THE LOUISVILLE CHAPTER

SOCIETY for NEUROSCIENCE

34th Annual Neuroscience Day

Friday, March 27, 2026

Neural Networks in Action:

Mechanisms, modulation and medicine

Presenting Guest Speaker

Warren Grill, PhD
Professor of Bioengineering,
Duke University

Program of Events

09:00 – 09:45 COFFEE AND POSTER SETUP

09:45 – 10:00 WELCOME AND INTRODUCTION

10:00 – 10:35 DATA DASH • preview of 8 selected posters: 3 slides, 3 minutes

Myelotomy Preserves Long-Distance Propriospinal Signaling: Kinematic Evidence from Bipedal vs. Quadrupedal Stepping in Porcine SCI (poster #1)
David Abel • UofL, Department of Neurological Surgery

The effects of Wnt/β-catenin upregulation on regeneration and recovery post-spinal cord injury (SCI) (poster #21)
Sonia Ali • Western Kentucky University, Department of Biological Sciences,

Impaired intraspinal hemodynamics and neurovascular unit in the chronically injured spinal cord (poster #43)
Dr Preeja Chandran • UofL, Department of Neurological Surgery

Preoperative Sleep Medication Use is Associated with Adverse Outcomes Following Lumbar Spine Surgery (poster #44)
Dr. Nick Dietz • UofL, Department of Neurological Surgery

Can Exercise Improve Learning, Memory and Motor Function Following Developmental Exposure to Benzo[a]pyrene?
Christina Gogzheyan • Northern Kentucky University, Biological Sciences (*poster #6)*

Role of the integrated stress response kinase HRI/EIF2AK1 in EAE model of Multiple Sclerosis (poster #28)
Divya Mohan • UofL, Department of Neurological Surgery

Aducanumab treatment drives APOE4 specific increases in glial reactivity (poster # 33)
Akhil Pallerla • University of Kentucky, Department of Physiology

Edge AI Based Gait Phase Detection for Closed-Loop Neuromodulation in SCI Mice (poster #50)
Dr Ahnsei Shon • UofL, Department of Neurological Surgery, KSCIRC

10:40 – 11:10 LOCAL SPOTLIGHT I

From Stars to Synapses: Parallels in Cosmic and Neural Discovery—from the Cosmic Microwave Background to Listening for Basal Ganglia Signals

Adolfo Ramirez-Zamora, MD • Professor, University of Louisville, Department of Neurology, UofL Health

11:15 – 12:15 PLENARY LECTURE I

Spaghetti or Meatballs? Ontogenetic Deconstruction of Deep Brain Stimulation

Warren Grill PhD • James B Duke Distinguished Professor of Biomedical Engineering, Duke University, Durham,

12:15 – 2:15 LUNCH AND POSTER SESSION • poster judging starts 12:45

2:15 – 2:45 LOCAL SPOTLIGHT II

Visualizing injury evolution in 4D for better neuroprotection after spinal cord injury

Zin Khaing, PhD • Associate Professor, University of Louisville, , KSCIRC, Department of Anatomical Sciences and Neurobiology

2:50 – 3:20 LOCAL SPOTLIGHT III

Cancer Immunotherapy Resistance: Translating Biological Insights into Improved Clinical Outcomes

Kavitha Yaddanapudi, PhD • Professor, University of Louisville, Brown Cancer Center, Department of Surgery

3:25 – 3:45 COFFEE BREAK

3:45 BUSINESS MEETING, BOARD ELECTION AND AWARDS

Learn more about the Louisville Chapter of the Society for Neuroscience at: www.sfnlouisville.org • Questions, email us: SFNChap@louisville.edu

About The Speaker

Dr. Warren M. Grill is a prominent neuroscientist specializing in neural engineering and neuromodulation . He is a James B. Duke Distinguished Professor of Biomedical Engineering at Duke University. He received the B.S. in biomedical engineering in 1989 from Boston University and the Ph.D. in biomedical engineering in 1995 from Case Western Reserve University.

Professor Grill teaches courses on circuits and instrumentation, bioelectricity, and the fundamentals and applications of electrical stimulation. He received the Capers & Marion McDonald Award for Excellence in Teaching and Research at Duke University on 2008 and again in 2018, in 2013 was awarded Outstanding Postdoc Mentor at Duke University, and in 2014 received the Duke University Scholar/Teacher of the Year Award.

His research interests are in neural engineering and neuromodulation and include design and testing of electrodes and stimulation techniques, the electrical properties of tissues and cells, and computational neuroscience with applications to restoration of bladder function, treatment of movement disorders with deep brain stimulation, electrical stimulation for treatment of pain, and vagus nerve stimulation for regulation of organ function. Dr Grills extensive body of work includes over 280 journal articles and he has been awarded 83 US patents.

Dr. Grill cofounded NDI Pelvic Health which developed a novel approach to treat overactive bladder and was acquired by Medtronic. He is Co-Founder, Director, and Chief Scientific Officer of NDI Medical, a medical device incubator, and serves as Chief Scientific Advisor at SPR Therapeutics, developer of a novel PNS treatment demonstrating sustained relief of chronic pain, as well as on the Scientific Advisory Boards of Boomerang Medical and Cala Health.

Dr. Grill serves as a Consultant to the Neurological Devices Panel of the FDA Medical Devices Advisory Committee, is Editor in Chief of the Journal of Neural Engineering, and is on the editorial boards of Brain Stimulation, Current Opinion in Biomedical Engineering, and Neuromodulation.

He was elected as Fellow of the American Institute of Medical and Biological Engineering in 2007, Fellow of the Biomedical Engineering Society in 2011, Fellow of the International Academy of Medical and Biological Engineering in 2022, and Fellow of the National Academy of Inventors in 2023.

Dr. Grill has been recognized with several prestigious awards. He was awarded a Javits Neuroscience Investigator Award by NIH-NINDS in 2015, his team was a Phase 1 winner of the NIH SPARC Neuromod Prize in 2022, and he was the inaugural winner of the inaugural NANS Clinical and Basic Science/Engineering Innovator Award in 2023.

THE LOUISVILLE CHAPTER

SOCIETY for NEUROSCIENCE

34th Annual Neuroscience Day

Friday, March 27, 2026

Neural Networks in Action: Mechanisms, modulation and medicine

Louisville Chapter, SfN Program Committee

Dr. Nelleke van Wouwe • President
Dr. Sujata Saraswat • Secretary/VP
Rofyontsa Shanti • Outreach Liaison
Dr. Joseph Neimat • Past President
Dr. Brian Williams • Treasurer
Nicole Aguirre • Outreach Liaison

Board Members Drs McCall, Ostrov, Samuelsen and Annike White

Special Thanks

Lesley Roberson

All Poster Judges

University of Louisville Participating Departments

Anatomical Sciences and Neurobiology
Arts and Sciences
Bioengineering
Law School
Microbiology & Immunology
Neurological Surgery
Neurology
Ophthalmology & Visual Sciences
Pediatrics
Pharmacology & Toxicology
Physiology
Psychiatry
Public health
Surgery

Participating Institutions

UNIVERSITY OF LOUISVILLE

NKU NORTHERN KENTUCKY UNIVERSITY

WKU

BELLARMINE UNIVERSITY

Cincinnati Children's

EKU

OHIO STATE

Learn more about the Louisville Chapter of the Society for Neuroscience at: www.sfnlouisville.org • Questions, email us: SFNChap@louisville.edu

THE LOUISVILLE CHAPTER

SOCIETY for NEUROSCIENCE

34th Annual Neuroscience Day

Friday, March 27, 2026

Neural Networks in Action:
Mechanisms, modulation and medicine

SfN SOCIETY for NEUROSCIENCE
Louisville Chapter

Support Provided by

KENTUCKY SPINAL CORD INJURY RESEARCH CENTER

UL Health | Brain & Spine Institute

NEURELIS®

University of Louisville
Anatomical Sciences and Neurobiology

Baxter

enovis™

Codman SPECIALTY SURGICAL | INTEGRA

ceribell®
Clarity When It's Critical

Boston Scientific
Advancing science for life™

RAPIDAI

stryker

DePuy Synthes

tobii dynavox

LifeNet Health®

GammaTile®

ZIMMER BIOMET
Your progress. Our promise.®

Pfizer

Learn more about the Louisville Chapter of the Society for Neuroscience at: www.sfnlouisville.org • Questions, email us: SFNChap@louisville.edu

THE LOUISVILLE CHAPTER
SOCIETY for NEUROSCIENCE
34th Annual Neuroscience Day
Friday, March 27, 2026

Abstracts

UNDERGRADUATE STUDENTS

ABSTRACT # 1

Myelotomy Preserves Long-Distance Propriospinal Signaling: Kinematic Evidence from Bipedal vs. Quadrupedal Stepping in Porcine SCI

Abel DR[1], Nibbe C[1], Miles D[1], Davidson S[1], Howland DR[12], Boakye M[1]

[1] Department of Neurological Surgery, UofL
[2] Robley Rex VA Medical Center

Introduction: Thoracic SCI severs long propriospinal (LPS) tracts required for inter-girdle coordination. We hypothesized that surgical myelotomy (evacuating intramedullary hemorrhagic necrosis) reduces glial scarring, preserving the substrate for quadrupedal coupling. We evaluated this by comparing kinematic efficiency of Bipedal vs. Quadrupedal stepping. Methods: Yucatan minipigs received T9-T11 contusions. In the full cohort (N=26), subjects were stratified into Myelotomy and Control groups across varied severities (700–4500 kdynes). Recovery was assessed via the Porcine Thoracic Injury Behavior Scale (PTIBS) and bladder voiding efficiency (BVE). To control for mechanical variance, a subgroup analysis isolated subjects meeting a "Moderate Contusion" threshold (1700–2300 kdynes; n=7). At 12 weeks, kinematics were recorded at 2.0 km/h. Results: In the heterogeneous cohort (N=26), varying severities masked treatment effects, yielding no significant difference in PTIBS (p>0.05). However, in the biomechanically matched subgroup (n=7), Myelotomy animals achieved significantly superior locomotor recovery (PTIBS: 7.30+/-0.50 vs. 4.50+/-0.58; p=0.0004, d=5.09) and improved autonomic recovery (BVE: 40.5% vs. 13.2%). Kinematically, the Myelotomy group successfully utilized forelimb engagement to stabilize hindlimb gait (100% quadrupedal task completion), whereas 50% of Controls exhibited "failure to step," suggesting an inability to functionally coordinate cervical and lumbar Central Pattern Generators (CPGs). Without LPS integrity, Control global coordination remained degraded, with Girdle Matching Ratios shifting from 1.09 to 2.54 (d=4.11). Conclusion: Isolating a strictly controlled biomechanical subgroup reveals Myelotomy provides significant improvements in functional recovery. The Myelotomy group's ability to utilize forelimb cues to enhance hindlimb kinematics generates the hypothesis that the intervention preserves LPS signaling. This sparing may protect the reticulospinal tract, which projects to cervical and lumbosacral interneurons and is highly plastic post-SCI.

ABSTRACT # 2

Chemogenetic inhibition of mPFC-BLA pathway does not alter risky choice

Adhikari S[12], Gastright CJ[1], Dowd MT[1], Forbes Blanco EV[2], Neeley JC[3], Rey Caldera A[1], Matone AC[1], Osborn E[1], Allgire EN[1], Yates JR[1]

[1] Department of Psychological Science, Northern Kentucky University
[2] Department of Chemistry and Biochemistry, Northern Kentucky University
[3] Department of Biological Sciences, Northern Kentucky University

Maladaptive risky choice is a defining feature of several psychiatric conditions such as gambling disorder and substance use disorders. The purpose of the present experiment was to determine if chemogenetic inhibition of the pathway between the medial prefrontal cortex (mPFC) and the basolateral nucleus of the amygdala (BLA) alters risky choice as assessed with an equivalent expected value (EEV) task. Sprague Dawley rats (n = 26 each sex) received bilateral injections of either hM4Di (human clone of the inhibitory muscarinic receptor) or mCherry (control) into mPFC or BLA. A retrograde virus was injected into the brain region that did not receive hM4Di/mCherry. After recovery, rats were trained in the EEV task in which they made choices between two food alternatives. The following probability/reinforcer magnitude combinations were used: 1.0/4 pellets vs. 0.8/5 pellets (EVs of 4), 0.67/3 pellets vs. 0.33/6 pellets (EVs of 2), 0.5/2 pellets vs. 0.1429/7 pellets (EVs of 1), and 0.2/1 pellet vs. 0.025/8 pellets (EVs of 0.2). The first 10 sessions of the EEV task consisted of forced-choice trials only, in which one lever was active during any trial. After the first 10 sessions, sessions consisted of free-choice trials only, in which both levers were made available. Both forced-choice and free-choice sessions lasted for 80 trials or 90 minutes, whichever occurred first. Once rats achieved stable responses, they received injections of deschloroclozapine (DCZ) (1 and 3 µg/kg; i.p.). A linear mixed effects (LME) model revealed a significant 3-way interaction between brain region, viral vector, and DCZ dose, $F(2, 449.42) = 3.95$, $p = .02$. A separate LME analysis for the mPFC revealed no main effects or a significant interaction, all F's ≤ 1.42, all p's ≥ .245. When injected into the BLA, there was a trend toward a significant interaction between viral vector and DCZ dose only, $F(2, 266.13) = 3.01$, $p = .051$. However, alterations in preference for the large, risky alternative were minimal following injection of DCZ in rats injected with the hM4Di viral vector (proportion of 0.47 following vehicle treatment vs. 0.42 following 3 µg DCZ). Chemogenetic inhibition of the mPFC-BLA pathway does not significantly alter risky choice as assessed with the EEV task. These results indicate that different neural circuits mediate decisions made between two alternatives that have equivalent outcomes.

ABSTRACT # 3

Kinematic strategies for obstacle negotiation following incomplete spinal cord injury in Minipigs

Boczek MS[12]*, Ahmed ZF[12]*, Ramey M[1], Mohamed-Hassan YE[12], Alrefai R[12], O'Steen WA[1], Konan ML[123], Howland DR[123]

[1]Kentucky Spinal Cord Injury Research Center
[2] Department of Neurological Surgery, UofL
[3] Department of Anatomical Sciences and Neurobiology, UofL
*Contributed Equally

Humans and animal models such as the Yucatan Minipig (YMP) can regain simple walking functions post spinal cord injury (SCI). However, recovery of adaptive gait features proves difficult and requires greater descending input from supraspinal systems. This study used low thoracic hemisection (Hx) to produce SCI the YMP. Subsequent recovery of the YMP was evaluated by monitoring level surface walking and negotiation of a 15cm high obstacle. Comparison of these two tasks provides insight into the ability of the YMP to recover adaptive gait features.\nKinematic data was collected on 5 intact, female YMPs. All were conditioned to traverse a level surface runway with and without a 15 cm obstacle at the midpoint. Hindlimb (HL) movements were tracked with 11 reflective markers. Task performance was captured using a Vicon Nexus system. Three of the YMPs received T9 lateral Hxs. Gait recovery was evaluated post-Hx at 4- and 8-weeks (w), using the same tasks. Procedures were approved by The University Committee for Animal Welfare (UCAW).\nIntact YMPs effectively clear the obstacle 100% of the time by increasing HL flexion during gait swing phase. In addition, they showed no dominant leading HL preference. Obstacle clearance is disrupted post Hx, after 4w only 56% of attempts clear the obstacle. Of the attempts in which the HL hits the obstacle, 73% resulted in a spinally-mediated, stumble correction response and 27% showed a passive (dragged) limb. After 8w, successful clearances had not improved, however a correlation between lead limb and effective clearance was observed. At both 4 and 8w 100% of ipsilesional HL leads resulted in failure to cross while ~/= 100% of contralesional leads resulted in complete clearance.\nTracking the 5th MT marker and angular kinematics revealed increased swing height and flexion of individual joints in the step pre and post obstacle negotiation in comparison to pre-Hx and post-Hx basic walking. Although swing time was not significantly altered, approach speed, cadence, and step length decreased in trials led by the ipsilesional HL. These results show that despite significant recovery post-Hx, adaptive limb features show permanent deficits that are dependent upon contributions of descending neural pathways. Thus, the YMP is a good preclinical model for testing gait features important for community ambulation in humans and potential therapies to improve function.\nFunding: CH Neilsen Found, RF Hammond Endow, KSCIRTF, and CMRU-KSCIRC core.

ABSTRACT # 4

Development of a Specialist Database for Applying Quantitative Analytical Tools to Selective Dorsal Rhizotomy in Cerebral Palsy

Fogle S[1], Khanjar T[2], Harris A[2], Amer A[3], Sokhadze T[14], Mutchnick I[45]

[1] Department of Bioengineering, UofL
[2] University of Louisville School of Medicine
[3] Evokes, LLC
[4] Norton Neuroscience Institute, Norton Children's Hospital
[5] Department of Neurological Surgery, UofL

Selective dorsal rhizotomy (SDR) is a neurosurgical procedure used to reduce spasticity in children with cerebral palsy by selectively cutting lumbar and sacral spinal cord dorsal sensory rootlets that contribute to abnormal reflex activity. Although intraoperative neuromonitoring is commonly used to assist in identifying abnormal rootlet responses, the neurophysiological data generated during surgery are rarely captured in a standardized and analyzable format. As a result, rootlet-level interpretations are often qualitative, center-specific, and difficult to compare across cases. This limits reproducibility and validation of rootlet interrogation techniques. This project addresses that limitation by focusing on the data infrastructure design that supports reproducible, rootlet-level neurophysiological analysis in SDR. This retrospective study used deidentified data from Norton Childrenâ€™s Hospital collected by co-mentors of the study. The objective of the study is to create a database that would allow for quantitative analysis of the dataset using advanced AI and Machine Learning methods. Intraoperative neuromonitoring output files, neuromonitoring technician documentation sheets, and operative reports were consolidated into a structured rootlet-by-rootlet database. The database was developed through multiple iterations to capture electrical stimulation parameters, EMG response characteristics, topography of evoked motor responses waveforms, anatomical identifiers, and surgical decisions, i.e., to cut or spare a tested rootlet depending on EMG response, in a consistent format, thereby reducing documentation variability. Binary and categorical encodings were selected where appropriate to improve consistency across cases and enable future statistical analysis. To support prospective data collection and formalize communication between the operating room and research analysis, a complementary intraoperative documentation tool was developed to align with the surgical workflow and an automation program was developed to directly convert the documentation tool information to the surgical database structure. Together, these tools establish a quantitative research analysis foundation for validating neuromonitoring guided approaches to SDR and supporting future studies of rootlet-level behavior to be correlated with surgical outcomes.

THE LOUISVILLE CHAPTER
SOCIETY for NEUROSCIENCE
34th Annual Neuroscience Day
Friday, March 27, 2026

ABSTRACT # 5

Resurgence of Oral Cocaine Seeking in Rats

Forbes Blanco EV[1], Rey Caldera A[2], Dowd MT[2], Neeley JC[3], Adhikari S[23], Osborn E[2], Rogers L[2], Gastright CJ[2], Allgire EN[2],

[1] Department of Chemistry and Biochemistry, Northern Kentucky University
[2] Department of Psychological Science, Northern Kentucky University
[3] Department of Biological Sciences, Northern Kentucky University

Contingency management is a common treatment strategy for addiction in which alternative reinforcers are provided (e.g., food voucher) when individuals abstain from substance use. While effective, one issue is that substance use often returns when individuals no longer receive alternative reinforcement. Resurgence is analogous to the recurrence of substance use following cessation of contingency management. When animals no longer receive an alternative reinforcement (e.g., food pellet), reinstatement of a previously extinguished response occurs (e.g., responding on a manipulandum paired with drug reinforcement). The purpose of the present experiment was to determine if the pathway between the medial prefrontal cortex (mPFC) and the basolateral nucleus of the amygdala (BLA) mediates resurgence of cocaine seeking in rats. Understanding the neuromechanisms that control resurgence is important for designing treatments that can help prevent recurrence of substance use following the end of contingency management. Sprague Dawley rats (8 male, 6 female) received bilateral injections of either hM4Di (human clone of the inhibitory muscarinic receptor) or mCherry (control) into the mPFC. A retrograde virus was injected into the BLA. Rats were first trained to emit a nose poke response in one aperture to earn delivery of an oral cocaine solution (0.3 mg/ml in 0.05 ml of 0.1% saccharin). Eventually, responses no longer led to cocaine reinforcement. At this point, a lever was extended into the operant chamber. Responses on the lever led to delivery of a food pellet. Eventually, rats were given a resurgence test, in which operant responses never led to cocaine or food reinforcement. Following the first resurgence test, rats received additional sessions in which they could respond on the lever to earn food. Rats then received a second resurgence test. Before each resurgence test, rats received an intraperitoneal injection of dimethyl sulfoxide (DMSO; 1 ml/kg) or deschloroclozapine (DCZ) (3 µg/kg), with order counterbalanced across rats. A mixed factor ANOVA revealed a main effect of session only, $F(2, 20) = 3.90$, $p = .037$. Relative to baseline, rats injected with DMSO responded more on the "active" aperture. While we found some evidence for resurgence of oral cocaine seeking in rats, chemogenetic inhibition of the mPFC-BLA pathway did not alter such resurgence. Additional work is needed to determine the neuromechanisms underlying resurgence of drug seeking.

ABSTRACT # 6

Can Exercise Improve Learning, Memory and Motor Function Following Developmental Exposure to Benzo[a]pyrene?Benzo[a]pyrene Exposure

Gogzheyan C, Feltner M, Lillar S, Fox D, Easybuck T, Shakya A, Easton A and Curran CP

Department of Biological Sciences, Northern Kentucky University

Rationale: Benzo[a]pyrene (BaP) is a neurotoxic polycyclic aromatic hydrocarbon (PAH) that can be found in grilled foods, air pollution, car exhaust, and more. Children born to pregnant women with high exposure to PAHs had a higher risk of cognitive and behavioral deficits. Exercise is known to improve brain function, but little is known about how exercise during pregnancy and early life can affect the developing brain. In this study, we wanted to find out if exercise could protect against exposure to BaP and mitigate adverse effects on learning and memory and motor function. Methods: We compared Cyp1b1(-/-) knockout and Cyp1b1(+/+) wild type mice, because our previous studies showed the knockouts were more susceptible to developmental BaP exposure. Dams were exposed to 10mg/kg/day BaP or the corn oil vehicle from gestational day 10 until weaning at postnatal day 25 (P25). Offspring had access to running wheels 1hr/day from P30 to P60 when behavioral testing began. We used Novel Object Recognition and Morris Water Maze to test hippocampal-dependent learning and memory. Results: There was a significant gene x treatment interaction in the Novel Object Recognition test with BaP-exposed offspring spending less time observing the novel object in the test phase. Wildtype Cyp1b1(+/+) mice had the greatest impairments while BaP-exposed Cyp1b1(-/-) knockout mice performed similarly to corn oil control mice. In Morris water maze, there was a main effect of BaP exposure in the Acquisition phase. Offspring exercise improved performance on Day 2 of the Acquisition phase and on Days 2 and 4 of the Shift-reduced phase. Offspring exercise had significant benefits in the Rotarod test, but only for Cyp1b1(-/-) knockout mice. Together, these data suggest regular exercise can mitigate some, but not all of the adverse effects of early life BaP exposure.

ABSTRACT # 7

Microglia development following maternal helminth inoculation: role of neonatal infection in morphology

Hagan T, Williamson LL

Department of Biological Sciences, Northern Kentucky University

Rat dams inoculated with helminths, intestinal parasitic worms, reduced their pups' neuroinflammatory responses to E. coli infection. Maternal helminths combined with weanling helminths also attenuated cognitive deficits compared to rats without helminth exposure. In addition, pups born to dams treated with helminths also show some of the same effects at very early life stages, i.e. postnatal day 5 (P5), even though they do not have helminths (Williamson et al. 2016). The current study aims to characterize microglia morphology within developing pup brains in response to maternal helminth inoculation, E. coli infection at P4, or the combination of the two challenges. We examined microglia in the hippocampus at several timepoints in early development – P1, P4, P5, and P7. Brain tissue was sectioned at 20 um, mounted on slides, then stained to target the Iba1 protein. Then, microglia were counted and categorized by morphology. There is an effect of maternal helminth treatment on pup microglial development, but data on neonatal infection is ongoing.

ABSTRACT # 8

It's Not Just the Nicotine: A Systematic Review of Smoking and Vaping on Intracranial Aneurysm Formation and Rupture Physical Engagement

Hill NG[1], Gomes DC[12], Conklin DJ[23], Rahmani R[12]

[1] Department of Neurological Surgery, UofL
[2] Department of Pharmacology & Toxicology, UofL
[3] UofL Center for Cardiometabolic Science, UofL

Introduction: Intracranial aneurysm rupture results in significant morbidity and mortality. Smoking is known to be one of the most strongly associated risk factors of intracranial aneurysm (IA) formation and rupture. While smoking and the formation of IA is linked, the mechanisms that are responsible are still largely unexplored. Despite decades of data on the profound impact that smoking has on general health, the meteoric rise of vaping in the United States, especially in younger adults and teenagers, threatens new epidemics of diseases. Little is known about vaping and IAs, and there is limited scientific evidence for cerebrovascular-based public health statements to push for a decrease in the use of e-cigarettes. Methods: We conducted a systematic review of the physiological mechanisms behind vascular dysfunction in individuals who smoke or vape to provide a better understanding of what factors specifically impact IA formation and rupture. The online databases searched were EMBASE, PubMed, and MEDLINE. Covidence software was used for abstract and full-text screening, quality assessment, and data extraction. This review was conducted aligning with PRIMSA guidelines. Results: Examination of current literature on abdominal aortic aneurysm (AAAs) development and nicotine exposure, including individual components of cigarette smoke and vape (aldehydes, benzenes, PM2.5 and carbon monoxide) in the vascular endothelium, was reviewed to identify areas of interest for future research. Our review identified vascular inflammation associated with nicotine use, with a 2-3 times increase of IA formation in daily smokers and a correlation between smoking duration and multiple aneurysms. There was also a 4-5x increase in aneurysm formation risk with simply initiating smoking. Several biomarkers involved in vascular disease pathways (TRPA1, TGFB1, MCL1, CDKN1A) were identified as well. Evidence also suggests that smokeless nicotine consumption resulted in decreased IA formation and rupture. Clinical studies suggest that smokeless consumption is less harmful to vascular health due to combustion products, oxidants, and toxicants. Conclusion: Understanding the effects of smoking and vaping on aneurysm rupture can provide a means of supporting public education, specifically to adolescents who use vapes. This review combines basic science focused on mechanisms and clinical reports to understand patient outcomes for improved methods of prevention and treatment.

ABSTRACT # 9

Conflict Processing in the STN: Evidence from Single Units

Marquette A[12]*, Albakri A[12]*, Shanti R[13], Fernandez R[1], Bowersock J[1], van Wouwe N[13], Neimat J[13]

[1] Department of Neurological Surgery, UofL
[2] Undergraduate Neuroscience Program, UofL
[3] Department of Anatomical Sciences and Neurobiology, UofL

The subthalamic nucleus (STN) is a major target for deep brain stimulation (DBS) to treat motor symptoms in Parkinson's disease (PD) and is well known for its role in motor control. However, the STN is also thought to contribute to cognitive control and response conflict. The mechanism by which individual neurons across functional subregions of the STN encode conflict remains unclear. This study examines single-unit (SU) activity in the dorsal motor and ventral associative STN to explore its role in conflict processing. SU activity was recorded intraoperatively from dorsal and ventral STN subregions in 15 patients with Parkinson's disease during DBS while they performed the Simon task, a paradigm that induces response conflict. The Simon task requires a left or right response to the color of a spatially lateralized stimulus. When the action signaled by the location and color of the stimulus are different, this induces conflict and the inappropriate action impulse must be suppressed. Data processing is ongoing. SU activity was sorted offline using Plexon software with a combination of automated clustering and manual refinement to isolate single units. Analyses were restricted to correct trials and classified as non-conflict or conflict based on task condition and response. Neural firing was examined using stimulus and response-aligned peri-stimulus time histograms (PSTHs). Conflict-related modulation was evaluated at the level of individual neurons using cluster-based permutation statistics, followed by characterization of population-level effects across STN units. Preliminary results of 1/15 patients from STN subregions reveal significant time-resolved modulation within the STN. Stimulus-locked analyses showed increases in firing with incongruent trials compared to congruent trials (min $p = 0.019$). Response-locked analyses revealed significant modulation around response execution (min $p = 0.021$), including both pre- and post-response effects. These findings suggest that STN single-unit activity may be involved in conflict processing during the Simon task. Preprocessing and analyses will continue for the complete dataset and examine whether conflict- related activity differs between dorsal and ventral STN subregions. Future studies will also compare STN SU activity related to conflict control with activity in other DBS targets, such as the Globus Pallidus internus, to understand their unique roles in cognition.

ABSTRACT # 10

An Investigation into the Role of Valence on Motor Control

Marquette A[12], Aleissa Y[12], Fernandez R[1], Shanti R[13], Stewart T[1], van Wouwe N[13], Neimat J[13]

[1] Department of Neurological Surgery, UofL
[2] Undergraduate Neuroscience Program, UofL
[3] Department of Anatomical Sciences and Neurobiology, UofL

People adjust their thoughts and actions in response to a changing environment every day and emotions could influence these actions. Understanding how emotion impacts action control in situations where emotion is central to the action (task-relevant) compared to when it is present in the environment as distracting information (task-irrelevant) is essential. Currently it is unclear when emotion most significantly modulates action control. This study seeks to compare how valence (positive versus negative emotion) impacts action control performance when valence is task-relevant and task-irrelevant by using two modified versions of the Simon conflict task. The Simon task is a paradigm to study response conflict by creating interference between a presented stimulus and a subsequent action response. Participants are instructed to respond to a lateralized stimulus on the screen. When the location of the stimulus conflicts with the trained response, this slows reaction times and reduces accuracy compared to when they do not conflict (Simon effect). We created two modified versions of the Simon task and used happy and angry faces as valenced task stimuli. In version 1, the spatial affective Simon task (ST), participants were instructed to respond to the emotional expression of a face (valence is task-relevant). In the extrinsic affective Simon task (EAST), the affective stimulus was a face with an emotional expression, but participants were instructed to respond to the color of the face (valence is task-irrelevant). We collected reaction times and accuracy rates for each task in 12 healthy participants. Valence did not significantly impact the Simon effect in either task and we did not find a significant Simon conflict effect in the EAST. However, the spatial task did show a significant conflict effect with slower and less accurate responses on conflict trials. Future studies will test alternative modifications to this paradigm's design to study how emotion could play a role in action control and motor response. Such knowledge will allow these tasks to be translated in clinical research in studying specific brain regions and their role in processing emotional stimuli in conflict response settings.

ABSTRACT # 11

Spontaneous, age-dependent loxP site recombination driven by the oligodendrocyte-specific and tamoxifen-dependent Cre recombinase in Ddit3fl/fl:Plp-Cre-ERT2 mice

Mathew M[1], Miller M[1], Andres KR[1], Howard RM[1], Saraswat Ohri S[12], Hetman M[123]

[1] Kentucky Spinal Cord Injury Research Center
[2] Department of Neurological Surgery, UofL
[3] Department of Pharmacology and Toxicology, UofL

The Cre recombinase-ERT2 fusion protein (CreERT2) is widely used to drive loxP recombination upon treatment with an ERT2 ligand, tamoxifen (Tam). The Plp-CreERT2 mouse line enabled many genetic studies of mature oligodendrocytes as it is known for high efficiency of loxP recombination selectively in these cells. CreERT2 may also mediate rare, Tam-independent recombination events that may accumulate as animals age. Therefore, effects of age on Tam-induced CreERT2 activity were investigated using Plp-CreERT2:Ddit3fl/fl mice. Genomic DNA was isolated from spinal cord or liver at 2 weeks after completion of the tamoxifen induction protocol that started 5, 13 and 23 weeks of age. LoxP-mediated recombination of the Ddit3fl locus was analyzed by qPCR. The recombination was observed in the spinal cord but not the liver, consistent with oligodendrocyte specificity of the Plp-CreERT2 construct. However, Tam inducibility of the recombination was strongest at 5 weeks of age. The induction was still present in 13-week-old mice but disappeared at 23 weeks. These results suggest that spontaneous loxP recombination events can quickly accumulate with age when Plp-CreERT2 is used. Consequently, such a spontaneous recombination may affect oligodendrocyte biology regardless of Tam usage. Moreover, high levels of CreERT2 expression are the likely reason for a limited age window of loxP recombination inducibility in the Plp-CreERT2 line.

ABSTRACT # 12

Spatial transcriptomics reveals molecular pathways underlying neural regeneration in larval sea lampreys

Meador CS, Katz HR

Department of Biological Sciences, Western Kentucky University

In mammals, spinal cord injuries typically lead to irreversible neurological deficits. In contrast, larval sea lampreys (Petromyzon marinus) exhibit striking regenerative capacity following spinal cord transection. To investigate the molecular mechanisms that support this recovery, we utilized spatial transcriptomics to characterize region- and time-specific gene expression in the lamprey spinal cord before and after injury. Transcriptional profiles from rostral and caudal tissues at 1- and 3-weeks post-injury were compared against uninjured controls. Differentially expressed genes were ranked by the product of significance and the sign of log2 fold change and subjected to functional enrichment analysis using Enrichr, drawing from the GO Biological Process 2021, Reactome 2022, KEGG 2021, and ARCHS4 TFs Coexp gene sets. This analysis revealed distinct spatiotemporal patterns of pathway activation above and below the injury site. We observed differential regulation of regenerative and inhibitory signaling networks including an upregulation of genes related to both the FGF and Notch signaling pathways in rostral tissue when compared to caudal tissue at 1-week post-injury. An additional ranking by log2 fold change with an adjusted p-value cutoff was conducted and analyzed using the Database for Annotation, Visualization, and Integrated Discovery (DAVID) suite where we found enrichment of specific protein-protein interaction motifs, namely the ARM-like domains. Our findings highlight key molecular processes that likely contribute to successful neural regeneration in lampreys and provide insight into potential therapeutic targets for spinal cord injury in humans. Building on these results, we have invested two conserved pro-regenerative transcription factors, ATF3 and c-JUN, using fluorescence in situ hybridization (FISH) to validate our spatial findings and quantify colocalization.

ABSTRACT # 13

Female rats display enhanced compulsive drug seeking for an oral cocaine solution

Neeley JC[1], Rey Caldera A[2], Forbes Blanco EV[3], Dowd MT[2], Adhikari S[12], Osborn E[2], Rogers L[2], Gastright CJ[2], Allgire EN[2],

[1] Department of Biological Sciences, Northern Kentucky University
[2] Department of Psychological Science, Northern Kentucky University
[3] Department of Chemistry and Biochemistry, Northern Kentucky University

Individuals with a substance use disorder (SUD) often use a substance despite negative consequences (e.g., loss of job, health complications, etc.). Such compulsive drug seeking can be modeled in rodents using a seeking-taking schedule. The purpose of the present experiment was to determine if chemogenetic inhibition of the pathway between the medial prefrontal cortex (mPFC) and the basolateral nucleus of the amygdala (BLA) alters compulsive cocaine seeking in rats. Elucidating the underlying neuromechanisms of compulsive drug seeking can allow for the development of novel treatment approaches for SUDs. Sprague Dawley rats (9 male, 6 female) received bilateral injections of either hM4Di (human clone of the inhibitory muscarinic receptor) or mCherry (control) into the mPFC. A retrograde virus was injected into the BLA. This ensured that the pathway between the mPFC and the BLA was selectively inhibited. Rats were trained in a seeking-taking chained schedule in which completing a variable interval (VI) 10-s schedule of reinforcement in one aperture (seeking component) allowed rats to respond in another aperture according to a fixed ratio (FR) 1 schedule of reinforcement to earn access to cocaine (0.3 mg/ml in 0.05 ml of 0.1% saccharin) (taking component). However, after completing the seeking component, rats could randomly receive a foot shock that was delivered with a probability of 0.5. The shock was titrated across individual rats to minimize floor effects and ceiling effects. Once rats achieved stable responses, they received an intraperitoneal injection of dimethyl sulfoxide (DMSO; 1 ml/kg) or deschloroclozapine (DCZ) (3 µg/kg), with order counterbalanced across rats. A mixed factor ANOVA revealed a main effect of sex, $F(1, 11) = 5.58$, $p = .038$, and a main effect of dose, $F(1, 11) = 5.59$, $p = .037$. Overall, females completed more responses during the seeking component relative to males. DCZ increased compulsive cocaine seeking, regardless of the type of virus injected into the mPFC. The current results indicate that females display enhanced compulsive cocaine-seeking behavior compared to males. These results also raise concerns about the use of DCZ as a DREADD activator. Additional work is needed to determine if DCZ binds to endogenous receptors, thus influencing compulsive drug seeking.

ABSTRACT # 14

Beyond Paw Placement: A 3D Kinematic Pipeline to Quantify Intralimb Coordination after Spinal Cord Injury

Pallavarapu A[12], Butler M[1], Shum-Siu A[1], Tata Ramalingasetty S[3], Morehouse J[1], Danner S[3], Magnuson DSK[12]

[1] Kentucky Spinal Cord Injury Research Center
[2] J.B. Speed School of Engineering, UofL
[3] Department of Neurobiology and Anatomy, Drexel University College of Medicine

Spinal cord injuries can severely disrupt motor functions necessary to perform daily tasks, highlighting the need for basic animal research aimed at understanding and promoting locomotor recovery. In rodent models, post-SCI locomotion has generally been assessed using gait analysis pre- and post-injury which examines change in paw placement timing and order (i.e., interlimb coordination). However, intralimb coordination, particularly the timing and extent of knee and elbow angular changes (kinematics), is rarely examined due to the difficulty and inaccuracy of directly tracking these joints, largely caused by the movement of skin relative to the joints and limited surface visibility of the joints. \n\nTo address this limitation, we developed a MATLAB-based and DeepLabCut 3D kinematic pipeline that predicts knee and elbow joint angles using known bone lengths and adjacent, more reliable joints (hip, ankle, shoulder, and wrist) that were digitized and calibrated to achieve their 3D coordinates. DeepLabCut, a machine-learning-based pose-estimation program, significantly reduced manual digitization time for these joint markers while improving consistency across trials. This estimation approach reduces digitization error while enabling continuous reconstruction during locomotion.\n\nBy integrating predicted joint angles with gait phase classification, this method provides a more complete characterization of limb coordination and speed-dependent gait expression following SCI. This framework offers a practical tool for assessing recovery-related changes in locomotor biomechanics and expands the resolution of behavioral outcomes in preclinical spinal cord injury research.

ABSTRACT # 15

Development of Minipig-appropriate Skilled Gait Challenges

Ramey MG, O'Steen WA, Boczek MS, Bishop RM, Ahmed ZF, Mohamed-Hassan YE, Konan ML, Howland DR

Kentucky Spinal Cord Injury Research Center
Department of Neurological Surgery, UofL
University of Louisville School of Medicine

The Yucatán minipig (YMP) is an important preclinical model for multiple neurodegenerative conditions. Walking ability is a common rehabilitation goal. YMP gait is typically assessed while stepping on a treadmill or during level surface over ground walking. Our goal is to expand these assessments and include gait challenges, which require greater accuracy in limb trajectory, hoof placement, and balance. This would allow researchers to behaviorally test the contributions of different levels of the neural axis from the activity of spinal pattern generators to the contributions of descending cortical control. Basic prototypes of an adjustable horizontal bar obstacle and an agility ladder were tested for proof of feasibility. These prototypes have been converted into durable systems using aluminum for the main structures. The bar on the obstacle has a continuous adjustable height feature with an easy lever locking mechanism. The agility ladder rungs are connected by steel cable with easy-to-clean plastic sheaths. The variable height couplers for the obstacle bar and contoured endcaps with cable guides for the ladder were custom designed via SolidWorks and printed in ABS plastic. The obstacle bar is fitted with an accelerometer to detect mechanical force (hoof strike) and send an electrical signal to trigger a light strip. Aluminum construction provides adequate weight to keep YMPs from easily moving either system. Parts meet cleaning standards required for USDA species. Systems have smooth edges/corners and are easy to duplicate via digital design files. The light expedites assessment of bar contacts/negotiation failures, but sensitivity of vibration detection is a challenge. Systems are easily gradable with respect to varying gait challenges, including flexibility in rung number and spacing and bar height. The systems expand our gait testing toolbox for YMPs. In combination with basic gait tests, these tools allow us to behaviorally test across different levels of the neural axis. They also increase accuracy, consistency, and ease of data collection and are easy to collapse or disassemble. Electrical components continue to be refined and will be applied to the ladder. Capacitive touch technology is being explored to replace the current vibration-triggered system. Trigger by touch is expected to be more consistent. Acknowledgements: CHNF, Rebecca F Hammond Endowment, KSCHIRTF, Bucks for Brains, CMRU-KSCIRC Core

ABSTRACT # 16

Emotion Recognition is Affected by Pharmacological Treatment in College Students with Anxiety and Depression

Ratliff W, Bolin J, White IM

Neuroscience Program, College of Science and Engineering, Morehead State University

TDecreased efficacy in perception of emotion has long been linked to psychiatric disorders, leading to decreased adaptability in social situations. The present study was to compare emotion recognition of college students with or without anxiety and depression, and to compare the effects of medication on emotion recognition. In Experiment 1, based on 98-100% correct responses by 116 students, a set of stimuli were selected: happy, sad, fearful, and angry. In Experiment 2, based on the self-report, student volunteers with or without anxiety and depression were tested. Subjects were presented with a set of selected emotional stimuli from Experiment 1, and the correct responses and the effects of medication were compared among groups: anxiety, anxiety with depression, and controls. Compared to controls, subjects with anxiety alone or both anxiety and depression made more errors, particularly in response to negative emotions, anger and sad stimuli, with fear-biased rating. However, their accuracy in recognizing happy or fear emotion was comparable to that of controls. Overall, medication effects on emotion recognition differed: a greater Improvement on the group with both anxiety and depression, minimal effects on anxiety-alone group. Present findings suggest that anxiety and depression affect perception of negative emotions, with fear-bias and medication tends to improve perception in college students. Differential effects of medication will be further discussed.

ABSTRACT # 17

Effects of early-life acetaminophen on juvenile cognition and neuroinflammation

Routt C, Williamson LL

Department of Biological Sciences, Northern Kentucky University

Acetaminophen is one of the most commonly used medications to treat fevers and pain in infants and children. We hypothesize that it affects cognitive function and neuroinflammation if given in early life and may be correlated with the increased incidence of autism spectrum disorder. Rat pups were treated with either acetaminophen (150mg/kg) or saline three times daily from postnatal day 4 to 10. Pups were also given a mock infection twice daily, mimicking how humans typically receive acetaminophen when they are sick. Juvenile cognitive function was examined when rats reached postnatal day 24 using context preexposure facilitation effect (CPFE) testing, a hippocampus-dependent type of fear conditioning. Previously, we assessed early-life acetaminophen exposure and its effect on juvenile rat cognition using context object discrimination testing and we compared the two hippocampus-dependent behavioral tasks and cellular and molecular outcomes. We harvested brain tissue and plasma directly after behavioral testing. Peripheral inflammation was examined by analyzing the concentration of cytokines in collected plasma. Microglia density was analyzed in three different regions of the hippocampus to examine neuroinflammation. No significant differences were found in the juvenile behavioral data. Rats who received acetaminophen showed increased peripheral inflammation, and there were sex differences found in the inflammatory response. Overall, this study highlights the sex and treatment differences present after early-life acetaminophen exposure.

ABSTRACT # 18

Role of Maternal Exercise in Shaping Early Motor Development in Mice

Shakya M, Felter M, Fox D, Easton A, Easybuck T, Fetzer A, Gogzheyan C, Lallai E, Curran CP

Department of Biological Sciences, Northern Kentucky University

Benzo[a]pyrene (BaP) is a carcinogenic polycyclic aromatic hydrocarbon (PAH) produced during incomplete combustion. Exposures are widespread from vehicle exhaust, power plants, wildfire smoke and grilled foods. Studies have linked high prenatal exposure to PAHs with impaired brain development and long-term neurobehavioral deficits in children. Exercise can improve cognitive and motor functions. Therefore, we investigated whether maternal exercise could mitigate the harmful neurodevelopmental effects of BaP. We hypothesized that regular daily exercise before and during early pregnancy would reduce BaP-induced impairments in early motor development in mice. Methods To look for genetic differences, pregnant Cyp1ab1(+/+) and Cyp1b1(−/−) dams received 10 mg/kg/day BaP delivered on corn oil–soaked cereal from gestational day 10 (G10) through weaning on postnatal day 25 (P25). Control groups received corn oil only. Exercised dams had access to a running wheel for 1h/d for two weeks before mating until G10. We assessed early motor development in offspring using the righting reflex and negative geotaxis tests. We measured the righting reflex on P5, P7, and P10. We measured negative geotaxis on P7, P10, and P14. Results: We found a significant gene x treatment interaction with wild type mice having longer latencies to complete the righting reflex test on P7 (P=0.06). However, BaP-treated wild type mice had improved performances if their dams exercised (P = 0.021). There was a gene x exercise interaction at P7 (P=0.039) and P14 (P=0.007) in the negative geotaxis test with Cyp1b1(−/−) knockout pups having shorter latencies to turn. At P10, Cyp1b1(−/−) knockout pups exposed to BaP had improved performance over offspring from dams that did not exercise, but the differences didn't reach significance (P=0.069). Conclusions: Our preliminary results indicate that maternal exercise is beneficial for offspring exposed to BaP during early brain development.

ABSTRACT # 19

NeuroAD AI: A Multi-Modal Agentic AI Framework for Automated Alzheimer's Disease Screening and Diagnostic Orchestration

Tippana V

South Oldham High School

Early diagnosis of Alzheimer's Disease (AD) is vital for patient care, yet it is often hindered by "data siloing," where imaging, clinical labs, and cognitive assessments are reviewed in isolation. This project introduces NeuroAD AI, a novel, fully automated multi-modal agentic AI framework designed to synthesize disparate clinical data points into a unified diagnostic profile. The system utilizes the Google Gemini 3 Pro model to orchestrate four specialized virtual agents: a Radiology Agent (analyzing MRI/PET atrophy), a Cognitive Agent (tracking longitudinal MMSE decline), a Biomarker Agent (interpreting Amyloid/Tau concentrations), and a Neurophysiology Agent (processing EEG spectral reports). Unlike traditional static algorithms, this "agentic" approach employs an Orchestrator to simulate a clinical board, cross-referencing findings to identify diagnostic correlations. To ensure transparency, a Confidence Scoring System was implemented, requiring each agent to quantify its certainty (0.0 - 1.0). The software architecture, built with React and TypeScript, features a dashboard that visualizes longitudinal trends and multi-modal "Radar Variance" charts. Testing across diverse patient profiles ranging from healthy controls to late-stage AD, demonstrated that the system successfully fuses quantitative data (e.g., pg/mL biomarker levels) with qualitative clinical text (e.g., EEG narratives) to produce high-accuracy risk probabilities. By automating the synthesis of complex neuro-analytics, NeuroAD AI provides a scalable model to reduce diagnostic latency and enhance clinical decision support in neurodegenerative care.

ABSTRACT # 20

Assessing the role of microglial stromal interaction proteins in wound healing and tissue sparing after SCI.

Usmani D[1], Hill N[1], Gutti S[1], Leicht E[1], Stirling DP[123]

[1] Kentucky Spinal Cord Injury Research Center
[2] Department of Neurological Surgery, UofL
[3] Department of Anatomical Sciences and Neurobiology, UofL

Recent microglia specific deletion experiments have shown microglia are essential for wound healing and scar formation post-SCI (pSCI) limiting secondary degeneration; however, others have reported opposing effects suggestive of a detrimental role. Our previous work has shown that inhibiting store-operated calcium entry (SOCE) is neuroprotective after SCI. Specifically, we've found that targeting stromal-interaction molecules (STIM) improves neurological outcome pSCI, but the molecular and cellular mechanisms remain poorly understood. We hypothesized that deletion of STIM1 and STIM2 in microglia would reduce excessive microglial proliferation, motility, and release of proinflammatory mediators, resulting in improved tissue sparing pSCI. We used the Cre: lox system to conditionally knock out STIM1 or -2 specifically in microglia. Three tamoxifen-inducible mouse strains containing the cx3cr1cre driver (to restrict gene deletion to microglia) were bred in-house and used for this study: one with microglia-specific deletion of STIM1 (mSTIM1KO), one with microglia-specific deletion of STIM2 (mSTIM2KO), and a control strain (mSTIMWT). All strains carried the Ai9(tdTomato) reporter to visualize microglia and the YFP+ reporter to visualize axons. Following T9, 50 kdyn contusive SCI, mice were euthanized at 14d pSCI (n=5-7/group) and 42d pSCI (n=8-12/group). Cords were sectioned, and epicenters were imaged using confocal microscopy. Investigators blind to genotype assessed tdTomato+ microglia density, their spatiotemporal response, and assessed spared YFP+ axons. We found a significant decrease (t-test (10) = -3.076, p = 0.012) in % microglia density at the epicenter of injury in mSTIM2KO (mean ± SD,19.619 ± 2.566) versus mSTIMWT (23.811 ± 1.147) mice at 14d pSCI, corresponding with improved white matter sparing. Gross assessment of the spatiotemporal response of microglia reveals that microglia from mSTIM2KO expand less laterally and ventrally at the lesion site at 14d pSCI compared to mSTIMWT mice. In addition, the microglia appear more dispersed around the lesion border at 42d pSCI in comparison to the more cohesive border formed at 14d pSCI. Moreover, at 42d pSCI, mSTIM1KO mice exhibit a greater presence of large, circular microglia than the mSTIM2KO and mSTIMWT mice within the lesion core. Collectively, our preliminary results suggest a negative role for microglial specific STIM2 in part through increased microglial dispersion and lesion expansion.

GRADUATE STUDENTS

ABSTRACT # 21

The effects of Wnt/β-catenin upregulation on regeneration and recovery post-spinal cord injury (SCI)

Ali SS, Katz HR

Department of Biological Sciences, Western Kentucky University

The Wnt/β-catenin signaling pathway is a well-established driver of cell proliferation and regeneration and is of particular interest in the field of spinal cord regeneration. This pathway can be effectively studied in the larval sea lamprey (Petromyzon marinus). Following a complete spinal cord transection, lampreys exhibit significant functional recovery, regaining forward swimming within 3 weeks and near-complete swimming abilities by 11 weeks post-injury (wpi). During this recovery period, increased expression of β-catenin is observed in the spinal cord, indicating the role this pathway plays in the regeneration process. While recent studies using the Wnt pathway inhibitor Wnt-C59 (PORCN) demonstrate a significant reduction in functional recovery and axon regeneration following spinal cord injury (SCI), the therapeutic potential of Wnt upregulation remains unknown in the spinal cord. This study addresses that gap by evaluating the effects of pharmacological activation of the Wnt/β-catenin pathway using a Wnt agonist (Calbiochem). Recovery was assessed through anterograde bulk labeling and cell survival assays of reticulospinal (RS) neurons, swimming kinematics at 11 wpi, and behavioral scoring of swimming performance throughout recovery (0.5-11 wpi). While it was expected that chemical upregulation of the Wnt/β-catenin pathway would accelerate functional recovery and promote axonal regeneration, preliminary findings demonstrate reduced swimming recovery in agonist-treated animals compared to vehicle controls by 3 wpi. Additionally, Nissl-stained whole-mount brain tissue at 11 wpi revealed a lower survival rate of giant RS neurons in treated animals. However, spinal cord tissue from the same treated group exhibited an increased number of axons below the injury site relative to controls, suggesting a positive structural response to treatment. These findings indicate that, while Wnt/β-catenin upregulation had a positive effect on structural plasticity, it did not translate into improved functional recovery or enhanced neuronal survival. By comprehensively evaluating post-SCI recovery following Wnt agonist treatment, this work provides new insights into the effects of Wnt/β-catenin upregulation. These findings may inform future therapeutic strategies for mammalian neural repair, and ongoing trials will further clarify whether Wnt agonism actively promotes axon regeneration.

ABSTRACT # 22

Functional Connectivity Analysis Pipeline for Thalamocortical Networks in Epilepsy Using intracranial sEEG Data

Almadani I[1], Scraper A[2], Mutchnick I[2], Karakas C[3], El-Baz A[1] , Sokhadze E[2]

[1]J.B. Speed School of Engineering, UofL
[2]Norton Neuroscience Institute, Norton Children's Hospital
[3]Children's National Hospital

Epilepsy is a clinical disorder defined as the tendency to have recurrent and excessive seizures. Stereoelectroencephalography (sEEG) provides unique opportunities to identify approaches to understanding what brain structures and networks are directly involved in the process of seizures onset and propagation. Patients with drug-resistant epilepsy who are considered for neurosurgery undergo implantation of intracranial electrodes to obtain their sEEG recording which is used to localize the seizure onset. This work develops a pipeline for quantitative sEEG analysis using two functional connectivity measures, coherence (Coh) and directed Phase Lag Index (dPLI), to investigate the involvement of thalamic network in epileptic activity's onset, propagation, and termination. sEEG advances the understanding of the mechanisms contributing to seizure generation, propagation, and control by permitting precise and minimally invasive recording of the thalamus activity, along with recording from other structures of the cortical networks. Thalamic involvement in epilepsy has received increasing recognition due to its connectivity with networks directly involved in epileptic activity. The analysis of functional connectivity in thalamocortical networks during interictal, ictal (seizure) and post-ictal sEEG are performed using MATLAB toolboxes and Brainstorm software. The thalamocortical network sEEG connectivity analysis aimed at identifying regions (e.g., thalamic, prefrontal, temporal, and parietal regions) involved in these epileptic processes will allow for evaluation of their role in seizures onset, propagation, and termination. Deidentified sEEG recordings of pediatric patients who had undergone intracranial monitoring and were considered for neurosurgery treatment of refractory epilepsy were retrieved from stored databases for retrospective analysis using MATLAB. The regions of interest included were contacts in thalamus nuclei, prefrontal, temporal, and parietal regions. The two functional connectivity measures (Coh and dPLI) were analyzed using Brainstorm and a flowchart was developed to detail the analysis pipeline and emphasize reproducibility.

ABSTRACT # 23

Novel Large Animal Model of Anal-Rectal Neurogenic Dysfunction and Spinal Cord Epidural Stimulation After Spinal Cord Injury in Female Yucatan Mini-pig

Almosawi M, Medina Aguinaga D, Gallagher J, Rosado L, Knibbe C, Ahmed RU, Konan LM, Young D, Schmitt E, Ugiliweneza B, Davison S, Hubscher C, Boakye M

Department of Neurological Surgery, UofL
Kentucky Spinal Cord Injury Research Center

Spinal cord injury (SCI) leads to severe complications including paralysis, chronic pain, anorectal and bladder dysfunction, and cardiometabolic disorders. Anal-Rectal Neurogenic Dysfunction (ARND) is among the most prevalent and disabling consequences of SCI. Spinal cord epidural stimulation (scES) has emerged as a promising therapeutic strategy. The Yucatan minipig (YMP) model is increasingly used in SCI research since it offers significant advantages for studying SCI-related pathophysiology and developing effective therapies. The aim of this study was to establish a translational large-animal model of ARND and examine the effects of scES on anorectal manometry (ARM) after SCI. Fifteen adult female YMPs were divided into three groups: (1) SCI only, (2) bowel scES, and (3) stand-and-step scES (S&S). A severe contusion was induced at T10 using a 50-g impactor dropped from 20 cm, followed by 5 min of 100-g compression. A Medtronic stimulator was implanted at L6 or S1. Group 1 received no treatment. After 4 weeks of recovery, Group 2 underwent S1 neuromodulation (1 h/day), and Group 3 received L6 scES combined with locomotor training (1 h/day). Anorectal function was measured pre-injury and 8 weeks post-injury using ARM (rectum: 10 cm; internal anal sphincter [IAS]: 5 cm; external anal sphincter [EAS]: 0 cm), surface anal electromyography, and defecatory video monitoring. SCI alone reduced rectal and IAS maximum pressures before and after balloon challenge (BCh) and increased EAS pressures during the recto-anal inhibitory reflex (RAIR). These changes were associated with loss of normal circadian defecatory rhythm. In animals receiving bowel scES, IAS minimum and maximum pressures were reduced both pre- and post-BCh, while rectal pressure changes were limited to reduced minimum pressure post-BCh. EAS pressures during RAIR were reduced compared with pre-injury values, and this group preserved circadian defecation frequency at 8 weeks post-injury. In contrast, animals receiving scES with S&S training showed reductions in rectal minimum and maximum pressures pre- and post-BCh, along with reduced IAS minimum pressure post-BCh. EAS pressures were reduced across parameters except for baseline relaxation pressure. These findings demonstrate the feasibility of evaluating ARND using ARM in a translational large-animal model and provide experimental evidence that scES differentially modulates anorectal dynamics after SCI, supporting further translational investigations.

ABSTRACT # 24

Lower urinary tract response to spinal cord epidural stimulation pre- and post-select peripheral neurectomy in spinally injured rats

Beasley KM, Medina-Aguinaga D, Perez de Corcho Vazquez B, Hubscher CH

Department of Anatomical Sciences and Neurobiolgy, UofL
Kentucky Spinal Cord Injury Research Center

Spinal cord injury (SCI) often leads to severe impairment of multiple body systems, greatly impacting quality of life. While the urinary bladder is initially areflexic during spinal shock following SCI, reflexive voiding usually develops within 2-12 weeks in humans and 1-2 weeks in the rat. However, voiding post-SCI is often impacted and may display detrusor-sphincter dyssynergia (DSD), which is characterized by uncoordinated bladder and external urethral sphincter (EUS) contractions, causing inefficient emptying and smooth muscle hypertrophy. Likewise, the frequency of bladder contractions may increase and contribute to dangerously high intravesical pressures and storage dysfunction, a condition known as neurogenic detrusor overactivity (NDO). Spinal cord epidural stimulation (scES) is a novel therapy that has been shown to improve lower urinary tract (LUT) function in both humans and pre-clinical experimental models post-SCI. Our group hypothesized that the improvements in LUT function seen with scES result from modulation of the neural networks which project to the bladder or EUS that are located within these sites of stimulation. To gain insight into the neural mechanisms behind scES-induced effects on the LUT, the Hubscher laboratory has developed a model combining thoracolumbar or lumbosacral scES with a neurectomy of either the pelvic, hypogastric, or pudendal nerves in female rats with moderate-severe SCI (215 kdyn) during urethane-anesthetized cystometry-electromyography at 7-, 14-, or 28-days post-injury. Current acute post-transection data indicates both a loss as well as re-emergence of voiding and storage effects by the 28-day timepoint, depending on the nerve and/or site of scES stimulation. These findings indicate that the T13 and L6 level scES mediated improvements in LUT function may be due to post-SCI neuroplasticity and/or by the involvement of multiple peripheral nerves innervating the urinary bladder rather than a single source of output.

ABSTRACT # 25

APOE4 drives changes in microglial reactivity after low-dose Aducanumab immunotherapy

Lucido C[1], Pallerla A[1 2], Arbones-Mainar J[1], Saito K[3], Stephens I[1], Funnell J[1], Nolt G[1], Hernandez G[1], Territo P[4], Morganti J[3] , Johnson L[135]

Dept. of Physiology[1], MD/PhD Program, College of Medicine[2], UK, Sanders Brown Center on Aging[3], Indiana University School of Medicine[4], Dept. of Neuroscience[5], UK

Background: Anti-amyloid β (Aβ) monoclonal antibodies (mAbs), such as Aducanumab and Lecanemab, are the first disease modifying therapies for Alzheimer's disease (AD). However, adoption of these drugs has been slowed due to concerns over amyloid related imaging abnormalities (ARIA) of edema or microhemorrhages. While the cause of ARIA is unknown, there is a strong link with APOE4 (E4) – the strongest genetic risk factor for late onset AD – making it essential to understand the mechanisms of E4-associated ARIA. Methods: Female E4FAD mice (human E4 + 5xFAD model of amyloidosis) were treated for 12 weeks with chimeric Aducanumab (chAdu) or IgG isotype control (1.56 mg/kg). A subset of n=3 brains/group were cryosectioned (10mm), mounted on 10X Xenium cassettes, and run on the Xenium Analyzer using a custom 480-gene panel. Post-run, slides were stained with Thioflavin-S for downstream image co-registration and plaque-proximity analyses. scRNAseq was conducted on the mirroring hemibrain to increase transcript depth and data validation. Analyses were performed in R using Seurat(v5) and DESeq2. SPLIT and Squidpy were used for cell purification and image analyses. CellChat was used to infer interactions between vascular and immune cells . Results: After purification, over 346k cells were analyzed, including 35k microglia. Ten unique clusters of microglia were identified including multiple disease-associated (DAM), interferon responsive (IRM), and antigen presenting (APM) clusters. Treatment with chAdu increased DAM and APM subpopulations and decreased homeostatic microglia relative to IgG controls. Plaque-proximity analyses revealed distinct microglial states near parenchymal plaques vs cerebral amyloid angiopathies (CAA). Additionally, chAdu treatment drove alterations in spatial neighborhoods for immune and vascular populations, particularly infiltrating immune cells. Conclusions: Xenium spatial transcriptomics provides a powerful tool for visualizing subcellular changes following anti-Aβ treatment. Treated animals showed expanded microglial subpopulations involved in disease response and antigen presentation, suggesting increased inflammatory signaling, particularly in perivascular and CAA-associated niches. CellChat supported this, with elevations in pathways involving immune chemotaxis and vascular inflammation in chAdu mice. Together, these findings provide a window into the potential immune-vascular interactions driving E4-associated ARIA.

ABSTRACT # 26

Novel Genetic Models for Descending Spinal Tracts

Miozza L, Farris G, Morehouse J, Petruska JC

Department of Anatomical Sciences and Neurobiology, UofL
Kentucky Spinal Cord Injury Research Center

Research into the normal function and the response to injury and treatment of the corticospinal tract (CST) has been significantly enhanced by the availability of CST-specific genetic models (CST-reporters). Other spinal long-tracts have different functions and responses to injury and treatment and would benefit from similar genetic reporter models. We examined public databases for annotations that would indicate suitable signal-patterns for reporters of descending spinal tracts. We obtained commercially-available mice with Cre-recombinase controlled by the promoter for the transcription factor Phox2b. Phox2b-Cre mice were crossed with LSL-tdTomato mice (Ai9). These "Phox2b-tdTom" mice were examined for signal in the spinal cord. We injected retrograde tracer into the spinal cord to identify brain/brainstem neural cell bodies-of-origin of the Phox2b-tdTom spinal axons. We injected Cre-dependent viral vectors (AAV2-LSL-eYFP) into target nuclei to determine both the functional expression of Cre in the adult and the characteristics of eYFP transport throughout the Cre-expressing neurons. We performed spinal contusion injuries and screened for expression of Phox2b and/or Cre in the spinal cord and brainstem. Preliminary data indicated that the Phox2b-tdTom mice had labeled axons distributed throughout the lateral aspects of the VentroMedial and VentroLateral Funiculi. This limited the potential sources of labelled axons to the (ascending) SpinoThalamic, SpinoCerebellar, Spino-Olivary, and SpinoReticular Tracts and the (descending) Ventral/Medial CorticoSpinal, ReticuloSpinal, OlivoSpinal, and VestibuloSpinal Tracts. Preliminary retrograde tracing from the lower thoracic spinal segments indicated that, of those possibilities, the Phox2b-tdTom mice reported specifically on the VestibuloSpinal Tract to the exclusion of all others. Experiments are ongoing to determine 1) whether Phox2b-Cre reports on the LVST and/or MVST, 2) the proportion of the VST reported by Phox2b, 3) whether Phox2b-Cre is expressed into adulthood, and 4) the pattern of Phox2b and reporter expression after SCI. We have validated our data-mining approach for identifying candidate genetic models for spinal long-tracts. Phox2b is a promising genetic model system for the VST and appears to maintain specificity and sensitivity in the spinal-injured condition. ** We encourage collaborations to determine the validity of the reporter in a greater variety of injury and disease conditions.

ABSTRACT # 27

Role of Artificial Intelligence and Genomics in Early and Accurate Identification of Autism Spectrum Disorders (ASD)

Mohamed YB, Saleh I, Karam S, Buckley A, Shehata M, Barnes G, Contractor S, El-Baz A

School of Public Health and Information Sciences, UofL

Background / Introduction: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by social communication deficits and repetitive behavioral patterns. Early diagnosis remains a major challenge due to the heterogeneity of symptoms and the lack of objective biological diagnostic tools. Recent advances in genomics and artificial intelligence (AI) offer promising opportunities to improve the early detection and diagnostic accuracy of ASD. Research Question and Hypothesis: This study aims to evaluate the role of integrating genomic data with artificial intelligence techniques in improving the early and accurate identification of ASD. We hypothesize that combining genomic markers with AI-based analytical models enhances diagnostic performance compared with traditional or genomics-only approaches. Methods: A systematic review was conducted following the PRISMA protocol. Five major scientific databases were searched, including PubMed, Scopus, Google Scholar, IEEE Xplore, and ResearchGate. Search terms included combinations of "Autism," "genomics," "artificial intelligence," and "machine learning." Studies were included if they investigated genomic markers associated with ASD and applied AI or machine learning approaches for detection or prediction. Studies that lacked genomic data, did not utilize AI methods, or were not peer-reviewed research articles were excluded. A total of 80 studies were initially identified, and after removing duplicates and applying inclusion and exclusion criteria, 47 studies were included in the final qualitative analysis. Results: The reviewed studies consistently demonstrated improved diagnostic performance when genomic information was integrated with AI algorithms. Several genomic markers were frequently associated with ASD, including NBEA, HOXB3, HERC1, NR2F2, and MID2. Among AI methods, Convolutional Neural Networks (CNN), Random Forest, and Gradient Boosting models showed the strongest predictive performance. Many studies reported diagnostic accuracy exceeding 95%, with AUC-ROC values reaching up to 0.88. The integration of genomics and AI also highlighted important biological pathways related to ASD, including chromatin remodeling, neuronal signaling, and synaptic development. Conclusion: The integration of artificial intelligence with genomic data demonstrates strong potential for improving the early and accurate identification of Autism Spectrum Disorder. These approaches may enable earlier intervention, support personalized treatment strategies, and improve long-term outcomes for individuals with ASD. Future research should explore emerging areas such as radiogenomics, combining imaging and genomic data to further enhance non-invasive diagnostic approaches.

ABSTRACT # 28

Role of the integrated stress response kinase HRI/EIF2AK1 in an EAE model of Multiple Sclerosis

Mohan D, Mathew M, Andres KR, Russel M Howard RM, Hetman M, Zheng J, Saraswat Ohri S

Department of Anatomical Sciences and Neurobiology, UofL
Department of Neurological Surgery, UofL
Kentucky Spinal Cord Injury Research Center

Experimental autoimmune encephalomyelitis (EAE) results in inflammatory damage of the white matter that resembles multiple sclerosis (MS). Heme regulated inhibitor (HRI) is a protein kinase that initiates the integrated stress response (ISR) pathway under heme deficiency, mitochondrial stress or innate immunity activation. In the latter context, HRI supports full inflammatory response promoting anti-bacterial defenses, but also, enhances secondary damage of host tissues. Our recent preliminary data showed attenuated EAE severity in mice with a germline deletion of the Hri/Eif2ak1 gene (Hri-/-) compared to wild type controls. This correlated with reduced transcript levels of proinflammatory cytokines (Tnf-α, Il-1β, Il-6, and Nos2) and increased transcript levels of oligodendrocyte markers (Mbp, Plp) in Hri-/- mice after EAE induction. Interestingly, analysis of transcript levels from spinal cord and lymph nodes show differential effects on CD4+ T-cell subtypes in the two genotypes. These data suggest that HRI plays a detrimental role in the pathogenesis of neuroinflammation and white matter damage in EAE. Such a role may include direct contributions to neuroinflammatory activation of innate and/or adaptive immune cells or the cytotoxic ISR in oligodendrocytes.

ABSTRACT # 29

Age, Sex, and Race in Brain Metastases: Patterns of Survival Across Five Less Studied Primary Cancers Using the SEER Database

Mullick M, Abo Kasim R, Rama N, Ostrov P, Kaur A, Froman-Glover C, Ugiliweneza B, Williams B

Department of Neurological Surgery, University of Louisville School of Medicine, Washington University in St. Louis, Department of Mechanical Engineering, UofL

Introduction Brain metastases are a complication of systemic malignancies and are associated with poor outcomes. Limited data exist comparing survival patterns and demographic disparities among non-lung primary cancers that metastasize to the brain. This study evaluates the influence of age, sex, and race on overall survival in patients with brain metastases from breast, colorectal, renal, liver, and melanoma primaries. Methods 2010–2022 data were obtained from the Surveillance, Epidemiology, and End Results program. Adults diagnosed with primary breast (females only), colorectal, kidney parenchyma, liver, or melanoma cancers with brain metastases at presentation were included (n = 11,252). Median survival was estimated using Kaplan–Meier methods. Survival differences across demographic groups were assessed with log-rank tests and Cox proportional hazards models. Results Median survival varied across primary cancers: breast (10 months), colorectal (4 months), kidney (5 months), liver (2 months), and melanoma (5 months). Increasing age consistently predicted decreased survival probability. For breast cancer, the hazard ratios (HR) for ages 45–64 and ≥65 were 1.31 (95%CI: 1.16–1.48) and 1.88 (95%CI: 1.66–2.13), respectively, compared with ages 18–44 ($p < 0.0001$). Similar age gradients were observed for colorectal cancer, with an HR of 2.06 (95%CI: 1.58–2.69) for patients ≥65 ($p < 0.0001$); renal cancer, HR 1.32 (95%CI: 1.07–1.62) for patients ≥65 ($p < 0.0001$); liver cancer, HR 1.28 (95%CI: 1.00–1.63) for patients ≥ 65 ($p = 0.0254$); and melanoma, HR 1.50 (95%CI: 1.31–1.71) for patients ≥65 ($p < 0.0001$). Sex had no significant effect on survival for colorectal, kidney, or liver cancers; however, females with melanoma had 11% lower hazard of mortality compared to males (95%CI: 0.82–0.96; $p = 0.0023$). No significant survival differences were observed between White and non-White patients for any primary cancer. Conclusion Across five primary cancer types, age was the strongest predictor of survival following brain metastasis. Race showed no association. Sex-based survival differences were limited to melanoma. These findings underscore the poor prognosis of brain metastases and highlight the need for bias-free management strategies.

ABSTRACT # 30

Cancer-associated Trends in Spinal Cord Injury: Perspectives from a National Inpatient Sample

Mullick M, Rama N, Ostrov P, Kaur A, Froman-Glover C, Abo Kasim R, Ugiliweneza B, Williams B

Department of Neurological Surgery, UofL

Introduction Epidural spinal cord compression occurs in ~5% of patients who die of metastatic cancer. Prior single-center series may indicate high complication rates among tumor-related spinal cord injuries (SCI). We queried a national database to characterize trends, injury severity, and outcomes among SCI hospitalizations for patients with and without cancer. Methods Using the 2016–2022 National Inpatient Sample (NIS), we identified adult hospitalizations for initial encounter SCI and classified records by presence or absence of cancer. SCI and cancer were identified using the International Classification of Disease 10th edition (ICD-10). Individual characteristics (age, sex, race, Elixhauser comorbidity index, zip-code income, SCI severity) and hospital characteristics were extracted. Outcomes included length of stay, inflation-adjusted hospital charges (2022 US$), in-hospital mortality, and discharge disposition. Outcomes were compared between the groups using regression analysis, adjusting quantile regression to the median, and logistic regression. Estimates were presented with adjusted median, median absolute deviation, and adjusted percentages. Results Among the estimated 155,300 SCI admissions, 7,165 (4.6%) had cancer, and the incidence increased by 44 cases per year ($p=0.0076$). Patients with cancer were older (median 68 vs 58 years), more often female (35% vs 29%), and had greater comorbidity burden (≥3 comorbidities: 78% vs 51%; $p< 0.0001$). SCI severity differed markedly: cervical complete and incomplete injuries were less frequent in the cancer group (respectively 59% vs 67%; $p< 0.0001$, and 2% vs 4%; $p=0.0025$), while thoracic complete injuries were more frequent (24% vs 15%; $p< 0.0001$). Compared to patients without cancer, those with cancer had longer hospital stays (9±1 vs 8±2 days; $p=0.0138$) and higher in-hospital mortality (5% vs 4%; $p=0.0369$). Conclusion Cancer-associated SCI exhibits distinct epidemiology, affecting an older and more comorbid population with greater female representation compared to non-cancer SCIs. It also demonstrates a distinct severity profile accompanied by longer hospital stays and modestly higher in-hospital mortality. Recognition of these demographic and severity patterns may inform earlier detection, triage, and tailored management strategies for this vulnerable subgroup.

ABSTRACT # 31

Microglia-derived APOE2 improves remyelination even in the presence of endogenous APOE4

Nolt GL[1], Golden LR[12], Thorpe SP[1], Funnell JL[1], Stephens IO[1], Hernandez G[1], MacLean SM[12], Lucido CL[1], Brock CR[1], Pallerla AV[1], Adreon DR[1], Williams HC[1], Morganti JM[23], Johnson LA[12]

1 Department of Physiology, University of Kentucky
2 Sanders Brown Center on Aging
3 Department of Neuroscience, University of Kentucky

Demyelination occurs with aging and is exacerbated in neurodegenerative diseases. During demyelination, microglia upregulate expression of APOE, the gene encoding for the brain's primary lipid transport protein apolipoprotein E (ApoE), which also mediates microglial engulfment and elimination of myelin debris. Compared to the E3 allele of APOE, the E2 allele decreases risk for Alzheimer's disease (AD), while the E4 allele increases AD risk and is associated with an increased severity and progression of multiple sclerosis. Previous work shows that mice expressing E2 exhibit improved microglial function and remyelination compared to mice expressing E4. However, whether microglial-derived APOE is responsible for driving these differences following demyelination, and if microglia-selective expression of E2 is sufficient to provide protection, is unknown. We sought to determine if microglia-specific replacement of the E4 allele with E2 can rescue myelin loss and promote remyelination, even in the presence of continued E4 expression by other central nervous system (CNS) cells. Using a novel APOE allelic "switch" model in which we can induce a replacement of E4 with E2 exclusively in microglia, we characterize the glial cell response and lipid profile of mice that underwent either lysophosphatidylcholine (LPC) or cuprizone (CPZ)-induced demyelination and subsequent remyelination. We found that although alterations to the brain lipid profile were subtle, microglial E2 replacement significantly improved remyelination, lessened microgliosis, and decreased astrocytic lipid droplet load following CPZ-remyelination. Our results indicate that microglia-specific E2 expression, in the presence of continued E4 expression, may provide protection against myelin loss via both cell-autonomous and non-autonomous immunometabolic mechanisms..

ABSTRACT # 32

Expedient, High-Resolution MRI Sequence to Visualize the Globus Pallidus for Deep Brain Stimulation Targeting: a Proof-of-Concept Study

Omair J, Abo Kasem R, Fernandez R, Dietz N

Department of Neurological Surgery, UofL

Introduction Deep brain stimulation (DBS) is an established treatment for medically refractory movement disorders, with therapeutic efficacy dependent on accurate electrode placement within subcortical targets such as the globus pallidus internus (GPi). Visualization of the GPi on conventional MRI remains challenging, particularly during asleep DBS procedures where intraoperative testing cannot be performed. Fast Gray Matter Acquisition T1 Inversion Recovery (FGATIR) imaging improves gray–white matter differentiation but requires high-field MRI systems and specialized acquisition protocols. Optimization of low-field MRI sequences may provide a practical alternative for reliable GPi visualization. Objective To evaluate an optimized inversion-recovery sequence on a 0.5T MRI system for GPi border delineation for DBS planning compared to standard FGATIR and T1-weighted sequences. Methods Fifteen healthy volunteers underwent imaging on a head-only 0.5T MRI scanner using 3D MPRAGE acquisitions with multiple inversion times (250, 450, and 550 ms). Manual and automated segmentation of the globus pallidus was performed following image conversion and co-registration. Regions of interest were defined for the GPi, globus pallidus externus (GPe), and adjacent internal capsule. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated to quantify target boundary delineation. Statistical analysis included repeated-measures ANOVA and comparison with a clinical benchmark CNR value of 10.0 for reliable visualization. Results The optimized sequence (TI ≈ 250 ms) demonstrated effective white-matter suppression and improved GPi–GPe boundary visualization. Mean SNR across hemispheres was 45.43. The mean CNR was 10.74, meeting the clinical visualization threshold, with 60% of hemispheres exceeding a CNR of 10. Variability was observed across subjects, with CNR values ranging from 5.51 to 15.10. Conclusion An optimized 0.5T MRI sequence provides high-resolution visualization of the GPi with CNR comparable to current standards of 1.5T and 3.0T MRI. This accessible approach enhances DBS targeting precision without requiring high-field infrastructure, with potential implications for broader implementation and lower-cost preoperative planning.

ABSTRACT # 33

Aducanumab treatment drives APOE4 specific increases in glial reactivity

Pallerla A[1], Lucido C[1], Satish D[1], Nolt G[1], Stephens I[1], Funnell J[1], MacLean S[1], Adreon D[1], Olmsted S[1], Hernandez G[1], Persohn S[2], Territo P[2], Morganti J[34], Johnson L[134]

Department of Physiology, University of Kentucky[1], Indiana University School of Medicine[2], Sanders Brown Center on Aging[3], Department of Neuroscience, University of Kentucky[4]

Background: Anti amyloid monoclonal antibodies such as Aducanumab and Lecanemab are the first disease modifying therapies for AD. Although they provide cognitive benefits, they frequently cause amyloid related imaging abnormalities (ARIA), MRI detected edema or microbleeds that can lead to severe symptoms or death. The mechanisms of ARIA remain unclear, but APOE4 (E4)—the strongest genetic risk factor for late onset AD—is strongly associated with ARIA incidence. Because E4 carriers represent ~65% of individuals with AD, understanding E4-driven ARIA is critical for improving the safety of amyloid lowering treatments in this high risk population. Methods: Nine month old human APOE expressing mice (E2, E3, or E4) crossed to the 5xFAD model ("EFAD") received 12 weeks of chimeric Aducanumab (chAdu) or IgG control (1.56 mg/kg). Mice underwent susceptibility weighted MRI to assess ARIA like microhemorrhages, followed by Prussian Blue histological confirmation. MRI scans were registered to the Allen Common Coordinate Framework (ACCF) to annotate hypointense regions and identify bleed prone areas. Additional histological quantification of plaque burden (AmyloGlo), gliosis (IBA1, GFAP, P2ry12, CD68, Dectin), and vascular structure (isolectin), were also conducted. Results: ChAdu treatment induces plaque clearance and increased microbleeds detected by MRI and Prussian Blue staining in E4FAD mice. MRI hypointensities align with Prussian Blue positive regions, validating microbleed quantification. ACCF registered images reveal genotype and treatment dependent patterns of bleed distribution. E4FADs treated with chAdu showed increased hypointensities in the thalamus, CA1/CA3, and subiculum compared to IgG controls, and more dentate gyrus and piriform cortex hypointensities than chAdu treated E3FADs. Only E4FADs demonstrated elevated parenchymal and vascular microgliosis, along with increased GFAP in both compartments. Activated myeloid cells (CD68+, Dectin1+) were elevated in E4FADs without changes in P2ry12+ homeostatic microglia. Vascular complexity was altered after chAdu treatment in E2 and E3FADs but unchanged in E4FADs. Conclusion: E4 increases microbleed occurrence following chAdu therapy and is accompanied by enhanced perivascular gliosis and microglial activation. Unlike E2 and E3, E4FADs do not exhibit vascular remodeling after treatment. These findings suggest an E4 driven perivascular immune response as a key contributor to ARIA.

ABSTRACT # 34

Investigating bowel dysfunction after thoracic contusion in male rats

Perez De Corcho Vazquez B, Hoey RF, Medina Aguinaga D, Fell J, Hubscher CH

Department of Anatomical Sciences and Neurobiology, UofL Kentucky Spinal Cord Injury Research Center

The high occurrence of bowel-complications in spinal cord injury (SCI) patients often leads to rehospitalization, affecting morbidity and quality of life of individuals with SCI. In humans, SCI leads to various functional changes that collectively disrupt the ability of the gastrointestinal tract to store and evacuate efficiently. Approximately 75% of the SCI population has symptoms of neurogenic bowel dysfunction which can present as constipation, fecal incontinence, abdominal distension, fecal impaction, among others. The mechanisms behind these deficits, however, are not well understood. In the present study, a clinically relevant rodent T3 or T9 contusion model with graded injury severities (mild, moderate, and severe) was utilized to examine SCI induced bowel dysfunction. In addition, the effect of chronicity in rodents with moderate contusion was studied by performing terminal experiments at different timepoints post-injury (acute, sub-acute, chronic). Outcome measures included both external anal sphincter electromyography (EAS-EMG) and anorectal manometry, which is commonly used in clinical settings to assess colonic dysfunction in individuals with SCI. Significant differences were found in EAS response latency and duration of contractile activity in terms of chronicity of SCI. Frequency of giant contractions, which are primarily responsible for mass propulsion of material through the colorectum varied across groups. The T3 group of animals had higher frequencies of giant contractions, indicating a greater level of dysfunction relative to the T9 group. For T9 chronicity groups, GC were reduced below sham levels at the chronic timepoint (84-DPI), consistent with long-term dysfunctions related to inefficient emptying when considered in combination with a hyperactive sphincter. The findings to date illustrate multiple variables contributing to neurogenic bowel dysfunction following incomplete SCI, all of which are likely to contribute to existing challenges. A complete understanding of the existing complexities surrounding both continence and defecation will be informative for clinical management and provide specific targets for the development of novel therapeutic strategies.

ABSTRACT # 35

Characterization of Tolerance and Association with the Neurobehavioral Domain Responses in Patients with Alcohol Use Disorder

Shah A[1], Gul I1, Flynn C[1], Gulia B[2], Jala S[1], Nasme F[1], Jayanty D[1], Zhang W[1], Goswami A[3], Singal AK[1], Kong M[1], Schwandt ML[4], Stewart C[1], Vatsalya V[1]

University of Louisville[1], University of California, Los Angeles[2], Baptist Health Louisville[3], National Institute on Alcohol Abuse and Alcoholism[4]

Introduction: Heavy drinking is dependent on the craving phenotype of the reward mechanism. However, the role of alcohol tolerance and craving remains unclear. This study examined the role of tolerance and markers of heavy drinking in the characterization of craving severity in AUD patients. Methods: This is a single-time-point clinical observational investigation. After consent, 223 male and female adult AUD patients (diagnosed using DSM-IV TR) were grouped as "No Change in Tolerance" (NCT, n=23), Increased Tolerance" (IT, n=130), and "Reduced Tolerance" (RT, n=70) as assessed by the timeline followback for the past 90 days (TLFB90). Data on demographics, drinking history, and craving were collected. Craving scores were calculated from PACS (Penn Alcohol Craving Scale). Total drinks (TD90), Heavy drinking days (HDD90), Average drinks per week (AvgD90), and Number of Drinking Days (NDD90) were computed from the TLFB90, retrospectively recorded from the time of enrollment. Tolerance data was also derived from the same TLFB90 logs as total drinks per 10-day interval (Total nine recordings coded as TD1=total drinks in the earliest 10 days, TD2 for subsequent 10 days, likewise till TD9 for the latest 10 days just before enrollment). Results: 45 out of 223 females participated. The ages of all the patients ranged in the mid-40s, and they weighed between 180 and 200 lbs., without any statistical significance. IT had the least HDD90 and the highest Avg90, which was statistically different than the RT and NCT. IT patients reported a significant ($p<0.001$) lowest TD1 vs. NCT (104.5±53.2 vs. 126.7±33.94) and vs. RT (vs. 45.02±56.94). This response significantly ($p=0.001$) somersaults at TD9 in IT (=151.63, increase of 47 units) and RT (=112.39) patients, without much change in the RCT groups. A potential cause for this tolerance is attributed to the significant association of TD1 values and the frequency of heavy drinking in the IT group of patients (Adjusted $R^2=0.212$, $p<0.001$, moderate effect); this effect was non-existent in the RT and NCT patients. Notably, TD9 or the latest interval of assessment showed a significant association of TD9 and Avg90 (Very robust effect, Adjusted $R^2=0.835$, $p<0.001$) in the IT patients, regardless of whether Avg90 was very similar in IT and RT groups.

ABSTRACT # 36

Single-Neuron Dynamics in Human GPi During Cognitive Interference

Shanti RF[12], Bowersock J [1], Fernandez R[1], Neimat J [12], Van Wouwe N [12]

1 Department of Neurological Surgery, UofL
2 Department of Anatomical Sciences and Neurobiology, UofL

The globus pallidus internus (GPi) serves as a principal output structure of the basal ganglia and is thought to play a critical role in regulating action selection under competing demands. Although GPi involvement in cognitive control has been inferred from models and clinical observations, how individual human GPi neurons respond during response conflict remains unclear. We investigated single-unit GPi activity recorded intraoperatively from 13 patients with Parkinson's disease during performance of the Simon task, while undergoing deep brain stimulation surgery. The Simon task is a well-established paradigm that induces motor response interference. Analyses were restricted to correct trials, which were classified based on conflict conditions (conflict vs non-conflict) and response laterality relative to the recording hemisphere. Neural firing was examined using stimulus-aligned and response-aligned peri-stimulus time histograms, with firing rates normalized to a pre-stimulus baseline window (−350 to −100 ms). Conflict-related modulation was evaluated at the level of individual neurons using cluster-based permutation statistics, followed by population-level characterization across units. Across 26 GPi neurons, conflict-related modulation was present in a subset of units and varied in both direction and timing, with some neurons showing transient increases and others showing suppressions. Significant conflict-associated clusters were observed in both stimulus-locked and response-locked epochs, including a stimulus-locked window at 37.5–162.5 ms post-stimulus and response-locked windows spanning −487.5 to −412.5 ms, −362.5 to −262.5 ms, and −212.5 to 37.5 ms relative to response. These findings suggest that cognitive interference is represented in human GPi through diverse, neuron-specific temporal patterns that extend from early post-stimulus processing into peri-response dynamics. While single-unit analyses reveal substantial heterogeneity in conflict-related modulation, understanding GPi contributions to inhibitory control will require integrating these neuron-level dynamics within broader network-level mechanisms of basal ganglia function in humans.

ABSTRACT # 37

Uremic Tumoral Calcinosis of the Cervical Spine with Symptomatic Myelopathy: An Illustrative Case

Sheth A, Dietz N, Becerril-Gaitan A, Ham E, Sieg E

Department of Neurological Surgery, UofL

Background: Tumoral calcinosis is a rare pathology characterized by extraarticular soft tissue calcium deposition, commonly near large joints. Tumoral calcinosis may be idiopathic or associated with underlying disorders, such as end stage renal disease (ESRD), sarcoidosis, and hyperparathyroidism. The cervical spine is a rare location for tumoral calcinosis, with only 11 cases of uremic tumoral calcinosis previously reported in the literature. Observations: We report a case of cervical tumoral calcinosis in a 46-year-old man with end stage renal disease. He presented with unilateral extremity weakness and was found to have a C2-C6 soft tissue calcific mass. His hospital course was complicated by medical instability, and he eventually underwent mass resection, laminectomy, and posterior spinal fusion. After surveying the literature, we found that 36 cases of cervical tumoral calcinosis have previously been reported. Scleroderma was the most common etiology, with ESRD contributing to 30.5% of reported cases. Laminectomy and further medical management are reasonable treatment strategies to alleviate symptoms and prevent recurrence. Patients with ESRD represent a high-risk population, with increased complications seen postoperatively. Lessons: Although tumoral calcinosis rarely occurs in the spine, it is an important condition for spinal surgeons to be aware of as tumoral calcinosis may be a more frequently encountered pathology due to the rising prevalence of chronic kidney disease.

ABSTRACT # 38

Advancements in robot assisted spine surgery with highlights from the 10th Annual Seattle Science Foundation Course

Sheth A[1], Dietz N[1], Drazin D[2]

1 Department of Neurological Surgery, UofL
2 Department of Neurosurgery, Providence Neuroscience Center Everett

Background: The use of robotics in spine surgery has been rapidly evolving over the past several decades, with significant progress occurring over the past five years. Now used in pedicle screw placement, preoperative planning, intraoperative navigation, robotics has increased accuracy and safety for spinal procedures. Newly developed technology includes augmented reality, three-dimensional imaging, and artificial intelligence. This scoping review summarizes recent advancements in robot assisted spine surgery, with additional commentary from the Annual Seattle Science Foundation Course. Methods: A scoping review of the literature was conducted in January 2026. Search terms included "robotics", "spine surgery", and "preoperative planning" on the PubMed database. Additional studies and highlights were added from the 10th Annual Seattle Science Foundation Course. Results: Robot assisted spinal surgery consistently improves surgical accuracy, while decreasing intraoperative radiation exposure. Robot assisted pedicle screw placement has an accuracy rate of over 97%, with radiation exposure time of 3 seconds per screw. New avenues such as augmented reality and artificial intelligence can be used to assist preoperative planning and provide real time intraoperative guidance. The use of robots in spinal deformity and cervical spine cases has shown promising results in technically challenging surgeries, with increased accuracy and decreased postoperative complications compared to freehand surgery. Learning curves for robotic surgery have been reported as 25 cases or less, with junior surgeons having shorter learning curves with robot assisted surgery compared to conventional methods. While a reported drawback of robot assisted surgery is increased operating times, robotic assistance decreases the cumulative time lost to failed screw placement, intraoperative strategy changes, and adjunct fixation. Conclusion: Robotics has made significant progress in spine surgery, with studies showing clinically favorable outcomes compared to conventional freehand surgery. Future studies should continue to validate the long-term outcomes of robotic use, regarding safety, economics, and sustainability.

POST-DOCTORAL/STAFF/RESIDENT STUDENTS

ABSTRACT # 39

Automated 3D Tracking of Taste Bud Cells for Morphological & Lifespan Analysis

Walters BN[1], Alston DC[12], Krimm RF[1]

Department of Anatomical Sciences and Neurobiology, UofL
Department of Opthalmology and Visual Sciences, UofL

Taste bud cells continually die and are replaced, necessitating methods to study their dynamics. This project uses in vivo dual channel two-photon microscopy, performed in mice, to collect the same taste buds over time. Here, we present an analytic pipeline for 3D automated segmentation and tracking of individual taste bud cells over time. Due to the densely packed nature of cells in taste buds, manual cell segmentation and tracking are labor-intensive and inefficient. Automating these processes allows for more efficient analysis of cell morphology, spatial position, and lifespan, significantly increasing the volume of data that can be analyzed. Napari, a Python-based tool for image processing, is used to render volumetric reconstructions and generate ground-truth segmentations of individual cells. For preprocessing, we used Noise2Void, and for preprocessing of taste bud volumes collected at successive time points, we used the Fast4DReg plugin in ImageJ. Concerning automated segmentation, we used a UNet that uses transformers (SeUNet), while Ultrack tracks segmentations of individual cells over time. We have established proof of concept demonstrating that the affinity-based segmentation model performs well in sparsely populated taste buds. Based on this, we are refining the affinity model to improve performance in densely packed taste buds. Cell morphological measurements will be quantified using the MorphoLibJ plugin in ImageJ. To our knowledge, this is the first integrated tool specifically designed for automated 3D segmentation and longitudinal tracking of individual taste bud cells. It enables analysis of cell morphology and spatial position within the taste bud, measures total cell lifespan, and provides a framework for other 3D time-lapse imaging studies.

ABSTRACT # 40

Parkinson's Disease in the Dual Diagnosis of Traumatic Spinal Cord Injury and Traumatic Brain Injury: 22-Year Nationwide MarketScan Analysis

Alvarez-Madrid EL[1], Gartner K[2], Castillo C[23], Kaelin D[23], Ugiliweneza B[4]

Kentucky Spinal Cord Injury Research Center[1], Department of Neurological Surgery[2], Division of Physical Medicine and Rehabilitation[3], Department of Anatomical Sciences and Neurobiology[4], UofL

Objective: To evaluate the rates of Parkinson's disease (PD) in dual diagnosis (DD) of traumatic spinal cord injury (TSCI) and traumatic brain injury (TBI) compared to TSCI and TBI alone. Background: TSCI and TBI each independently increase the risk of developing PD. TBI has long been recognized as a major risk factor, and recent evidence also links TSCI to higher PD risk, likely through neuronal damage, inflammation, and neurodegeneration. Although the mechanisms connecting TSCI and TBI to PD have been studied separately, their combined effects remain unclear. Given that up to 76% of individuals with TSCI also experience TBI, it is important to determine whether concomitant injury further elevates PD risk beyond either condition alone. Methods: MarketScan Database from 2000 to 2022 was used to extract data from adults, 55 years and older, with TSCI, TBI, and DD. PD rates were adjusted for age, sex, insurance, cardiometabolic, and psychiatric chronic conditions. Results: The cohort was composed of 96,672 adults: 1,680 DD; 6,242 TSCI; and 88,750 TBI. Median age ranged from 65 to 72 years old. Those with a DD were 3 to 7 median years younger compared with isolated TSCI or TBI. After adjusting for demographics and chronic conditions, the rate of PD was significantly higher in DD cases (119 per 100,000 person-years) compared to isolated TSCI (23 per 100,000 person-years, $p<0.0001$) and isolated TBI (39 per 100,000 person-years, $p<0.0001$). The rate of PD after TBI was significantly higher than after TSCI ($p<0.0001$). Rates were similar across levels and completeness of injury for TSCI. However, the rate of PD was significantly higher for severe TBI (172 per 100,000 person-years) compared to mild TBI (44 per 100,000 person-years, $p<0.0001$) and moderate TBI (38 per 100,000 person-years, $p<0.0001$). For DD cases, the rate of PD in complete cervical/thoracic TSCI with moderate/severe TBI (114 per 100,000 person-years) was significantly higher than that of incomplete cervical/thoracic TSCI with moderate/severe TBI (24 per 100,000 person-years, $p=0.0478$). Rates across all other categories of DD were similar. Conclusion: Our findings indicate that individuals with DD have a significantly higher risk of developing PD compared with those with either injury alone. These results underscore the importance of early screening and targeted monitoring in this population. Further research is needed to better understand the underlying mechanisms and inform clinical management.

ABSTRACT # 41

Impact of neuromodulatory locomotor rehabilitation parameters on body composition in individuals with chronic spinal cord injury

Amirova L[1], Willhite A[1], Kondaurova I[12], Cirnigliaro CM[34], Bullock A[1], Siu R[15], Stanis N[16], Gerasimenko Y[78], Castillo C[910], Ovechkin A[110]

Kentucky Spinal Cord Injury Research Center[1], Division of Environmental Medicine, UofL[2], Bronx Veterans Medical Research Foundation[3], Department of Physical Medicine and Rehabilitation, Rutgers University[4], Case Western School of Engineering, Case Western Reserve University[5], Indiana University School of Medicine[6], Department of Physiology, UofL[7], Pavlov Institute of Physiology[8], Division of Physical Medicine and Rehabilitation, UofL[9], Department of Neurological Surgery, UofL[10]

Spinal cord injury (SCI) leads to profound restructuring of body composition, resulting in atrophy, obesity, and bone fractures. Activity-based locomotor training (ABLT) with spinal cord transcutaneous stimulation (scTS) may better activate spinal networks, improving effects on bone, muscle, and fat than ABLT alone. Understanding how different parameters influence body composition in SCI can provide insights into personalized interventions. This study is the first to examine bone mineral density (BMD) and body composition following ABLT combined with scTS interventions. Collecting a large amount of training data across all intervention sessions and accounting for high subject variability allowed us to use principal component analysis (PCA) to identify interactions between key intervention parameters and BMD/body composition in SCI. Five adults with SCI (3m/2f; age 32.4 ± 6.8 years; 9.9 ± 6.0 years post-injury) received 85–361 ABLT sessions with multisite scTS. Whole-body and regional dual-energy X-ray absorptiometry scans were obtained pre- and post-intervention. Linear mixed-effects models were used to analyze pre–post intervention effects and individual changes in BMD and body composition ($\alpha = 0.05$). The PCA included only continuous variables with no missing data. Data were mean-centered and scaled prior to analysis. Four of the five participants showed significant improvements in body composition, with no loss of BMD. Group-level changes were not significant due to high variability and the small sample size. PCA showed unidirectional changes in BMD and bone mineral content associated with the number of overground interventions, and a negative association between fat tissue mass and locomotor training intensity. Lean tissue mass was inversely related to scTS intensity; however, this relationship is likely indirect, as scTS intensity depended on SCI severity. Our results provide preliminary evidence that ABLT with scTS can favorably modulate body composition and potentially mitigate BMD loss in individuals with SCI. Higher-intensity training (i.e., more sessions, greater weekly training volume, and higher treadmill speed) has shown to be more effective for fat loss, while greater weight-bearing may be beneficial for bone density. Spinal cord transcutaneous stimulation may partially alleviate ABLT intervention for SCI by facilitating movement and enabling a higher level of training than without it. This study was supported by NIH R01 NS102920.

ABSTRACT # 42

Exploring effective treatment window for intradetrusor botulinum toxin in a rodent model of SCI

Cates LN[12], Valenti BR[3], Hudson MP[4], Yang CC[5], Khaing ZZ[12]

Department of Anatomical Sciences and Neurobiology[1], Kentucky Spinal Cord Injury Research Center[2], UofL, Department of Neurological Surgery[3], Department of Physiology and Biophysics[4], Department of Urology[5], University of Washington

Despite modern bladder management methods, lower and upper urinary tract complications still contribute significantly to morbidity and diminished quality of life in persons with spinal cord injuries (SCIs). Neurogenic overactive bladders (OAB) often develop after SCI, and this can result in loss of compliance and concomitant urinary tract complications. Currently, there is no treatment available to prevent the development of neurogenic bladder for patients with SCI. However, intradetrusor injections of botulinum toxin A (BoNT-A) are approved and often performed at the chronic state of OAB to chemodenervate and relax bladder muscles. We theorize that the prolonged state of overactivity of the bladder after SCI which precedes the BoNT-A intervention results in muscle, nerve, and tissue damage that can be prevented by acute and/or early chemodenervation. Here we present the results of bladder functional studies in which rats sustained contusion type spinal cord injury at T7/8 or a sham injury (n=3) and either received saline (n=7) or intradetrusor BoNT-A injections immediately (acute, n=8), 3 days post injury (dpi, n=7), 1 week post injury (wpi, n=7), or 2wpi (n=5) and we performed cystometry studies at 6 – 8 wpi for all animals. We found that acute BoNT-A treatment after SCI resulted in improved bladder capacity and compliance, increased regularity of voiding contractions, and shortened intermicturition intervals compared to 3dpi, 1wpi, 2wpi, or saline treated SCI animals. While not all differences we noted in bladder functions reached statistical significance we are greatly encouraged by the pattern in our findings; the longer the delay in chemodenervating the overactive bladder appears to result in poorer preservation of normal bladder function. Additionally, significant decreases in CGRP-positive sensory fibers in the dorsal horn and GAP-43 expression were seen in acute BoNT-A treated SCI animals compared to SCI animals with no bladder treatment. Acute treatment with BoNT-A shows promising results in maintaining normal bladder function after SCI. Future studies exploring the effective length of time and potential for redosing could help establish a more translatory treatment protocol for SCI patients. Supported by the Craig H. Neilsen Foundation, and the DoD CDMRP TRA.

ABSTRACT # 43

Impaired intraspinal hemodynamics and neurovascular unit in the chronically injured spinal cord

Chandran P[12], Odarenko A[12], Cates LN[12], Ng M[2], Senthil H[2], Bruce MF[3], Khaing ZZ[12]

Department of Anatomical Sciences and Neurobiology[1], UofL, Department of Neurological Surgery[2], Applied Physics Laboratory[3], University of Washington

Vascular disruption and remodeling at the injury epicenter after spinal cord injury (SCI) are well documented, however it remains unclear if these changes extend beyond the lesion site or vary with injury severity. A recent study suggested that the spinal cord below a chronic injury is hypoxic state, with oxygenation levels at 40% of preinjury levels. We hypothesize that intraspinal hemodynamics and vascular associated cells are altered below the injury in chronic SCI. We examined intraspinal hemodynamic using intravital contrast enhanced ultrasound (CEUS) imaging at L3 in rats with chronic SCI at T8/9. We found that while a moderate injury did not show significant alterations in vascular resistance (GM: 1.206 ± 0.099 vs 1.143 ± 0.044 sec; p= 0.582 and WM: 1.481 ±0.078 vs 1.366 ± 0.052 sec; p= 0.43), a severe SCI resulted in a significantly elevated vascular resistance in both GM (1.576 ± 0.144 vs 1.143 ± 0.044 sec; p<0.023) and WM (1.682 ± 0.122 vs 1.366 ± 0.052 sec; p<0.017) compared to baseline hemodynamics. Moreover, vascular response during a short episode of metabolic challenge was impaired in both groups compared to sham (27-34% reduction). Pericyte coverage, which can regulate blood flow in the microcirculation, found preserved following a moderate injury, but was markedly reduced after a severe SCI (p<0.0005). Additionally, serotonergic innervation from the brainstem nuclei, which controls the neurovascular tone, was significantly reduced in both injury severities (p=0.001). While microglial activation increased across both severities in a graded manner, astrocyte density remained unchanged. Importantly, we found that increased vascular resistance was highly correlated with both spared serotonin percentage (r=-0.712; p=0.002; d=1.89) and pericyte loss (GM: r= -0.856; p=0.144; WM: r= -0.575, p= 0.425). Combined our findings suggest that moderate injury retains partial vascular regulation whereas severe injury resulted in pronounced intraspinal vascular impairments that included increased resistance, impaired vascular reactivity, and substantial cellular disruptions caudal to the injury in chronic SCI. This study provides new insights into the interplay between hemodynamics alterations and remodeling of cells in the neurovascular unit, caudal to the injury in chronic SCI. These findings highlight the potential for targeting the neurovascular unit to restore blood flow below the injury and enhance functional recovery.

ABSTRACT # 44

Preoperative Sleep Medication Use is Associated with Adverse Outcomes Following Lumbar Spine Surgery

Dietz N[1], Sheth A[1], Ugiliweneza B[1], Bjurstrom M[2], Boakye M[1]

1 Department of Neurological Surgery, UofL
2 Department of Surgical Sciences, Uppsala University

Background: Although postoperative sleep disruption adversely affects recovery, the prognostic impact of preoperative sleep disturbance remains underexplored. This study investigates whether preoperative sleep disturbance, proxied by long-term sleep medication prescriptions, is associated with poorer postoperative outcomes following lumbar spine surgery. Methods: A retrospective cohort analysis was conducted using the Merative MarketScan Databases (2000-2021). Adults undergoing lumbar fusion or decompression for degenerative disorders were included. Patients were stratified by preoperative polypharmacy and sleep medication use (defined as consistent use ≥6 months). Primary outcomes were healthcare utilization (length of stay [LOS], payments, readmissions), complications, mental health diagnoses, and opioid use over 24 months. Adjusted regression analyses controlled for demographic factors and comorbidity burden. Results: Among 118,434 patients, 15.8% were preoperative sleep medication users. In patients without polypharmacy (n=37,682), sleep medication use was associated with significantly higher hospitalization costs, long-term healthcare payments, and markedly increased rates of high postoperative opioid utilization (19% vs. 10% at 6 months, q=0.0002). In the polypharmacy cohort (n=80,752), sleep medication use was linked to worse outcomes across all domains: longer LOS, lower home discharge rates, higher costs, increased complications (e.g., surgical site infection, renal injury), significantly elevated rates of depression and anxiety, and substantially higher short- and long-term opioid use (61% vs. 49% high use at 6 months, q=0.0002). Conclusion: Preoperative sleep medication use is a significant marker for increased postoperative healthcare utilization, complications, mental health diagnoses, and prolonged opioid use after lumbar spine surgery, with effects most pronounced in patients with polypharmacy. These findings highlight the need to integrate sleep health assessment into preoperative optimization strategies.

ABSTRACT # 45

Utilizing the HTr3a-FlpO Mouse Line to Define Gustatory Neuron Innervation of Type III Taste Bud Cells

Eze N, Krimm R

Department of Anatomical Sciences and Neurobiology, UofL

The gustatory system is a complex sensory system relying on various cell types, each expressing distinct receptor types that contribute to the perception of different taste stimuli. Type III taste bud cells transduce sour, bitter, and salt taste stimuli. In response to stimulation, Type III cells release Serotonin (5-HT), which activates Serotonin Receptor 3a- expressing nerve fibers (HTr3a-flpo). However, a definitive genetic marker for Type III associated gustatory nerve fibers has yet to be clearly defined. Here we utilized the HTr3a-flpo mice bred with reporter mice to examine the innervation patterns with Type II and Type III taste bud cells of neurons undergoing gene recombination. We found that HTr3a-flpo was expressed in (38%) of Phox2b-labeled geniculate neurons that project to the oral cavity. Furthermore, HTr3a-expressing neurons were found to innervate (94%) of fungiform taste buds. Examining the proximity between HTr3a-flpo nerve fibers and taste transducing cell types (II &III) revealed significantly greater HTr3a-flpo innervation of Type III compared to Type II taste bud cells. These findings suggest Type III taste bud cells receive preferential innervation from HTr3a-flpo nerve fibers. However, further investigation into innervation density revealed that Type III taste bud cells may inherently receive increased innervation in comparison to Type II taste bud cells, independent of neuron subtype. Perhaps the longer lifespan of Type III taste bud cells contributes to this increased innervation pattern. Consistent with this idea, using intra vital imaging we determined that newly appearing Type III cells are less well innervated than the full population. We conclude that for taste neurons the relationship between neuron subtype structure and function is complicated by plasticity.

ABSTRACT # 46

Moodin- a new brain protein uniquely targeted by chronic mood stabilizers treatment

Ibrahim M[1], Vadnal RE[1], Parthasarathy LK[2], El-Mallakh RS[1], Parthasarathy RN[1]

1 Department of Psychiatry, UofL
2 Department of Pathology and Lab Services, Robley-Rex VA Medical Center

Although lithium is widely used as a gold standard medication to treat bipolar disorder (BD) especially during mania, its exact therapeutic role is unclear. To gain insight into its mechanism of pharmacological action other than brain inositol signal pathways, we have used proteomic and mass spectroscopy analyses to identify differentially expressed proteins in rat cortex tissue, a region mostly affected in BD, after six weeks of lithium and valproate (VPA) feeding in their diets. Several proteins from control and lithium/VPA treated brain tissues were separated by 2-dimensional differential in-gel electrophoresis (2D-DIGE) and individual protein spots were identified by mass spectrometry. Of the 2198 protein spots resolved with lithium treated samples, the abundance of 23 proteins was found to be significantly altered (with the levels of 5 proteins increasing and those of 18 decreasing). Of the 2826 protein spots resolved with VPA treated samples, the abundance of 19 proteins was found to be significantly altered (with the levels of 3 proteins increasing and those of 16 decreasing). Serendipitously, we observed a unique protein level sharply decreased in both lithium and VPA treated samples. This protein is derived from the human C12ORF24 gene called FAM216A protein. Since this brain protein is specifically targeted by both mood stabilizers (lithium and VPA) we call this FAM216A protein as "Moodin" to underscore its specific response to mood stabilizers treatment. We have also found that this protein Fam216a level was also decreased in lithium treated rat serum samples facilitating to study in human blood samples during mania. In 2D-gels this FAM216A protein exists as four different molecular forms possibly by post translational modifications (PTMs). Further work from our team will reveal whether this protein is specifically linked to human mood control and acts as a "Mania Factor" as well. Our studies demonstrate that FAM216A protein (derived from human C12ORF24 gene) is specifically modulated by chronic mood stabilizers treatment and therefore we call this protein as "Moodin".

ABSTRACT # 47

Blood pressure augmentation to improve intraspinal blood flow following cervical spinal cord injury in rats

Jensen DE[1], Odarenko AA[1], Cates LN[1], Bruce MF[2], Khaing ZZ[1]

1 Department of Anatomical Sciences and Neurobiology
2 Applied Physics Laboratory, University of Washington

Blood pressure maintenance is a common clinically used strategy for acute spinal cord injury (SCI) management. Maintenance of mean arterial pressure (MAP) between 85 - 90mmHg is used to limit loss of blood flow to the spinal cord associated with the injury. However, it is unclear whether maintaining MAP within the recommended range results in better intraspinal blood flow. Here, we aim to use a novel ultrafast contrast-enhanced ultrasound (CEUS) to observe vascular changes and evaluate the therapeutic potential of elevated acute MAP via norepinephrine (NE) administration. Mature female Long Evans rats were anesthetized, and a femoral catheter was inserted for real-time systolic and diastolic pressure monitoring. Each rat underwent a three-level laminectomy, followed by a moderate cervical (C6) contusion injury and a subsequent subcutaneous injection of either saline control (0.9% NaCl, N=4) or NE treatment (0.5 mg/kg, N=6) immediately after injury. CEUS imaging was performed at three time points: baseline (pre-injury), acutely post-injury, and at 4 hours post-injury (hpi). MAP was measured pre-injury and up to 5 hpi. As expected, after cervical SCI, there was a rapid decline in MAP (87 to 46 mmHg) which remained below baseline for at least 60 minutes post-SCI. Treatment with NE restored blood pressure to baseline levels quicker (27 min; $p<0.01$, mixed-effects ANOVA) and elevated MAP to a greater extent (+47 mmHg above baseline; $p<0.0001$, t-test) compared to control animals. At 4 hpi, NE-induced MAP elevation resulted in measurable hemodynamic changes via CEUS imaging, including a reduced perfusion deficit volume and a smaller medial-lateral extent of perfusion deficit. These data demonstrate a first direct connection between bolstered MAP after injury and improved intraspinal blood flow and tissue perfusion. Future studies will adopt a longitudinal approach to investigate the enduring impact of acute MAP augmentation on intraspinal hemodynamics.

ABSTRACT # 48

Dissociating Target vs. Limb Representations in Human Precentral Gyrus: Implications for Intracortical BCI Control

Ostrov PB[1], Rao K[12], Jenkins H[3], Simeral JD[13], Vargas-Irwin CD [246], Hochberg LR[124567]

School of Engineering[1], Robert J. and Nancy D. Carney Institute for Brain Science[2], Biomedical Engineering Graduate Program, School of Engineering[3], Brown University, VA Center for Neurorestoration and Neurotechnology, VA Medical Center[4], Center for Neurotechnology and Neurorecovery, Harvard Medical School[5], Department of Neuroscience, Brown University[6], Department of Neurology, Harvard Medical School[7]

Introduction: Intracortical brain-computer interfaces (iBCIs) have demonstrated potential in restoring function to individuals with tetraplegia. However, the degree to which neuronal ensembles in the precentral gyrus encode the spatial target of a movement versus the specific kinematics of the limb remains a fundamental question in motor control. Distinguishing between these representations is critical for developing more intuitive and adaptable BCI decoders. Objectives: The primary objective of this study is to characterize the neural representation of movement intent within the precentral gyrus by isolating target-dependent activity from limb-dependent activity during visually guided tasks. Methods: Data will be collected from a participant with tetraplegia enrolled in the BrainGate2 Pilot Clinical Trial (NCT00912041), implanted with intracortical microelectrode arrays. The experimental paradigm utilizes the a virtual posture-tracking environment and a wearable soft robotic arm (SRA). To decouple neural features, we employ a "visual inversion" task: 1. Standard Trials: Virtual representation of intended upper extremity movement matches the participant's intent. 2. Inverted Trials: The visual feedback of the limb movement is inverted relative to the participant's intent. Data Analysis Pipeline: Neural features are extracted from broadband signals recorded at 30k samples/second across 384 intracortical channels. We will evaluate selective tuning and firing rate modulation in response to both the target location and the visual limb trajectory. Specifically, spike train similarity space analysis will be utilized to quantify the variability of single-unit activity and channel level features across the varying visual conditions. Significance: By identifying how the precentral gyrus primarily encodes extrinsic targets or intrinsic limb kinematics, this work aims to optimize the neurosurgical placement of intracortical recording devices for restorative neurotechnologies and refine decoding algorithms.

ABSTRACT # 49

AHR–Driven Reprogramming of the Glioblastoma Microenvironment Enhances Oncolytic Zika Virus Therapy

Rehman H[1], Cashman KS[1], Ghosh S[12], Jala VR[12], Nair S[12]

1 Department of Microbiology and Immunology, UofL
2 Brown Cancer Center, UofL

Glioblastoma (GBM) is a lethal primary brain tumor plagued by glioma stem–like cells (GSCs) that drive recurrence and therapeutic resistance within a highly immunosuppressive tumor microenvironment (TME) of the central nervous system. Tumor-associated myeloid cells dominate the GBM TME and constrain effective $CD8^+$ T cell responses. Oncolytic Zika virus (ZIKV) is designed to exert therapeutic efficacy through a dual mechanism: first, by leveraging its intrinsic tropism to selectively target and eliminate GSCs; and second, by promoting antitumor immune programs. Notably, we identified that systemic activation of the aryl hydrocarbon receptor (AHR) markedly enhances ZIKV therapy by boosting antitumor immunity and extending survival in GBM. Using Ahrflox/flox LysM-Cre^+ and Villin-Cre^+ mice, our study demonstrates that myeloid-intrinsic, but not epithelial, AHR signaling is critical for this synergistic enhancement of ZIKV therapeutic efficacy. AHR activation primes ZIKV-driven myeloid cell responses, which are subsequently recruited into the tumor to enhance $CD8^+$ T cell recruitment and effector functions, including perforin-1 and Granzyme B activity, without altering anti-ZIKV immunity. These findings identify modulation of neuro-immune interactions through oral delivery of AHR ligands as a viable strategy to improve oncolytic virotherapy in GBM.

ABSTRACT # 50

Edge AI Based Gait Phase Detection for Closed-Loop Neuromodulation in SCI Mice

Shon A, Vernam JT, Wu W

Department of Neurological Surgery, UofL
Kentucky Spinal Cord Injury Research Center

Detecting gait phase in real time presents a significant obstacle for closed-loop neuromodulation systems designed to restore movement following spinal cord injury (SCI). Many current gait analysis methods depend on post-processing or resource-heavy computational models that cannot support rapid, embedded implementation. This research introduces a combined hybrid AI sensing framework that achieves real-time kinematic measurement and on-device gait phase identification for closed-loop neuromodulation in mice with SCI. A computer vision AI component conducts marker-based, rapid pose tracking to capture hindlimb joint angles during treadmill walking, while a compact edge AI model running on a microcontroller identifies gait phase and produces immediate phase-specific stimulation signals for closed-loop neuromodulation. The complete system adapted to previously unseen SCI gait characteristics without requiring injury-specific recalibration and delivered accurate phase-synchronized biphasic stimulation during benchtop closed-loop testing. This research establishes a rapid-response, contact-free sensing and control platform for gait-adaptive neuromodulation, advancing future development of wearable or implantable closed-loop neurorehabilitation technologies.

THE LOUISVILLE CHAPTER
34th Annual Neuroscience Day
Friday, March 27, 2026

ABSTRACT # 51

Subpopulations of gustatory neurons differ in their sensitivity to BDNF

Stout M, Krimm R

Department of Anatomical Sciences and Neurobiology, UofL

Peripheral taste neuron survival and targeting is dependent on expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF). When BDNF is overexpressed (OE) in basal epithelium of tongue and skin, the number of neurons increases in the geniculate ganglion, but in the tongue these neurons fail to innervate the correct location. Taste neurons are genetically and functionally diverse, and genetic subpopulations could vary in the responsiveness to BDNF. To determine if genetic populations are impacted differently by BDNF overexpression, we investigated the defined proenkephalin (Penk+) expressing population and compared results to the full population defined by expression of the transcription factor paired like homeobox 2B (Phox-2b+) in wildtype and OE mice. We found that the number of Penk+ neurons decreased in OE mice ($p<0.05$) whereas the Phox2b+ neurons remained unchanged. We then hypothesized that another genetic subpopulation increases in OE mice, but so far, have found no such population. The decrease in Penk+ geniculate neurons could be due to disrupted target innervation. Consistent with this possibility, by P60, innervation of fungiform taste buds by Penk+ neurons is disrupted when compared to Phox2b+ neurons. Specifically, the percentage of taste buds innervated by Penk+ fibers decreases in OE mice ($p<0.05$) whereas Phox2b+ innervation remains unchanged. In addition, the volume occupied by Penk+ fibers in the taste bud decreased significantly ($p<0.05$) in OE mice compared to controls. Whereas the Phox2b+ nerve fiber volume did not decrease. Our data suggests that subpopulations of taste neurons are impacted differently by BDNF overexpression. Thus, different gustatory neuron types are regulated differentially by developmental factors.