTHealth Houston NRC Executive Committee Member, **Linda Ewing-Cobbs, PhD**, as she rolls off the Executive Committee. Dr. Ewing-Cobbs is a professor of pediatrics and the Harriet and Joe Foster Chair in Cognitive Neuroscience, as well as a Neuropsychologist at the Duncan Children's Neurodevelopmental Clinic. She has served on this committee since 2007, providing invaluable guidance over the past 17 years.

DeMaster

We would also like to welcome **Dana M. DeMaster, PhD** of the Children's Learning Institute to the Executive Committee. Dr. DeMaster is an assistant professor of pediatrics. Her research program examines developmental improvements in learning and memory in both infant and child populations. For several years, she has been an avid contributor to the NRC, publishing in our Newsletter and volunteering at Brain Night for Kids, as well as having plans to participate in our 2025 Public Forum. We are thrilled to have her participation in this leadership role.

news & information

The Children's Learning Institute at UTHealth Houston established its Texas School Ready-Registered Apprenticeship Program (TSR-RAP), a program which supports career advancement and pathway opportunities for early childhood education professionals in Texas.

Jose Arriola Vigo, MD, MPH, assistant professor of psychiatry and behavioral sciences, was recently elected to be a Fellow of the American Psychiatric Association (APA). This fellowship is awarded to outstanding psychiatrists with a large breadth within the field who have made significant contributions in at least five of the following areas: administration, teaching, scientific and scholarly publications, volunteering in mental health and medical activities of social significance, and community involvement.

Elaheh Ashtari, PsyD, associate professor of psychiatry and behavioral sciences and director of psychology services at UTHealth Houston Behavioral Sciences Campus, shared her experience as a leader at the Women in Leadership Seminar.

Carmen Dessauer, PhD, professor, chair, and John P. and Kathrine G. McGovern Distinguished Chair in the Department of Integrative Biology and Pharmacology, was recently featured in the Women Faculty Forum, a professional and networking forum at the McGovern Medical School. In May, Dr. Dessauer was highlighted as a leader in medicine, research, and education.

David A. Lee, MD, MBA, clinical professor of ophthalmology & visual science, served as author and committee member for the 2023-24 development and revision process for the Basic and Clinical Science Course, Section 1, Update on General Medicine book. This book is part of the comprehensive curriculum for residents in the field of ophthalmology and an invaluable education resource.

The first UTHealth Houston Brain Collection Research Symposium was held by **Thomas Meyer, PhD**, and **Consuelo Walss-Bass, PhD**, co-directors of the UTHealth Houston Brain Collection Program in May. The symposium highlighted novel studies in postmortem brain research, which included multiomic approaches and understanding the brain-behavior interplay.

Elda Ramirez, PhD, the Dorothy T. Nicholson Distinguished Professor in the Department of Graduate Studies at Cizik School of Nursing, has recently been appointed associate dean of strategic initiatives and community engagement at the School of Nursing.

Jair C. Soares, MD, PhD, founding dean of UTHealth Houston School of Behavioral Health Sciences, has appointed associate deans for this new School. **Scott D. Lane, PhD**, associate dean of academic and student affairs, will oversee academic program development, faculty and student management, policy administration, and strategic planning to enhance the overall functioning and success of the School. **Jeff R. Temple, PhD**, associate dean of clinical research, will oversee leadership in clinical research development, infrastructure establishment, faculty and student engagement, training programs, and mentorship within the School. **Lokesh Shahani, MD, PhD, MPH**, associate dean of clinical integration, will facilitate clinical integration, building partnerships, improving patient care quality, and expanding training opportunities within the School. Mary Lopez, MBA, acting associate dean of management, will oversee the comprehensive management of financial, operational, human resources, compliance, procurement, and strategic aspects within the School.

Sylvia Villareal, MEd, MPH, adjunct faculty, and **Anson Koshy, MD**, artist-in-residence and adjunct associate professor, both from the Center for Humanities and Ethics, published their first children's book, "Arun on the Run." The book is about a first-grade student who is exhibiting signs of attention-deficit/hyperactivity disorder (ADHD). His teacher is able to guide him and his parents, helping them find strategies to help calm his body and brain, and also introduce the family to physicians and other resources.

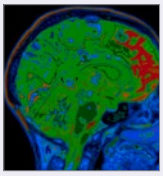
Jason Yu, PhD, assistant professor of psychiatry and behavioral sciences, led a the UTHealth Houston Well Connected podcast in February. Dr. Yu shared insight on the importance of mental health coaching in an episode titled, "How it Works, Benefits and More."

Jiajie Zhang, PhD, dean of McWilliams School of Biomedical Informatics, was named a 2023 Fellow of the American Association for the Advancement of Science (AAAS), for his "distinguished contributions to, and advocacy of, the field of biomedical informatics through outstanding research, as well as leadership and service across related research, higher education, and professional organization communities."

A record-breaking number of attendees logged in to the McWilliams School of Biomedical Informatics virtual workshop on AI in biomedicine and health care. The event was chaired by **Jiajie Zhang, PhD**. The workshop featured large language model applications, learning health systems, imaging applications, genetics, and clinical trials. It is available to be viewed at https://med.uth.edu/researchaffairs/collaborative-workshops

Upcoming Events

Neurobiology of Disease Course



Fall 2024

"Artificial Intelligence and the Brain"

Tuesdays at Noon; 1 credit hour

Open to Graduate Students, Medical Students, and Postdoctoral Fellows

Course Director: Amy Franklin, PhD
Associate Professor and Associate Dean for Student, Faculty, and Community Affairs, McWilliams School of Biomedical Informatics

Distinguished Lecture in the Neurosciences Series

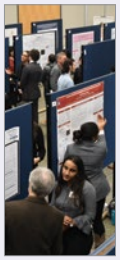
October 22, 2024 at Noon

McGovern Medical School; MSB 3.001

Grégoire Courtine, PhD
Professor
École Polytechnique Fédérale de Lausanne, Switzerland

30th Annual Neuroscience Poster Session

Saturday, December 7, 2024 at 10:30am



UTHealth Cooley University Life Center

Open to Undergraduate, Graduate and Medical Students, Postdoctoral Fellows, Residents, Faculty

UTHealth Houston, Baylor College of Medicine, Rice University

Please visit our website for more information

We welcome notices of your neuroscience seminars, grand rounds, research colloquia, and conferences (sponsored by UTHealth Houston, the Texas Medical Center, and area institutions) for our calendar (https://www.uth.edu/neuroscience-research-center/neurofax-calendar). Please send the event name, contact details, date, time and place to **UTHealth.NRC@uth.tmc.edu**

UTHealth Houston
Neuroscience Research Center

6431 Fannin St., MSB 7.046
Houston, TX 77030

NONPROFIT ORG.
U. S. POSTAGE
PAID
HOUSTON, TX
PERMIT NO. 209

ADDRESS SERVICE REQUESTED

Keep in Touch!

Website: https://www.uth.edu/neuroscience-research-center/

"Like" UTHealth Neuroscience Research Center at www.facebook.com/UTHealthNRC

@UTHealthNRC; www.Twitter.com/UTHealthNRC

Questions? Comments?

Contact us at 713-500-5538
or E-mail: UTHealth.NRC@uth.tmc.edu

This Newsletter is distributed by mail to individuals and groups engaged in neuroscience research within the TMC and worldwide and features research, neuroscience accomplishments and outreach efforts performed at UTHealth. Past issues are available on the NRC website.

If you prefer to receive a digital copy through email, please contact UTHealth.NRC@uth.tmc.edu with your information.

The Neuroscience Research Center Newsletter
Editor: Anne Hart, PhD
Design: Chad Inmon, ImageSet