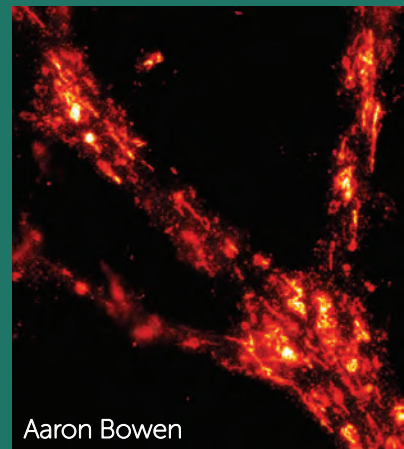
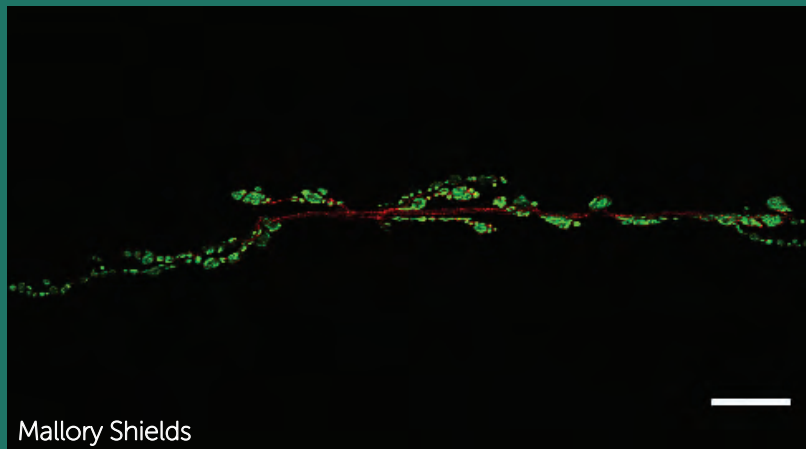
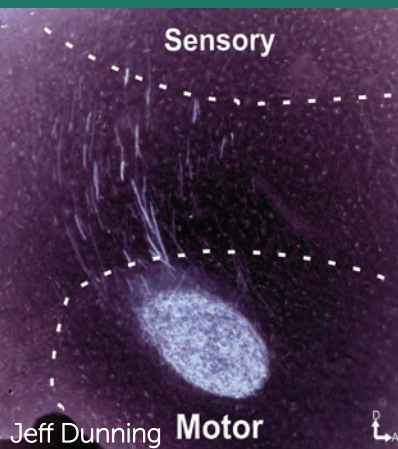


# 2016 CONFERENCE PROGRAM

# FRONT RANGE NEUROSCIENCE

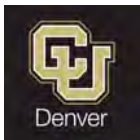
SfN CHAPTER OF THE YEAR



## 14<sup>TH</sup> ANNUAL MEETING

## December 7, 2016

## Lory Student Center



# 14<sup>TH</sup> ANNUAL MEETING

**DECEMBER 7, 2016**

Lory Student Center  
Registration opens at 9:30 AM

# SCHEDULE

**10:30 - 12:00**

## **Communication Workshop**

Hands on session moderated by Distinguished Toastmaster,  
Bob Sturtevant

**12:00 - 3:00**

## **Poster Session, Vendors, and Lunch**

12:30 - 1:45 Odd Posters; 1:45 - 3:00 Even Posters

**3:00 - 4:00**

## **Award-Winning Student Presentations**

Mallory Shields (Colorado State University)

Aaron Bowen (CU Denver - Anschutz)

Jeff Dunning (University of Wyoming)

**4:00 - 4:30**

## **Coffee Break**

**4:30 - 5:30**

## **Keynote Lecture:**

**"Stress and drugs alter synapses in brain reward pathways"**

**5:30 - 6:30**

## **Awards, Prizes, and Reception**

### KEYNOTE SPEAKER

## Julie Kauer, PhD

Professor, Department of Neuroscience  
Professor, Department of Pharmacology,  
Physiology, and Biotechnology  
Brown University  
<https://vivo.brown.edu/display/jkauer>



## ACKNOWLEDGEMENTS

Cover Page: Designed by Ashley Leek

Scientific images provided by *Mallory Shields (Colorado State University)*, *Jeff Dunning (Univ Wyoming)*, and *Aaron Bowen (CU Denver-Anschutz)*. Details will be in their oral presentations. The FRNG website (<http://FRNG.colostate.edu>) was created by Leif Saul in 2005 – see more images on our website.

### **Special Thanks!**

Special thanks to all of you that submitted abstracts for oral and poster presentations! We particularly thank the judges for the poster contest!! – and to ***Shane Hentges*** for managed the herculean task of organizing the judging operation for the meeting – no easy task!!!

Special thanks to the vendors listed in this program. These companies have declared by their contributions both in dollars and prizes that they value Front Range Neuroscience Group business. We encourage you to buy from these vendors that support you.

Special thanks to our Platinum Level Industry Supporters: DSM Nutritional Products, Olympus America, and Stoelting Inc. In addition, special thanks to the CSU Lory Student Center for stepping up to provide the ideal venue. Additional thanks to Jeremy Podany for making the new phone App (TheFairsApp) available to create an online access to the program.

Special thanks to the University departments and programs that provided financial support to help make the meeting possible; in particular Colorado State University, the University of Wyoming, the University of Colorado at Boulder, and finally the parent Society for Neuroscience.

Special thanks to the graduate student organizing committee for creating and polishing the program and fixing the details, and in particular for creating the program book. This includes Ashley Leek, Emily Maverick, and Nathan Byers from CSU, Paige Dingess and Kristen Smith from Univ Wyoming, Elizabeth McCullagh and Shelly Jones from UC Denver Anschutz Health Science Campus, Annie Miller and Lauren Chun from UC-Boulder, Stephanie Stout from DU, and Jonna Jackson from Univ Northern Colorado. Additional thanks go to Graduate Student Advisors Erin Bisenius (Biomedical Sciences, CSU) and Sara Neys (Biomedical Engineering, CSU) and the first year CSU MCIN students for helping with attendee registration.

Special thanks to you, the attendees, for making this a meeting that we can be proud to hold on a regular basis, and for forming Front Range Neuroscientists into a vibrant and interactive Community!

Stay tuned for information on our FRNG Website that helps us communicate position openings, course offerings, seminars and a whole lot more!!!

Sincerely yours,

The Front Range Neuroscience Steering Committee,  
Shane Hentges, Bob Handa, Bill Flynn, Serge Campeau, Kimberly Gorgens, Mark Basham, Sondra Bland, Mark Thomas and Stuart Tobet.

## KEYNOTE SPEAKER

### Julie Kauer, PhD

Professor, Brown University

#### BIOGRAPHY:

Dr. Julie Kauer is currently a Professor in the Department of Pharmacology, Physiology, and Biotechnology and Department of Neuroscience at Brown University, where she runs a lab dedicated to understanding synaptic plasticity that underlies reward and addiction.

Dr. Kauer received her Bachelor's degree in Psychology from Swarthmore College in 1979. Dr. Kauer graduated with her PhD in Pharmacology from Yale University in 1986 where she worked with Leonard Kaczmarek. After graduation, she continued on to do postdoctoral work in the labs of Dr. Roger Nicoll (UCSF; 1986-1989) and Dr. Richard Tsien (Stanford; 1989-1991). Thereafter, she became an Assistant Professor in the Department of Neurobiology at Duke University Medical Center (1991-2000), and in 2000, Dr. Kauer moved to her current home at Brown University.

Throughout her 30 year career, Dr. Kauer has contributed extensively to the field of synaptic plasticity at inhibitory synapses. In honor of her vast contributions, she was recently named a Fellow of the American Association for the Advancement of Science (AAAS). In addition to her contributions to research, Dr. Kauer has also served the field by acting as the chair of the Gordon Research Conference on Synaptic Transmission in 2006, a member of the NINDS Board of Scientific Counselors from 2008-2013, and an editor or editorial board member for publications such as the *Journal of Neuroscience* (2001-2006), *Journal of Neurophysiology* (2002-present), *Physiology* (2006-2012), and *Physiological Reviews* (2010-present).

#### ABOUT HER WORK:

Our work in the reward system underlines the idea that changes in synaptic strength contribute to neuroadaptations of many brain systems beyond those used to store memory per se. The interactions of drugs of abuse with long-term potentiation (LTP) mechanisms illustrate this idea: distinct environmental inputs may modify or perturb existing brain systems to bring about long-lasting behavioral changes. We have characterized a novel form of LTP at GABAergic synapses on VTA dopamine neurons. This LTP is entirely blocked 24 hours after exposure to brief stress or to opiate drugs and to other drugs of abuse as well. We have identified that kappa opioid receptors in the VTA must be activated during the stressor to block the synaptic changes. Our collaborators at the University of Pennsylvania found that delivery of a kappa opioid antagonist into the VTA prior to a stressor entirely prevented stress-induced reinstatement of drug seeking, a prime model of relapse in human substance abusers. Remarkably, even days after a single stressor, we have found that delivery of a kappa opioid antagonist can rescue both LTP and stress-induced reinstatement of cocaine seeking.



Study stops stress-based drug relapse in rats |  
News from Brown March 6, 2013  
<http://news.brown.edu/articles/2013/03/cocaine>

## MORNING COMMUNICATIONS WORKSHOP



**Bob Sturtevant (moderator and facilitator):** Bob Sturtevant spent much of his 35-year career as the Hiring Manager for the Colorado State Forest Service. In this role he read hundreds of resumes and cover letters and conducted numerous interviews. A Distinguished Toastmaster, Bob has been a member of the organization for 22 years. Currently he volunteers with several groups including the Society of American Foresters, Alpha Phi Omega National Coed Service Fraternity and the Coalition for the Poudre River Watershed.

Thank you to all of the faculty and expert communicators for helping with the session!

### Notes:

## ALYSON WELKER: FEATURED ARTIST



"My research began with looking at the brain and how the brain learns and retains information; however, the more I learned about the brain the more I realized how unique every individual brain is as well as how infinite factors are at work simultaneously within the brain at any given time. As a researcher, I was trying to generalize how students learned in online spaces, but after much investigation I found that it would be nearly impossible to understand how even one student learns in online spaces due to the numerous effects of technology and learning on the brain (not to mention the effects of sleep, food, career, family, time, space, genes etc.) that cannot all be controlled for. My art depicts how we often try to understand the brain in the same way that we try to understand people: by

separating them, labeling them, and looking at how they work. I have paintings that focus on parts of the brain including the cerebellum, hippocampus, amygdala, and thalamus. These separations are meant to demonstrate that all parts can be labeled separately, but none function without the others. There are small neurons that are depicted in other paintings that I created as I thought about how such small components can have such large affects. A final image looks at how researchers cut the brain into neat slices in order to further examine it, but my painting shows how my experience in looking at the brain did not have clean and even results, but rather became a complex mess of connections."



## **2016-17**

### **Society for Neuroscience**

- Chapter of the year award!

### **Colorado State University**

- Program in Molecular, Cellular and Integrative Neurosciences
- Department of Biomedical Sciences
- Program in Cell and Molecular Biology
- School of Biomedical Engineering

### **University of Colorado Boulder**

- Department of Psychology & Neuroscience
- Department of Integrative Physiology

### **University of Wyoming**

- Wyoming Neuroscience Center

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Open to faculty, postdoctoral fellows, graduate students, undergraduate students, professional research associates, research scientists, staff and those affiliated with neurobiology that have an interest in teaching neuroscience and research methods to teens.

- Share your knowledge about the nervous system, behavior and research
- Practice your skills in communicating science concepts and refine your teaching style

### Find out more:

*Stop by our BAW Table during the Poster Session of the FRNG conference*

Contact: Leslie Stone-Roy, PhD  
Dept. Biomedical Sciences, CSU  
email: [leslie.stone-roy@colostate.edu](mailto:leslie.stone-roy@colostate.edu)  
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## AWARD-WINNING STUDENT PRESENTATIONS

### 1) Mallory Shields, Graduate Student at Colorado State University

#### Synaptotagmin 2 mutation results in a presynaptic myasthenic syndrome

Mallory C Shields<sup>1,2</sup>, MR Bowers<sup>1,2</sup>, MK Bollig<sup>1</sup>, AD Vrillas-Mortimer<sup>3,4</sup>, H Lochmüller<sup>5</sup>, RG Whittaker<sup>6</sup>, R Horvath<sup>5</sup>, NE Reist<sup>1,2</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University <sup>2</sup>Molecular, Cellular, and Integrative Neuroscience Program, Colorado State University <sup>3</sup>Department of Biological Sciences, University of Denver <sup>4</sup>School of Biological Sciences, Illinois State University <sup>5</sup>John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University <sup>6</sup>Institute of Neuroscience, Newcastle University.

During chemical transmission, the function of synaptic proteins must be coordinated to efficiently release neurotransmitter. Synaptotagmin 2, the calcium sensor for fast, synchronized neurotransmitter release, has recently been implicated in a dominantly inherited human congenital myasthenic syndrome associated with a non-progressive motor neuropathy. In one family, a proline residue within the C2B calcium-binding pocket of synaptotagmin is replaced by a leucine. The functional importance of this residue has not been investigated. Here we examine the in vivo effects of a homologous mutation using *Drosophila*. When expressed in the absence of native synaptotagmin, this mutation is lethal, demonstrating for the first time that this residue plays a critical role in synaptotagmin function. To achieve expression similar to human patients, the mutation is expressed in flies carrying one copy of the wild type synaptotagmin gene. These mutants display behavioral deficits similar to the human patients. In addition, several of the human electrophysiological deficits are recapitulated in *Drosophila*. These results support a causative role for this synaptotagmin point mutation in disease etiology.

**Keywords:** congenital myasthenic syndrome, *Drosophila*, neuromuscular disease, synaptotagmin

### 2) Aaron Bowen, Graduate Student at University of Colorado Denver

#### Local forward trafficking of secretory cargo occurs through recycling endosomes in neuronal dendrites and spines

Aaron B. Bowen, MJ Kennedy. From the Department of Pharmacology, University of Colorado School of Medicine.

Long-term storage of memories in the central nervous system depends on the local dendritic synthesis and membrane trafficking of new synaptic proteins such as AMPA-type glutamate receptors (AMPA). While traditional cell biology dictates that newly synthesized integral-membrane proteins require processing and sorting by the Golgi apparatus (GA) for trafficking, the GA is notably absent from most neuronal dendrites. Consequently, the identity of the organelles responsible for trafficking dendritically synthesized proteins, as well the spatial scale over which these organelles operate, remain enigmatic. We have utilized live-cell fluorescence microscopy to define the organelles of the dendritic secretory pathway that traffic AMPA receptors in the absence of canonical GA. We found that after exiting the dendritic ER, AMPARs undergo spatially restricted entry into the dendritic secretory pathway and subsequently traffic through the recycling endosome (RE) network. Surprisingly, disrupting the function of REs drastically impairs the surface delivery of AMPARs. Thus, in addition to their canonical role in recycling membrane-proteins, REs are also critical mediator of biosynthetic protein trafficking in neuronal dendrites. Furthermore, RE-mediated surface delivery of AMPARs still occurred in the absence of normal GA function, indicating that locally translated proteins may be directly targeted to this pathway without requiring processing by the somatic GA. Overall, we have defined a dendritic, GA-independent trafficking pathway that facilitates the delivery of new synaptic proteins and could support translation-dependent forms of plasticity and consequently long-term memory storage.

**Keywords:** live-cell fluorescence microscopy, engineering fusion proteins, super-resolution microscopy

### 3) Jeffrey Dunning, Graduate Student at University of Wyoming

#### Anatomical links between auditory perception and motor behavior in female mate choice

Jeffery L Dunning<sup>1</sup>, S Maze<sup>1</sup>, EJ Atwood<sup>1</sup>, K Murphy, JF Prather<sup>1</sup>. From the Program in Neuroscience, Department of Zoology & Physiology, University of Wyoming

Females of many species use male courtship displays as a proxy of male fitness to inform decisions of mate choice. Female mate choice has been studied extensively in songbirds, in which females evaluate the quality of male songs for the purpose of choosing a mate. Female songbirds are superb in their abilities to discriminate amongst songs and will exhibit copulatory behaviors (i.e. copulation solicitation displays (CSDs) and calls) in response to songs played through a speaker. It remains unknown, however, how perception of song quality influences expression of copulatory behaviors. Studies of female responses to song have implicated specific auditory cortical regions, such as the caudal mesopallium (CM), in the expression of female mate preferences. Here we examined the projections from CM in female Bengalese finches using an anterograde neural tracer. Our results demonstrate a novel projection from CM to the robust nucleus of the arcopallium

(RA) as well as a region we suspect to be the ventral intermediate arcopallium (AIV). Ongoing experiments with dual tracers are examining the AIV projections more carefully. These arcopallial projections may enable CM to influence brain regions implicated in female courtship behaviors. In zebra finches, AIV projects to the ascending auditory stream, which in turn projects to the mediobasal hypothalamus (MBH), a region associated with female CSDs. In female Bengalese finches, RA projects to the dorsomedial nucleus of the intercollicular complex (DM), a site necessary for female call production. In addition, DM has been shown to project to the cloaca via the respiratory premotor nucleus retroambiguus (RAm) in canaries. Together, these data reveal putative pathways through which CM may influence both CSDs and calls in response to preferred song(s). To address the functionality of the projections emanating from CM in driving female courtship behaviors, we have begun using an adeno-associated virus (AAV) encoding the channelrhodopsin protein (ChR2) to selectively and reversibly manipulate CM neurons as female songbirds are engaged in evaluation of song quality. Our preliminary results demonstrate that CM displays expression of ChR2 and an increased firing rate in response to 420nm light. We are presently beginning tests of our expectation that manipulations of CM while females are listening to song will induce changes in female courtship behaviors via the projections of CM to the arcopallium.

Keywords: Behavior, IHC, stereotaxic injections, optogenetics, confocal imaging

- 1) **A comparison of selection methods for restudying information: EEG versus participant selection**  
P Freud<sup>1</sup>, K Beirise<sup>1</sup>, K Michael<sup>1</sup>, Alex Claxton<sup>1</sup>, & A Cleary<sup>1</sup>. From the <sup>1</sup>Department of Psychology, Colorado State University.
- 2) **In vivo electrochemical and optogenetic assessment of accumbal dopamine release events in a novel behavioral economics based footshock avoidance task**  
Katherine Pultorak<sup>1</sup>, SA Schelp<sup>1</sup>, G Krzystyniak, EB Oleson<sup>1</sup>. From the <sup>1</sup>Psychology Department, University of Colorado Denver.
- 3) **Cognitive deficits in a mouse model for schizophrenia**  
Amber Olson<sup>1</sup>, S Rolan<sup>1</sup>, D Restrepo<sup>1</sup>. From the <sup>1</sup>Center for Neuroscience University of Colorado Anschutz.
- 4) **The effect of 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) on extinction and reconsolidation of fear memory**  
EC Loetz<sup>1</sup>, Holly S. Hake<sup>1</sup>, BA Lloyd<sup>1</sup>, A Sanchez<sup>1</sup>, MR Mondragon<sup>1</sup>, BN Greenwood<sup>1</sup>. From the <sup>1</sup>Department of Psychology, University of Colorado Denver
- 5) **Response inhibition represented by the N200 in adults in a Go-NoGo task**  
Alexandra Bicket<sup>1</sup>, BK Taylor<sup>2</sup>, WJ Gavin<sup>2</sup>, PL Davies<sup>3</sup>. From Colorado State University <sup>1</sup>Department of Neuroscience, <sup>2</sup>Human Development & Family Studies, <sup>3</sup>Occupational Therapy.
- 6) **P200 Sensory Gating in Children with Autism**  
Stephanie The<sup>1</sup>, J Crasta<sup>2</sup>, PL Davies<sup>2</sup>, WJ Gavin<sup>3</sup>. From the <sup>1</sup>Department of Neuroscience, Colorado State University <sup>2</sup>Occupational Therapy, Colorado State University <sup>3</sup>Human Development & Family Studies, Colorado State University.
- 7) **Exercise increases mTOR signaling in brain regions involved in cognition and emotional behavior**  
Brian A. Lloyd<sup>1</sup>, HS Hake<sup>1</sup>, T Ishiwata<sup>1,2</sup>, CE Farmer<sup>1</sup>, EC Loetz<sup>1</sup>, MR Fleshner<sup>3</sup>, ST Bland<sup>1</sup>, BN Greenwood<sup>1</sup>. From the <sup>1</sup>Department of Psychology, University of Colorado Denver <sup>2</sup>Department of Sport and Wellness, Rikkyo University, Saitama, Japan <sup>3</sup>Department of Integrative Physiology, University of Colorado Boulder.
- 8) **Basic word processing and recognition in bilingual and monolingual individuals**  
Luis E. Gomez Wulschner<sup>3,4</sup>, BK Taylor<sup>2,3</sup>, PL Davies<sup>1,3</sup> & WJ Gavin<sup>2,3</sup>. From the <sup>1</sup>Department of Occupational Therapy, <sup>2</sup>Human Development and Family Studies Department, <sup>3</sup>Brainwaves Research Lab, <sup>4</sup>Molecular Cellular & Integrative Neurosciences Program.
- 9) **DREADD-induced activation of the nigrostriatal dopamine pathway modulates fear extinction and reduces fear renewal**  
Courtney A. Bouchet<sup>1</sup>, MA Miner<sup>2</sup>, AJ Rosberg<sup>2</sup>, NM Gray<sup>2</sup>, TM Nicastro<sup>2</sup>, BA Lloyd<sup>2</sup>, EC Loetz<sup>2</sup>, BN Greenwood<sup>2</sup>. From the <sup>1</sup>Department of Integrative Biology, University of Colorado Denver, and <sup>2</sup>Department of Psychology, University of Colorado Denver.
- 10) **Dopamine release in the medial dorsal striatum during voluntary exercise**  
Natalie M. Haddad<sup>3</sup>, SA Schelp<sup>1,2</sup>, KJ Plutorak<sup>2,3</sup>, GJ Gillan<sup>1</sup>, EB Oleson<sup>1</sup>, BN Greenwood<sup>1</sup>. From the Department of <sup>1</sup>Psychology, <sup>2</sup>Integrative Biology, <sup>3</sup>Chemistry; University of Colorado Denver.
- 11) **The MAGL inhibitor MJN110 decreases aggressive behavior after post-weaning social isolation in male and female adolescent rats**  
LM Dawud, Esteban C. Loetz, J Fontenot, T Khan, D Tauber, I Brailier, ST Bland.
- 12) **Early life exposure to predictable maternal behavior has a long-term influence on cognitive performance in rodents and humans**  
EP Davis<sup>1,2</sup>, Stephanie A Stout<sup>1</sup>, J Molet<sup>3</sup>, B Vegetabile<sup>4</sup>, LM Glynn<sup>5</sup>, CA Sandman<sup>2</sup>, H Stern<sup>4</sup>, TZ Baram<sup>3</sup>. From the <sup>1</sup>Department of Psychology, University of Denver <sup>2</sup>Department of Psychiatry and Human Behavior, University of California-Irvine <sup>3</sup>Department of Pediatrics, Anatomy/Neurobiology, Neurology, University of California-Irvine <sup>4</sup>Department of Statistics, University of California-Irvine <sup>5</sup>Department of Psychology, Chapman University
- 13) **Dorsal striatum neurons expressing dopamine-1 receptors are recruited during fear extinction and are activated by DREADD-induced dopamine**  
Megan A. Miner, CA Bouchet, BA Lloyd, HL Hake, TM Nicastro, NM Gray, EC Loetz, BN Greenwood. From the Department of Psychology, University of Colorado Denver.
- 14) **An exploratory examination of oscillations in patients with traumatic brain injury following neurofeedback training**  
Marielle Darwin<sup>1</sup>, LN Pantlin<sup>1</sup> <sup>1</sup>Cognitive Neuroscience, Department of Psychology, Colorado State University.
- 15) **Examining schizotypal personality disorder using mismatch negativity**  
Jenna L. Klippenstein<sup>1</sup>, Brad Stewart<sup>1</sup>, Lara N. Pantlin<sup>1</sup>. From the <sup>1</sup>Department of Psychology, Colorado State University.

## DEVELOPMENT

- 16) Developmental neuropathology of *Xenopus laevis* tadpoles exposed to bisphenol-A, a chemical found in treated wastewater effluent from Laramie, Wyoming**  
Katelynne B. Donnelly<sup>1</sup>, MA Merlino<sup>2</sup>, OF Javaid<sup>3</sup>, KG Pratt<sup>4</sup>. From the <sup>1</sup>Department of Zoology & Physiology, University of Wyoming.
- 17) Developmental expression of ERbeta in the dorsal raphe and prefrontal cortex of male and female mice**  
MA Holschbach, RJ Handa. From the Department of Biomedical Sciences, Colorado State University.
- 18) Prenatal dexamethasone exposure induces a female-specific alteration in the postnatal leptin surge in rat**  
Bradley Hammond<sup>1</sup>, C Royal<sup>1</sup>, MK Thompson<sup>1</sup>, L Madhavpeddi<sup>1</sup>, TM Hale<sup>1</sup> and RJ Handa<sup>1</sup>. From the <sup>1</sup>Department of Basic Medical Sciences, University of Arizona, College of Medicine – Phoenix.
- 19) Regulation of synaptic growth by FMRP-containing RNA processing bodies**  
Emily L. Starke<sup>1</sup>, J Furlong<sup>1</sup>, SA Barbee<sup>1,2</sup>. From the <sup>1</sup>Department of Biological Sciences and Eleanor Roosevelt Institute, University of Denver <sup>2</sup>Molecular and Cellular Biophysics Program, University of Denver.
- 20) Development of a *Drosophila* Vps54 model for motor neuron disease**  
PH Patel<sup>1</sup>, EL Starke<sup>1</sup>, M McGimsey<sup>1</sup>, JT Blankenship<sup>1,2</sup>, Scott A. Barbee<sup>1,2</sup>. <sup>1</sup>Department of Biological Sciences and Eleanor Roosevelt Institute, University of Denver <sup>2</sup>Molecular and Cellular Biophysics Program, University of Denver.
- 21) Coordinated regulation of translation by FMRP and the miRNA pathway**  
Navneeta Kaul<sup>1</sup>, SJ Pradhan<sup>1</sup>, NG Boin<sup>1</sup>, SA Barbee<sup>1,2</sup>. From the <sup>1</sup>Department of Biological Sciences and Eleanor Roosevelt Institute, University of Denver <sup>2</sup>Molecular and Cellular Biophysics Program, University of Denver.
- 22) A role of presenilin in the developing visual circuit of *Xenopus* tadpole**  
Zhenyu Liu<sup>1</sup>, AM Thakar<sup>1</sup>, KG Pratt<sup>1</sup>. <sup>1</sup>Department of Zoology & Physiology, University of Wyoming, Laramie WY.

## DISORDERS OF THE NERVOUS SYSTEM

- 23) Identifying genes potentially common to Schizophrenia pathways based on correlated gene expression analysis**  
Erin I. Liedtke<sup>\*1</sup>, S Zhang<sup>\*1</sup>, JA Thompson<sup>1</sup>, S Sillau<sup>2</sup>, J Gault<sup>1,3</sup>. \*These authors contributed equally. From the <sup>1</sup> University of Colorado Denver, Anschutz Medical Campus, Department of Neurosurgery, <sup>2</sup> University of Colorado Denver, Anschutz Medical Campus, Department of Neurology, <sup>3</sup> University of Colorado Denver, Anschutz Medical Campus, Department of Psychiatry.
- 24) Chronic vs. acute effects of subthalamic nucleus deep brain stimulation on olfactory bulb volume in patients with Parkinson's disease**  
Hermella Yilma<sup>1,2</sup>, JA Thompson<sup>1,3</sup>. From the <sup>1</sup>Master's Program in Modern Human Anatomy, <sup>2</sup>Department of Cell and Developmental Biology, <sup>3</sup>Department of Neurosurgery, University of Colorado School of Medicine, Aurora CO, 80045.
- 25) Cortical mitochondria from R6/<sup>2</sup> Huntington's disease mice have elevated iron and altered proteomic and functional markers**  
Sonal Agrawal<sup>1</sup>, JH Fox<sup>1</sup>. From the <sup>1</sup>Department of Veterinary Sciences, University of Wyoming, Laramie, WY 82070, USA.
- 26) Dietary docosahexaenoic acid alleviates autistic-like behaviors resulting from maternal immune activation in mice**  
Michael J. Weiser<sup>3</sup>, B Mucha<sup>1</sup>, H Denheyer<sup>1</sup>, D Atkinson<sup>1</sup>, N Schanz<sup>1</sup>, E Vassiliou<sup>2</sup>, and RH Benno<sup>1</sup>. From the <sup>1</sup>. William Paterson University, Dept. of Biology, Wayne, NJ, <sup>2</sup>. Kean University, Dept. of Biological Sciences, Union, NJ, <sup>3</sup>. DSM Nutritional Products, Human Nutrition and Health, Boulder, CO.
- 27) Contributions of brain-derived neurotrophic factor to exercise-induced attenuation of methamphetamine-induced neurotoxicity**  
Monica F. Murray, AE Simpson, and AN Fricks-Gleason. From the Department of Psychology & Neuroscience, Regis University.
- 28) Local and use-dependent effects of  $\beta$ -Amyloid oligomers on NMDA receptor function revealed by optical quantal analysis**  
Brooke Sinnen<sup>1</sup>, AB Bowen<sup>1</sup>, ES Gibson<sup>1</sup>, MJ Kennedy<sup>1</sup>. From the <sup>1</sup>Department of Pharmacology, University of Colorado Anschutz Medical Campus.
- 29) Stressor controllability is not protective in female rats**  
Nathan R. Leslie<sup>1</sup>, IP Fallon<sup>1</sup>, SD Dolzani<sup>1,2</sup>, J Amat, MV Baratta<sup>1</sup> LR Watkins<sup>1</sup>, SF Maier<sup>1</sup>. <sup>1</sup>Department of Psychology & Neuroscience, <sup>2</sup>Institute for Behavioral Genetics, University of Colorado Boulder, Boulder.

**30) Hypothalamic POMC neuron involvement in an activity-based anorexia rodent model**

Caitlin M. Daimon<sup>1</sup>, ST Hentges<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University.

**31) Characterization of multiple adeno-associated virus (AAV) serotypes for gene expression in neurons and astrocytes in vivo and in vitro**

Sean Hammond<sup>1</sup>, A Leek<sup>2</sup>, E Richman<sup>3</sup>, and R Tjalkens<sup>3</sup>. From the <sup>1</sup>Cell and Molecular Biology Program Colorado State University, Fort Collins, CO, <sup>2</sup>Center for Biomedical Sciences, Colorado State University, Fort Collins, CO, <sup>3</sup>Center for Environmental Medicine, Colorado State University, Fort Collins, CO.

**32) Automated dopaminergic cell counting in a viral induced Parkinson's disease CD-1 mouse model**

Collin M. Bantle<sup>1</sup>, AT Phillips<sup>2</sup>, SL Hammond<sup>3</sup>, R Tjalkens<sup>1</sup>. From the <sup>1</sup>Department of Environmental and Radiological Health Sciences, Colorado State University, <sup>2</sup>Microbiology, Immunology and Pathology, Colorado State University, <sup>3</sup>Department of Cell and Molecular Biology, Colorado State University.

**33) Mutant huntingtin alters the response of microglial cells to lipopolysaccharide stimulation**

Ryan M Nelson<sup>1</sup>, DW Donley<sup>2,3</sup>, JH Fox<sup>2,3</sup>. From <sup>1</sup>Department of Zoology and Physiology, University of Wyoming <sup>2</sup>Department of Veterinary Sciences, University of Wyoming <sup>3</sup>Neuroscience Program, University of Wyoming.

**34) Increased mortality of Huntington's disease mice with Toxoplasma gondii infection: a possible role of elevated indoleamine-2,3-dioxygenase**

David Donley<sup>1,2</sup>, A Olson<sup>3</sup>, M Raisbeck<sup>1</sup>, JH Fox<sup>1,2</sup>, and J Giggley<sup>4</sup>. From the <sup>1</sup>Department of Veterinary Sciences and <sup>2</sup>Neuroscience Graduate Program, University of Wyoming <sup>3</sup>Department of Psychology, University of Wyoming <sup>4</sup>Department of Molecular Biology, University of Wyoming.

**35) Determining the role of PrPC-mediated signaling during prion-induced neurodegeneration**

Lindsay E Parrie, JAE Crowell, GC Telling, RA Bessen. From the Prion Research Center; Microbiology, Immunology, and Pathology; Colorado State University.

**36) Unexpected early proteomic changes in Alzheimer's disease model mice synaptosomes**

Kerri Ball<sup>1</sup>, A Pisconti<sup>1</sup>, K Grounds<sup>1</sup>, WM Old<sup>1,\*</sup>, MHB Stowell<sup>1,2</sup>. From the <sup>1</sup>The Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder <sup>2</sup>The Department of Mechanical Engineering, University of Colorado, Boulder.

**37) Quantitative measures of brain MRI as a potential predictive factor of cognitive outcomes after Subthalamic Nucleus Deep Brain Stimulation for Parkinson's disease**

Laura J Weinkle<sup>1,2</sup>, O Klepitskaya<sup>2</sup>, J Tanabe<sup>3</sup>, J Honce<sup>3</sup>, JA Thompson<sup>4</sup>, B Hoyt<sup>4</sup>. From the <sup>1</sup>Modern Human Anatomy Program, University of Colorado: Anschutz School of Medicine, <sup>2</sup>Department of Neurology, University of Colorado: Anschutz School of Medicine, <sup>3</sup>Department of Neuroradiology, University of Colorado: Anschutz School of Medicine, <sup>4</sup>Department of Neurosurgery, University of Colorado: Anschutz School of Medicine.

**38) Voluntary exercise attenuates methamphetamine-induced monoaminergic neurotoxicity**

Abigail E. Simpson<sup>1</sup>, MF Murray<sup>1</sup>, and AN Fricks-Gleason<sup>1</sup>. From the <sup>1</sup>Department of Psychology & Neuroscience, Regis University.

**39) Intermittent imaging of cultured hippocampal slices during long term incubation**

Ben Fixman<sup>1</sup>, Laurie Minamide<sup>2</sup>, Alisa Shaw<sup>2</sup>, Jeff Field<sup>2,3</sup>, James Bamberg<sup>1,2</sup>. From the <sup>1</sup>Neuroscience Program, <sup>2</sup>Department of Biochemistry and Molecular Biology, and <sup>3</sup>Microscope Imaging Network, Colorado State University, Fort Collins, CO.

NEURAL EXCITABILITY, SYNAPSES, AND GLIA

**40) Somatostatin not parvalbumin interneurons mediate feedforward inhibition in the basolateral amygdala**

Ethan M. Guthman<sup>1,2</sup>, D Restrepo<sup>1,3</sup>, MM Huntsman<sup>1,2,4</sup>. From the <sup>1</sup>Neuroscience Program, <sup>2</sup>Department of Pharmaceutical Sciences, <sup>3</sup>Department of Cell and Developmental Biology, <sup>4</sup>Department of Pediatrics, University of Colorado | Anschutz Medical Campus, Aurora, CO, USA.

**41) Membrane insertion by both C2 domains of the calcium sensor, synaptotagmin, are critical for neurotransmitter release**

Matthew R. Bowers<sup>1</sup>, NE Reist<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University.

**42) Role of NFAT in the Inactivity-Dependent Regulation of Kv4 Channels**

Abdunaser Eadaim, S Tsunoda. From the Department of Biomedical Sciences, Colorado State University.

**43) Synaptic homeostasis contributes to Aβ42-induced changes in cholinergic neural activity**

Euteum Hahm, R Nagaraja, S Tsunoda, From the Department of Biomedical Sciences, Colorado State University, Fort Collins, CO.

**44) Potential neuroprotective role of slo2 during over-excitation**

Nathan S. Byers<sup>1</sup>, A Rothe<sup>1</sup>, S Sorensen<sup>2</sup>, S Tsunoda<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, <sup>2</sup>Department of Biological Sciences, Colorado State University.

**45) Local synaptic activity dynamically regulates recycling endosome cargo trafficking**

Ashley M. Bourke<sup>1</sup> and MJ Kennedy<sup>1</sup>. From the <sup>1</sup>Department of Pharmacology, University of Colorado Anschutz Medical Campus.

**46) Illuminating the opioid epidemic: opioids inhibit retinal cells responsible for the photoentrainment of circadian rhythm**

Allison M. Cleymaet<sup>1</sup>, AS Hoag<sup>2</sup>, and J Vigh<sup>2</sup>. <sup>1</sup>Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO. <sup>2</sup>Department of Biomedical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO.

**47) Requirement of AKAP79/150 palmitoylation in synaptic plasticity**

Alicia Purkey, K Woolfrey, and M Dell'Acqua. From the Department of Pharmacology, University of Colorado Anschutz Medical Campus

**48) Influence of perineuronal nets on the firing properties of neurons within the prefrontal cortex after exposure to cocaine**

Emily T. Jorgensen<sup>1</sup>, CM Cassidy<sup>1</sup>, BA Sorg<sup>2</sup>, and TE Brown<sup>1</sup>. From the <sup>1</sup>Department of Neuroscience, University of Wyoming, Laramie, WY 82071, <sup>2</sup>Department of Integrative Physiology and Neuroscience, Washington State University, Vancouver, Washington 98686.

**49) Exposure to a high-fat diet attenuates perineuronal net intensity in the prefrontal cortex**

Paige Dingess<sup>1</sup>, M Slaker<sup>3</sup>, J Harkness<sup>3</sup>, B Sorg<sup>3</sup>, T Brown<sup>1,2</sup>. From the <sup>1</sup>School of Pharmacy, University of Wyoming, Laramie, WY 82071, <sup>2</sup>Neuroscience Program, University of Wyoming, Laramie, WY 82071, <sup>3</sup>Department of Integrative Physiology and Neuroscience, Washington State University, Vancouver, Washington 98686.

**50) Somato-dendritic mu opioid receptors inhibit the activity of pro-opiomelanocortin neurons in the arcuate nucleus of the hypothalamus through multiple effector pathways**

Philip D. Fox<sup>1</sup>, ST Hentges<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Division of Neuroscience, University of Colorado, Fort Collins.

**51) AgRP neurons do not contribute tonic GABAergic inhibition onto POMC cells**

Andrew R. Rau<sup>1</sup>, ST Hentges<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University, Fort Collins.

NEUROENDOCRINE

**52) Effects of chronic caffeine exposure on rat brain serotonergic systems**

Matthew R. Arnold<sup>1</sup>, SR Archuleta<sup>2</sup>, TM Smith<sup>1</sup>, PH Williams<sup>1</sup>, JA McArthur<sup>1</sup>, CE O'Neill<sup>2</sup>, CA Lowry<sup>1</sup>, RK Bachtell<sup>2</sup>. From the <sup>1</sup>Department of Integrative Physiology, University of Colorado Boulder, <sup>2</sup>Department of Psychology, University of Colorado Boulder.

**53) The effect of Fgfr3 deficiency on HPG axis function**

Samantha J. Bonelli<sup>1</sup>, LR Brooks<sup>1</sup>, SN Kalavity<sup>1</sup>, SI Kavanaugh<sup>1</sup>, and P-S Tsai<sup>1</sup>. From the <sup>1</sup>Department of Integrative Physiology and Center for Neuroscience, University of Colorado Boulder.

**54) Compensatory mechanisms for GnRH production in Fgf8-deficient mice**

Alexa Ary, SJ Bonelli, A Miller, L Brooks, P-S Tsai, From the Department of Integrative Physiology, University of Colorado Boulder.

**55) Multicellular signaling in the gut: linguistic convergence?**

Luke A. Schwerdtfeger<sup>1</sup>, T Weingarten<sup>1</sup>, SA Tobet<sup>1,2</sup>. From the <sup>1</sup>Department of Biomedical Sciences, <sup>2</sup>School of Biomedical Engineering, Colorado State University.

**56) Effects of acute systemic corticosterone (CORT) treatment on clock gene expression in the male rat brain**

Matthew J. Hartsock<sup>1</sup>, AC Tomczik<sup>1</sup>, AM Janas<sup>1</sup>, NA Droeger<sup>1</sup>, LE Chun<sup>1</sup>, ER Woodruff<sup>1</sup>, RL Spencer<sup>1</sup>. From the <sup>1</sup>Department of Psychology and Neuroscience, University of Colorado Boulder.

**57) Chronic variable stress reduces oxytocin and fos immunoreactivity in the paraventricular nucleus (PVN) of the female mouse**

Amanda P. Borrow<sup>1</sup>, RJ Handa<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University.

**58) Cortisol responses to stress are blunted among infants delivered by Cesarean section**

Leticia D. Martinez<sup>1</sup>, CD Driver<sup>1</sup>, LM Glynn<sup>2</sup>, CA Sandman<sup>3</sup>, EP Davis<sup>1</sup>. From the <sup>1</sup>Department of Psychology, University of Denver, <sup>2</sup>Department of Psychology, Chapman University, <sup>3</sup>Department of Psychiatry and Human Behavior, University of California, Irvine.

**59) Corticotropin-releasing hormone (CRH) regulation by acute glucocorticoid receptor activation and restraint stress**

Ashley L. Turnidge<sup>1</sup>, RJ Handa<sup>1,2</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University <sup>2</sup>Department of Basic Medical Sciences, University of Arizona College of Medicine.

**60) Alternative mechanisms for HPA axis regulation following selective paraventricular nucleus (PVN) deletion of estrogen receptor beta 3rd exon**

Mario G. Oyola<sup>1</sup>, A Acevedo-Rodriguez<sup>3</sup>, AM Malysz<sup>1</sup>, D Carbone<sup>2</sup>, SK Mani<sup>3</sup>, and RJ Handa<sup>1,2</sup>. <sup>1</sup>Colorado State University, <sup>2</sup>Univ. of Arizona, and <sup>3</sup>Baylor College of Medicine.

SENSORY AND MOTOR SYSTEMS

**61) Representation of calls in the activity of neurons in the songbird premotor nucleus HVC**

Karagh Murphy<sup>1</sup>, JF Prather<sup>1</sup>. From the <sup>1</sup>Program in Neuroscience, Department of Zoology/Physiology, University of Wyoming.

**62) Identification of metabolite-sensing muscle afferents in vivo using GCaMP6s**

Kristen M. Smith-Edwards<sup>1,2</sup>, AR Light<sup>3</sup>, and CJ Woodbury<sup>1</sup>. From the <sup>1</sup>Department of Zoology & Physiology, University of Wyoming, Laramie, WY, <sup>2</sup>Graduate Neuroscience Program, University of Wyoming, Laramie, WY; <sup>3</sup>Department of Anesthesiology, University of Utah, Salt Lake City, UT.

**63) A role for glycine in altered excitation and inhibition in the auditory brainstem of fragile X mice**

Elizabeth A McCullagh<sup>1</sup>, S Minkowicz<sup>2</sup>, M Huntsman<sup>3</sup>, A Klug<sup>1</sup>. From the <sup>1</sup>Physiology and Biophysics University of Colorado Anschutz <sup>2</sup>Florida Gulf Coast University, <sup>3</sup>Pharmaceutical Sciences University of Colorado Anschutz.

**64) A comparison of autism-spectrum quotient (AQ) factors in non-clinical populations using mismatch negativity**

Asher Augustinis, L Hirt, B Stewart, L Pantlin. From the Department of Cognitive Neuroscience, Colorado State University.

**65) Manual and automated approaches for quantification of fungiform papillae on the tongue**

Zoe J. Zrelhoff<sup>1</sup>, J Moritz, Jr.<sup>2</sup>, LM Stone-Roy<sup>1</sup>. <sup>1</sup>Department of Biomedical Sciences, Colorado State University, <sup>2</sup>Department of Mechanical Engineering, Colorado State University.

**66) An analysis of cortical and subcortical white and gray matter volume in patients with movement disorders prior to deep brain stimulation treatment**

Jeanelle K. France<sup>1</sup>, J Thompson<sup>2</sup>. <sup>1</sup>From Department of Neuroscience, University of Colorado Boulder <sup>2</sup>Department of Neurosurgery, University of Colorado Anschutz Medical Campus.

**67) Temporal processing in college students indicating high-anxiety**

Zach Thorvaldson<sup>1</sup>, LN Pantlin<sup>1</sup>, D Davalos<sup>1</sup>. From the <sup>1</sup>Cognitive Neuroscience, Department of Psychology, Colorado State University.

**68) Fungiform papillae density across the human tongue correlates with perceived intensity and discrimination ability during electrotactile stimulation for sensory substitution**

Tyler S. Allison<sup>1</sup>, A Danish<sup>1</sup>, J Moritz Jr.<sup>1</sup>, L Stone-Roy<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University.

**69) The relationship between cortical resource allocation, behavior, and neurocognitive function in adults with hearing loss (withdrawn)**

Hannah Glick<sup>1</sup>, Erin Duncan<sup>1</sup>, Anu Sharma<sup>2</sup>. From the <sup>1,2</sup>Department of Speech, Language, & Hearing Science, University of Colorado Boulder.

OTHER TOPICS

**70) Spectral analysis of EEG activity during weekend recovery sleep**

Sarah J. Morton<sup>1</sup>, CM Depner<sup>1</sup>, EL Melanson<sup>2,3</sup>, JR Guzzetti<sup>1</sup>, KP Wright Jr<sup>1,2</sup>. From the <sup>1</sup>Sleep and Chronobiology Laboratory, Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO, USA, <sup>2</sup>Division of Endocrinology, Metabolism, and Diabetes, <sup>3</sup>Division of Geriatric Medicine University of Colorado Anschutz Medical Campus, Aurora, CO, USA.

**71) Culturing primary neurons on patterned adhesive substrate allows for the separation of pre and post synaptic neuronal components**

Marissa J. Metz, ST Hentges. From the Department of Biomedical Sciences, Colorado State University.

**72) Increased c-fos regulation in neocortical subregions in response to social interaction in young and adult female rats**

Angela C Tomczik<sup>1</sup>, AE Perkins<sup>2</sup>, TL Doremus-Fitzwater<sup>2</sup>, RL Spencer<sup>1</sup>, EI Varlinskaya<sup>2</sup>, MM Conti<sup>2</sup>, C Bishop<sup>2</sup>, T Deak<sup>2</sup>. From the <sup>1</sup>Department of Psychology and Neuroscience, University of Colorado Boulder <sup>2</sup>Department of Psychology, Binghamton University.

**73) Machine learning classification of lifestyle intervention outcomes on diffusion imaging data in older adults**

Yun Zhang<sup>1</sup>, M Wadley<sup>1</sup>, O Koyejo<sup>2</sup>, E McAuley<sup>3</sup>, AF Kramer<sup>4</sup>, AZ Burzynska<sup>1</sup>. From the <sup>1</sup>Department of Human Development and Family Studies, Colorado State University, <sup>2</sup>Department of Computer Science, University of Illinois at Urbana-Champaign, <sup>3</sup>Departments of Kinesiology and Psychology, University of Illinois at Urbana-Champaign, <sup>4</sup>The Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign.

## 74) Agonist dependent alterations of mu opioid receptor mobility

Reagan L. Pennock<sup>1</sup>, D Krapf<sup>2</sup>, ST Hentges<sup>1</sup>. From the <sup>1</sup>Department of Biomedical Sciences, Colorado State University, <sup>2</sup>School of Biomedical Engineering and Department of Electrical and Computer Engineering, Colorado State University.

## 75) Role of KChIP in the stability of Kv4 channels in neurons

Derek Schaeuble, G Waro, S Tsunoda. From the Department of Biomedical Sciences, Colorado State University

## 76) Altered encoding of motivational stimuli in the basolateral and central amygdala in cocaine-experienced rats

Katherine J. Stansfield, KL Agster, KS McConomy, CN Brown, MR Payne, MP Saddoris. From the Department of Psychology and Neuroscience, University of Colorado Boulder.

## 77) Serum GFAP levels as a predictor of prion related neurodegeneration.

Joshua D. Estep<sup>1</sup>, SJ Kane<sup>1</sup>, MD Zabel<sup>1</sup>. From the <sup>1</sup>Department of Microbiology, Immunology and Pathology, Colorado State University.

## 78) Neuromorphology of gigantopyramidal cells across artiodactyls, perissodactyls, feliformia, caniformia, primates, a rodent, a lagomorpha, and a diprodontia

B Jacobs<sup>1</sup>, Madeleine Garcia<sup>1</sup>, B Shea<sup>1</sup>. From the Laboratory of Quantitative Neuromorphology, Department of Psychology, Colorado College.

**1) A comparison of selection methods for restudying information: EEG versus participant selection**

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Recently, real time EEG has been used to identify items that will and will not be subsequently recalled. However, to our knowledge, no studies have yet compared how EEG selection compares to individuals' metacognitive judgements regarding what was well versus poorly encoded and thus could benefit from further study. In this experiment, 40 undergraduate students participated in either the self-selection group or the EEG selection group. Each participant was fitted with a B-Alert x10 wireless EEG cap and completed three baseline tasks. Participants then studied 30 words. For all items in both conditions, they indicated whether they would like to restudy the item; the EEG classifier's indication of engagement was also recorded. Next they were given a restudy list based on their condition; items self-selected for restudy appeared for the self-selection group and items selected as low engagement by the EEG classifier appearing for the EEG-selection group. After completing a five minute distractor task all participants had ten minutes to freely recall as many words from the original study list as they could. A moderated regression of number of items studied and group was run on proportion recalled and showed no significant relationship between the number of items self-selected and items recalled ( $p = .15$ ) nor between condition and items recalled ( $p = .82$ ); however, there was a significant negative relationship between the number of items selected in the EEG condition and items recalled ( $p = .05$ ). This indicates that the EEG selection criteria is indeed identifying participants in need of additional learning opportunities, but simple restudy is not sufficient to increase their recall. Further, the present study is consistent with the idea that EEG classifiers can identify trials for which additional assistance with the materials at hand is needed. **Keywords:** EEG, Subsequent Memory, Metacognition

**2) In vivo electrochemical and optogenetic assessment of accumbal dopamine release events in a novel behavioral economics based footshock avoidance task**

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The mesolimbic dopamine (DA) system has historically been implicated in motivational processing under appetitive contexts. Within an appetitive context, mounting evidence supports that transient accumbal DA release events increase in response to reward predictive cues, represent intrinsic reward value, and causally modify reward-seeking. Less, however, is known regarding the role DA plays in an aversive context. Using fast-scan cyclic voltammetry (FSCV), we recently demonstrated that accumbal DA release events are increased in response to aversive stimuli both when animals are presented with a cue signaling the opportunity to actively avoid electric foot shock as well during successful avoidance behavior. Here we investigate whether DA concentration scales as a function of the value of footshock avoided and whether optical stimulation of DA neurons causally modifies the price animals are willing to pay to avoid footshock. Here we first developed a novel behavioral economics task in which rats are provided the opportunity to operantly avoid electrical footshock across epochs wherein unit-price (response requirement/mA shock avoided) increases on a semi-exponential array. In congruence with previous appetitive research, the concentration of DA observed at the avoidance-predictive cue as well as at successful avoidance decreased as a function of increasing unit-price. To assess causality, we optogenetically activated channelrhodopsin-2 expressing DA neurons within the ventral tegmental area to selectively augment DA release at either cue onset or during successful avoidance. Our preliminary results suggest that augmenting release at cue onset decreases the maximal price paid to avoid footshock; whereas augmenting release at successful avoidance increases the maximal price paid to avoid footshock. Next, we sought to assess the role of anxiety in our behavioral economic avoidance task by pre-treating rats with the benzodiazepine, diazepam. While at low doses, diazepam increased the maximal price animals pay to avoid footshock, a decrease in avoidance occurred in a high dose range—an effect perhaps due to the sedative effects produced by high dosages. Together, these findings suggest that transient, accumbal DA release events play an integral role in the assessment of and behavioral response to aversive stimuli as well as suggest that the neuronal circuitry underlying anxiety strongly influence the valuation of avoidance. **Keywords:** dopamine, motivation, aversive, Fast-scan cyclic voltammetry

**3) Cognitive deficits in a mouse model for schizophrenia**

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Schizophrenia is a neuropsychiatric disorder estimated to affect about 1.1% of the world's population, with an estimated 2.2 million suffers in the U.S. Symptoms are debilitating and spilt into three types: positive, negative, and cognitive. Historically, research has focused on the positive and negative symptoms, with little focus on the cognitive deficits, which include working memory, executive function, and impaired ability to maintain focus. Recently missense mutations of the CaMKII $\alpha$  gene have been identified in human schizophrenic patients (Purcell et. al., 2014). This is interesting because CaMKII $\alpha$  is involved in long term potentiation and, therefore, these mutations may underlie learning deficits in these patients. Our research focuses on whether decreased expression

of CaMKII $\alpha$  elicits deficiencies in associative learning and whether cognitive deficits are accompanied by changes in neural oscillatory activity in the CA3 region of the hippocampus. We used an olfactory associated learning task (oALT) to compare behavioral performance between mice heterozygous for CaMKII $\alpha$  (Hets) and wild type controls (WT). The oALT is a go/no go behavioral task where water deprived mice learn to respond to one of two odorants to obtain a water reward. We also performed extracellular local field potential (LFP) recording in the CA3 region of the hippocampus, to record the theta phase amplitude coupling studies of gamma local field potential oscillations that are thought to play a role in hippocampal learning. In preliminary studies we found that the Het underperformed the WT in the oALT, and also we found differences in the theta phase for gamma LFP amplitude for Hets compared to the WT. We are following up on these findings to determine whether deficiency in associative learning in the Hets is correlated with differences in phase amplitude coupling in CA3 in the hippocampus.

**Keywords:** Schizophrenia, CaMKII $\alpha$ , long term potentiation, electrophysiology

#### 4) The effect of 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) on extinction and reconsolidation of fear memory

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Traumatic memories are the central cause of posttraumatic stress disorder (PTSD). Current therapeutic strategies for PTSD thus focus on inhibiting fear memories, or the establishment of stronger competing memories. Currently, these strategies have poor long-term efficacy. New techniques to enhance the standard therapies are greatly needed. In human studies psychotherapy paired with moderate-dose 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) has shown promise in reducing symptoms of PTSD, but the means by which MDMA reduces fear is unknown. MDMA administered during psychotherapy could either enhance fear extinction (the learning that trauma cues no longer predict threat) or impair fear memory reconsolidation (the process of strengthening fear memories after recall). The goal of these experiments is to determine whether MDMA enhances fear extinction or impairs fear memory reconsolidation in a rodent model of fear. Adult, male Long Evans rats were exposed to a traumatic event consisting of an auditory tone co-terminated with a mild footshock. This conditioning procedure results in strong fear memories in rodents-characteristic of trauma memories in PTSD. The day after fear conditioning, rats were given either saline or MDMA (1, 2, or 3 mg/kg; i.p.) 30min prior to fear extinction learning. Memory for fear extinction was then tested 1 and 7 days later. Rats were also re-exposed to the conditioning context after the extinction protocol to test for general memory impairment from MDMA administration. To determine the effect of MDMA on fear memory reconsolidation, rats were briefly re-exposed to the conditioning context to reactivate the fear memory. Saline or MDMA (3 or 5 mg/kg; i.p.) was administered immediately after fear memory recall, during their fear memory reconsolidation phase. Strength of the fear memory was tested the next day. MDMA (3 mg/kg) enhanced short-term fear extinction memory, and did not influence generalized memory impairment. Fear extinction could therefore be a target of MDMA-paired psychotherapy. Future studies will investigate if MDMA has a differential effect on long-term memory. **Keywords:** Fear, memory, extinction, reconsolidation, MDMA, ecstasy, PTSD, anxiety

#### 5) Response inhibition represented by the N200 in adults in a Go-NoGo task

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Researchers are developing biomarkers for human functioning using measures derived from electroencephalography (EEG) such as event related potentials (ERPs). For example, the inhibitory N2 ERP component is elicited following "NoGo" stimuli of a Go-NoGo task and is believed to represent one's inhibitory abilities. Despite abundant research on the inhibitory N2, to date, no studies have examined the test-retest reliability of the component. Additionally, a variety of stimuli in Go-NoGo tasks have been used to elicit the inhibitory N2 across studies (letters, pictures, sounds), yet no research has determined whether different stimuli elicit the same neural response (i.e., validity of the Go-NoGo paradigm). Establishing the psychometric properties of ERPs and paradigms is essential for the development of robust biomarkers. The purpose of this study is to establish the psychometrics of the inhibitory N200 in a Go-NoGo task. Thirty young adults aged 18-25 will be recruited from the community to complete two sessions of EEG data collection. During each session, participants will complete two versions of a Go-NoGo task. Test re-test reliability of the inhibitory N2 will be established using correlations. I predict reliability will be high. To establish validity of the paradigm, differences in N2 amplitudes will be measured using a repeated measures ANOVA. I expect to see differences in amplitude due to emotional valence associated with different stimuli in the two versions of the Go-NoGo task. This study could inform scientists and professionals in the medical field about the development of N200 as a biomarkers of inhibitory control.

## 6) P200 Sensory Gating in Children with Autism

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Sensory gating is the neurological process that filters out irrelevant stimuli to prevent sensory overload of higher brain functions. Gating is commonly studied using electroencephalography (EEG) via a paired click paradigm. Most studies examine gating at the P50 ERP (event-related potential) component, which is a positive deflection occurring around 50 ms after stimulus onset and relates to pre-attentional inhibitory mechanisms. In neurotypical individuals, there is an attenuation of second click amplitude compared to first click amplitude, indicating sensory gating. Impaired gating has been documented in children with autism spectrum disorders (ASD) at the P50 component. However, sensory gating has not been studied at the P200 component, which is a positive deflection that occurs around 200 ms post-stimulus onset and relates to the registration of stimuli. The purpose of this study was to analyze gating in the P200 component in children with ASD. Based on previous studies, we hypothesized that there will be impaired sensory gating at the P200 component in children with ASD. A cross-sectional quantitative study was employed to compare two groups when performing the paired click paradigm. To date, EEG data has been recorded from 20 children with ASD and 20 neurotypical controls. Data will be analyzed using statistical procedures to compare the two groups with regards to the processing of click stimuli and sensory gating for the P200 component. These results can help practitioners understand aspects of sensory processing that appear difficult for children with ASD and may suggest more effective treatment strategies for children with ASD.

## 7) Exercise increases mTOR signaling in brain regions involved in cognition and emotional behavior

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Exercise can enhance learning and memory and produce resistance against stress-related psychiatric disorders such as depression and anxiety. In rats, these beneficial effects of exercise occur regardless of exercise controllability: both voluntary and forced wheel running produce stress-protective effects. The mechanisms underlying these beneficial effects of exercise remain unknown. The mammalian target of rapamycin (mTOR) is a translation regulator important for cell growth, proliferation, and survival. mTOR has been implicated in enhancing learning and memory as well as antidepressant effects. Moreover, mTOR is sensitive to exercise signals such as monoamines and metabolic signals. The effects of exercise on mTOR signaling, however, remain unknown. The goal of the present study was to test the hypothesis that exercise, regardless of controllability, increases levels of phosphorylated mTOR (p-mTOR) in brain regions important for learning and antidepressant responses. Rats were exposed to 6 weeks of either sedentary (locked wheel), voluntary, or forced wheel running conditions. At 6 weeks, rats were sacrificed during peak running and levels of p-mTOR were measured using immunohistochemistry. Overall, both voluntary exercise and forced exercise increased p-mTOR-positive neurons in the medial prefrontal cortex, striatum, hippocampus, and amygdala compared to locked wheel controls. Exercise, regardless of controllability, also increased numbers of p-mTOR-positive glia in the striatum, hippocampus, and amygdala. For both neurons and glia, the largest increase in p-mTOR positive cells was observed after voluntary running, with forced exercise causing a more modest increase. Interestingly, voluntary exercise preferentially increased p-mTOR in astrocytes (GFAP+), while forced running increased p-mTOR in microglia (CD11+). Results suggest that mTOR signaling is sensitive to exercise, but subtle differences exist depending on exercise controllability. Increases in mTOR signaling could contribute to the beneficial effects of exercise on cognitive function and mental health.

**Keywords:** Exercise, mTOR, glia, cell signalling, learning, cognition

## 8) Basic word processing and recognition in bilingual and monolingual individuals

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Previous behavioral literature suggests that multilingual individuals use multiple processing systems that engage in simple word recognition; thus, delaying response time in picture-naming and word-recognition tasks presented. This study addresses the difference in word processing in monolingual and bilingual individuals, specifically, the delayed response time showed by bilingual individuals compared to monolingual individuals regarding basic word recognition. The study's main objective is to identify differences in neural processing that occur in basic word recognition, as well to examine those differences. To do so, two different tasks will be used, both tasks will be picture-naming related tasks, one will be an immediate response, while the other one will be a delayed response. The delayed response task will allow us to see if the delay is due to more complex word processing or simply due to individual delay. We believe that the delay observed in bilingual individuals is due to more complex neural processing in word recognition. That being said, will bilingual individuals actually be slower to respond than monolingual individuals? And will that delay/difference disappear in the "delayed response" task? The results will expand the understanding of language processing, as well as compare basic word-recognition processing in bilingual and monolingual individuals. **Keywords:** Word processing and recognition

## 9) DREADD-induced activation of the nigrostriatal dopamine pathway modulates fear extinction and reduces fear renewal

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Identification of novel strategies to reduce fear relapse after extinction is of high priority. Dopamine (DA) can enhance fear extinction, but the distinct DA circuits able to facilitate extinction are unknown. Although mesocortical DA can inhibit fear extinction, the effect of mesolimbic and nigrostriatal DA activity on fear extinction is unclear. Phasic DA release in the striatum increases as fear extinction is learned, due to the error in prediction that the unconditioned stimulus follows the conditioned stimulus (CS). Phasic DA increases signaling at low-affinity D1 receptors implicated in promoting movement and reward, and anatomically linked to fear circuitry. Dorsal striatum (DS) D1 receptors, in particular, are sensitive to manipulations that can enhance fear extinction and reduce fear relapse in new contexts (renewal), such as acute exercise. The DS supports learning strategies that do not involve hippocampal or contextual components, further implicating the DS in the learning of fear extinction memories resistant to contextual modulation. We utilized Designer Receptors Exclusively Activated by Designer Drugs (DREADD), receptors activated by CNO, to increase phasic activity of substantia nigra pars compacta (SNc) DA neurons, the origin of the nigrostriatal pathway, in order to test the hypothesis that activation of the nigrostriatal DA circuit enhances fear extinction. Following auditory fear conditioning, adult male wild-type or TH-Cre rats injected with AAV-hSynrM3DQ-mCherry into the SNc, received either vehicle or CNO (1 mg/kg i.p.) 30 min before 2 sequential fear extinction sessions. Twenty-four hours after the second extinction session, rats were placed (drug-free) into either the familiar extinction context or a novel context and exposed to the auditory CS to assess fear renewal. Activation of the nigrostriatal DA pathway during fear extinction enhanced fear extinction and prevented fear renewal. This effect of nigrostriatal DA activation was mimicked by pharmacological activation of DS D1 receptors elicited by intra-DS SKF38393 (5  $\mu$ g/ $\mu$ l; 2  $\mu$ l/side). Data suggest that phasic activity of the nigrostriatal DA circuit represents a novel target for rendering fear extinction memory resistant to contextual modulation and relapse. **Keywords:** Fear extinction, dopamine, DREADD

## 10) Dopamine Release in the Medial Dorsal Striatum During Voluntary Exercise

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Despite the clear health benefits of physical activity, the participation in exercise by the general public is in constant decline. Identifying factors contributing to motivation to participate in exercise could have dramatic effects on quality of life. The neurotransmitter dopamine has been shown to play a crucial role in movement, reinforcement, and goal-directed behavior. There are two well-characterized patterns of dopamine release: tonic and phasic. Tonic is characterized by spontaneously occurring baseline release, and phasic by high-frequency, burst-firing which can drastically increase dopamine efflux. Indeed, phasic DA increases signaling through low-affinity dopamine 1 receptors thought to be particularly important for reinforcement and the promotion of movement. There is a general assumption that physical activity increases dopamine concentrations in target brain areas that promote reinforcement and movement, however the effect of voluntary exercise on phasic dopamine release has not been investigated. We characterized phasic dopamine release events in rats during voluntary wheel running using fast-scan cyclic voltammetry. Phasic dopamine release was measured in the dorsal striatum before, during, and after an acute voluntary wheel running bout, in rats with a history of between 1 and 3 weeks of prior nightly exercise. Data indicates that Phasic DA release in the DMS increases during a running bout. As exercise behavior becomes habitual, the DA concentration decreases but the frequency of release events remains elevated. These data represent the first characterization of phasic dopamine release events during spontaneous, voluntary exercise, and could provide novel insight into the role of dopamine in guiding motivated behavior.

## 11) The MAGL inhibitor MJN110 decreases aggressive behavior after post-weaning social isolation in male and female adolescent rats

LM Dawud, Esteban C. Loetz, J Fontenot, T Khan, D Tauber, I Brailleur, ST Bland.

Post-weaning social isolation (PSI), also known as isolation rearing, interferes with normal social development and produces a behavioral phenotype that includes increased aggression. PSI also alters the endocannabinoid system in brain regions including the medial prefrontal cortex. The MAGL inhibitor MJN110 increases levels of the endocannabinoid 2-arachidonoylglycerol (2-AG) in the CNS, and we have previously shown that MJN110 impacts social behavior. Moreover, MJN110 differentially altered phosphorylation of mammalian target of rapamycin (p-mTOR) in neurons and astrocytes within the medial prefrontal cortex (mPFC). Here, we tested the hypothesis that MJN110 would decrease aggressive behavior after PSI. Male and female Sprague-Dawley rats were exposed to either 4 weeks of PSI or group housing starting on postnatal day (PSD) 21, and on PND 49 underwent a 15 min trial of social interaction with a novel, same-sex juvenile rat. Prior to the social interaction, rats received either 0, 1, or 5 mg/kg of MJN110. Behavioral trials were recorded and assessed, and brains were removed for p-mTOR immunohistochemistry. We observed that MJN110 dose-dependently decreased aggressive grooming while

having no effects on overall social behavior or on play behaviors. This effect was largely due to decreased aggressive grooming in isolates and was observed in both males and females. These results suggest that endocannabinoids are involved in appropriate social behavior during adolescence. **Keywords:** Endocannabinoids, 2-AG, Social Isolation, PFC

## 12) Early life exposure to predictable maternal behavior has a long-term influence on cognitive performance in rodents and humans

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Caregiving behaviors during early life have a persisting effect on offspring development. In humans, quality of caregiving is evaluated using global measures such as sensitivity and responsiveness to the infant's needs. However, global constructs provide little insight into specific processes by which maternal care may influence offspring development, limiting our ability to explore underlying biological mechanisms. Further, animal models demonstrate that the pattern of maternal signals influences long-term offspring vulnerability. As part of the Conte Center on Brain Programming in Adolescent Vulnerabilities, the current study uses novel methodology to characterize predictability of maternal behavior in humans and rats and explores the link between the predictability of maternal behavior and offspring cognitive development using a longitudinal study design. We observed 128 mothers and their 12-month-old infants during a 10-min play session. Maternal behaviors categorized as providing tactile, auditory, or visual stimulation to the child were recorded and used to calculate an entropy rate (predictability) score for each mother. Child cognitive development was assessed at 2 years of age using the Bayley Scales of Infant Development (BSID) and at 6.5 years using the WRAML. We also compared the hippocampal-dependent spatial memory of adolescent rats exposed to normal rearing conditions to those exposed to restricted bedding material from P2-P9, a manipulation that induces less predictable maternal behavior. We found that unpredictable maternal behavior (high entropy rate) at 12 months predicted lower cognitive performance on the BSID at 2 years ( $r = -.198$ ,  $p = .027$ ) and on delayed recall memory at 6.5 years ( $r = -.027$ ,  $p = .037$ ). In rodents, spatial memory was impaired among offspring exposed to unpredictable maternal behavior ( $p = .02$ ). The current study provides cross-species evidence that unpredictability of maternal signals during vulnerable periods of early life has a long-term influence on offspring cognitive development. These findings also demonstrate the importance of understanding maternal behavioral patterns and factors influencing them. Future work will examine the biological mechanisms underlying the observed links between maternal behavior and offspring development. **Keywords:** Early life experience, cross-species, cognitive development, stress, fetal programming

## 13) Dorsal striatum neurons expressing dopamine-1 receptors are recruited during fear extinction and are activated by DREADD-induced dopamine

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Previous studies suggest that dopamine (DA) can enhance fear extinction, but neural circuitry underlying this extinction modulation is largely unknown. Phasic activity of DA systems can be augmented during fear extinction using Designer Receptor Exclusively Activated by Designer Drug (DREADD). DREADD-induced DA efflux would be expected to increase low-affinity D1 receptor signaling in target regions, but this has yet to be verified. Using double fluorescent in situ hybridization (FISH) for *cfos* and D1 mRNAs, we investigated whether striatal neurons expressing D1 receptors are recruited during fear extinction, and if activity of these neurons can be augmented by DREADD-induced phasic DA. DREADD virus was microinjected bilaterally into the substantia nigra (1  $\mu$ l / side). After 4 weeks, to allow ample time for viral expression, adult, male wild-type or TH-Cre Long Evans rats underwent auditory fear conditioning. The following day, rats were injected intraperitoneally with the designer drug Clozapine-N-Oxide (CNO) 30 min prior to fear extinction learning or control conditions. Fear extinction learning increased *cfos* mRNA in D1-expressing neurons of the dorsal striatum (DS), suggesting that D1 receptors in the DS are recruited during fear extinction. Moreover, DREADD-induced DA increased activation of DS D1-expressing neurons, indicating that D1 receptors in the DS are a target of DREADD-induced augmentation of the nigrostriatal DA pathway. Activity of D1-expressing neurons in the ventral striatum is currently being analyzed. These results suggest that DS D1 receptors could be involved in fear extinction, and provide important new information regarding functional effects of DREADD-induced DA activity.

## 14) An exploratory examination of oscillations in patients with traumatic brain injury following neurofeedback training

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Over 1.7 million traumatic brain injuries (TBI) are diagnosed per year and TBIs account for 30.5% of injury-related death in the US. TBIs are the result of an assault to the head, often causing a loss of consciousness and long lasting or permanent cognitive, physical, and psychosocial deficits that prevent patients from fully readapting. Due to the

lack of long term treatment options, the practicality of EEG neurofeedback (NFB) training as an effective therapy has been assessed. NFB uses real-time neurophysiological activity (i.e. oscillations) to improve self-awareness of functioning and self-regulation. Oscillations are a defined frequency range that corresponds to specific cognitive functions or states of psychological arousal. Oscillations have demonstrated plasticity in training, which supports the exploratory component of this study: to examine if a specific bandwidths demonstrate a larger response to NFB training. The response is quantified by convergence back to normalized standards. Oscillations are pathological if they are  $\pm 2$  standard deviations outside of the normative database. The purpose of this study was to examine the overall effectiveness of NFB. The hypothesis was that (1) NFB would produce a significant change in average amplitude across sessions, indicating that the patient's oscillations patterns were approaching the normalized standards. To further address individualized treatment, this study also explored which bandwidths (delta, beta, etc.) would be more responsive to NFB. Participants (N=39) were patients at a TBI unit of a 280-bed inpatient rehabilitation center, had a history of post-injury aggressive behavior, and participated in 20 sessions. Sessions were individually specialized for each participant via QEEG analysis to identify amplitudes that were outside of the normative range, which were then targeted in session. Preliminary analyses indicated a significant change across sessions. Averages of both the first 5 sessions and the final 5 sessions (of 20) were compared. Overall, the delta bandwidth means approached significance across time points ( $t(38)=2.02$ ,  $p=.068$ ). Beta wave means did not demonstrate an effect. Initial trends demonstrated that patients' oscillations may be returning to a normative standard through NFB training; however, confirmatory analyses will be conducted by presentation date. Initial analyses supported oscillation plasticity and that certain bandwidths may be more responsive to NFB training.

**Keywords:** neurofeedback, traumatic brain injury, oscillation, bandwidth

### 15) Examining schizotypal personality disorder using mismatch negativity

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Previous research has examined the relationship between temporal processing disorders that are classified by temporal disturbances, such as schizophrenia (SZ). One electrophysiological paradigm that can be utilized to quantify this relationship is the event-related potential (ERP) mismatch negativity (MMN). Schizotypal personality disorder (SPD) and SZ both fall on the schizophrenia spectrum, but SPD differs from SZ in that SPD is a personality disorder as opposed to a psychotic disorder. While SPD patients might experience delusions, this disorder is not characterized by a loss of touch with reality. However, similarities do exist between patients with SPD and patients with SZ including cognitive deficiencies in the realm of verbal learning (Vogtmaier et al., 1997), early information processing impairments (Hazlett, Rothstein et al., 2015), and sensory gating disturbances (Hazlett et al., 2015). Given the previous commonalities between these disorders, patients who score high on the schizotypal personality disorder questionnaire (SPQ) may elicit MMN reductions similar to those observed in SZ patients. The present study aimed to examine the relationship between MMN amplitudes and participants who scored above the established cut-off score on the SPQ. The hypothesis was that individuals who were categorized as symptomatic for SPD would have less negative MMN amplitudes than those considered healthy controls. Participants (N=67) completed the SPQ and scores were coded. Those who scored above a 41 were grouped as symptomatic ( $n = 29$ ) and those who scored below a 41 were grouped as control ( $n = 38$ ). Brain activity was recorded using EEG while participants were listened to 2880 samples (120 cycles of 24 samples) of randomized tones that differed in duration (Standard = 500 ms; Deviant 1 = 425 ms; Deviant 2 = 250 ms). The results from Deviant 1 indicated there was a significant difference between groups at the Cz and Fz electrode locations (Fz:  $t(48) = 3.19$ ,  $p = 0.001$ ; Cz:  $t(53) = 2.88$ ,  $p = 0.003$ ; Pz:  $t(63) = 1.59$ ,  $p = 0.058$ ). The results from Deviant 2 indicated there was a significant difference between groups at the Cz electrode location (Fz:  $t(59)=1.02$ ,  $p = 0.157$ ; Cz:  $t(60)= 1.79$ ,  $p = 0.039$ ; Pz:  $t(60)= 0.43$ ,  $p = 0.334$ ). Current results support further investigation into the utility of MMN as a tool to distinguish between healthy individuals and those individuals who might develop SPD prior to the actual onset of the disorder. **Keywords:** mismatch negativity, schizotypal personality disorder, event-related potential, biomarker

## DEVELOPMENT

### 16) Developmental neuropathology of *Xenopus laevis* tadpoles exposed to bisphenol-A, a chemical found in treated wastewater effluent from Laramie, Wyoming

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The effluent discharged from the Laramie Wastewater Treatment Plant into the Laramie River contains a variety of prescribed and recreational drugs, personal care products, and industrial chemicals. Many of these compounds are neuroactive, meaning that they can affect neural system function. To study the neurological effects that these chemicals might have on a developing nervous system, we use the *Xenopus laevis* tadpole visual system as our model. This powerful model develops completely externally, allowing us to expose embryos to any desired chemical for the entirety of their development. To begin our investigation of the compounds found in the effluent,

we selected a chemical called bisphenol-A (BPA) as our initial compound of interest. This chemical is a commonly used plasticizer in many consumer products including plastic disposable water bottles, canned foods, and receipt paper. For this study, tadpoles were exposed to BPA at a range of sublethal concentrations during the developmental stages when visual circuit formation is known to occur. At 8 days post-fertilization, visual system function was evaluated at the behavioral, circuit, and cell levels. Our preliminary data indicate that BPA at a concentration of 15 $\mu$ M significantly impairs tadpole visual system function at the behavioral level. This was assessed using a visually guided avoidance behavior test based on the fact that tadpoles often avoid black moving dots projected onto the floor of their glass containers. We have also identified morphological abnormalities in axon targeting within tadpole brains that have been exposed to this same concentration of BPA (15 $\mu$ M). Retinal ganglion cell axons were visualized by filling them with the lipophilic dye, Dil and imaged using confocal fluorescence microscopy. These abnormalities could be indicative of improper circuit formation during development. These effects will be further characterized by carrying out a set of electrophysiological-based experiments to measure synaptic properties of the circuit. After we have identified and characterized the effects of BPA in the visual circuit of the developing tadpole, we plan to investigate the effects of other chemicals found in the effluent, including a neurologically active drug, gabapentin. Overall, these analyses will contribute to better evaluation of wastewater treatment plant effluents not only in Laramie, but also across the nation.

### 17) Developmental expression of ER $\beta$ in the dorsal raphe and prefrontal cortex of male and female mice

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Estrogen signaling is paramount in organizing sex differences in numerous brain functions, including stress responses, social behavior, and neurobehavioral disorders such as depression and anxiety. Midbrain regions, such as the dorsal raphe nucleus (DR), express estrogen receptors, particular estrogen receptor (ER)  $\beta$ , but few studies have examined their ontogeny or looked for sex differences. The DR is the main source of forebrain serotonin, which plays a critical role in many components of behavior and physiology. Moreover, sex differences in developmental expression of ER $\beta$  may contribute to, and potentially program, serotonergic output to many forebrain regions, including the prefrontal cortex (PFC), a major efferent target of the DR. In this study, we used immunohistochemistry to label serotonergic neurons within the DR of ER $\beta$ -EGFP transgenic mice to compare the distribution of ER $\beta$  in serotonergic and nonserotonergic populations of DR neurons in male and female mice on postnatal days 2, 4, and 14. Results suggest that young male mice have more serotonergic DR neurons than female mice do, but neonatal mice of both sexes have many ER $\beta$ -EGFP DR neurons that exist in both serotonergic and nonserotonergic neurons. We also measured differences in ER $\beta$  distribution in the PFC of these mice and used immunohistochemical labeling of doublecortin to assess whether ER $\beta$  was expressed in undifferentiated neurons. Preliminary results suggest that although both male and female mice express ER $\beta$  in many FC neurons, patterns may differ across development and between the sexes. Moreover, neither male nor female mice of any age had ER $\beta$  within undifferentiated neuroblasts (doublecortin-immunoreactive) in the PFC. These differences in ER $\beta$  expression indicate time- and sex-dependent mechanisms for lasting effects of estrogens on cognition, behavior, and physiology during adulthood.

### 18) Prenatal dexamethasone exposure induces a female-specific alteration in the postnatal leptin surge in rat

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Overexposure to glucocorticoids (GCs) during gestation increases the risk for developing disease such as metabolic syndrome in adulthood. However, little is currently known about the mechanisms underlying the developmental programming of adult disease by GCs. In rodents, a potential mechanism for the programming of metabolic syndrome is a surge of leptin during the 2nd week of postnatal life that allows the appropriate development of hypothalamic circuitry that controls food intake, metabolism and adiposity. In this study, we investigated the effects of maternal exposure to synthetic GCs on the postnatal surge of leptin as a candidate hormone for the fetal programming of adult disease by administering 0.1 and 0.4 mg/kg dexamethasone (DEX) to time-pregnant dams daily during days 18-21 of gestation. Blood was collected from offspring on postnatal days (PD) 0, 7, 10, 13, 17 and 21 and plasma was then assayed for leptin levels using an enzyme-linked immunosorbent assay. As we have previously reported, in utero exposure to DEX resulted in a significant reduction in birth weight and evidence of macrovesicular hepatic steatosis in adulthood, as detected by Oil Red O staining in liver. Relative to PD 0, there was an increase in plasma leptin levels during the 2nd postnatal week that peaked at PD 13 in vehicle-treated groups (VEH). However, in female offspring, in utero exposure to 0.1 mg/kg DEX resulted in a significant reduction in plasma leptin concentration, relative to VEH at PD 10 (VEH: 7.8  $\pm$  1.0 ng/ml vs. 0.1 mg/kg DEX: 4.6  $\pm$  0.9 ng/ml) and at PD 13 (VEH: 11.0  $\pm$  1.5 ng/ml vs. 0.1 mg/kg DEX: 4.7  $\pm$  0.6 ng/ml). Exposure to 0.4 mg/kg DEX in utero in female rats did not significantly reduce plasma leptin at any PD as compared to vehicle-treated controls. In contrast to females, male offspring showed plasma leptin levels that were highest at PD 13 (Veh: 8.65  $\pm$  1.68 ng/ml), but were not significantly altered by in utero DEX exposure at any age. We are currently determining the consequences of alterations in the leptin surge during early postnatal development by prenatal DEX treatment. An altered leptin surge

could dramatically alter the development of hypothalamic circuitry controlling food intake and adiposity, thereby shedding light on a potential mechanism by which maternal exposure to sGCs programs adult metabolic syndrome. **Keywords:** Leptin, Metabolic Syndrome

## 19) Regulation of synaptic growth by FMRP-containing RNA processing bodies

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Fragile X syndrome (FXS) is the most common form of inherited intellectual disability in children and is the best characterized monogenetic cause of autism. FXS is caused by loss of the Fragile X Mental Retardation Protein (FMRP), an RNA binding protein that has been implicated in the control of synaptic development and plasticity in the wild-type brain. FMRP acts as a translational regulator, presumably through the direct association with structural elements in the untranslated regions (UTRs) of target mRNAs, and to repress mRNA translation at the level of initiation and elongation. The absence of FMRP leads to translational dysregulation, a condition believed to underlie the cellular defects associated with FXS. We have previously shown that FMRP interacts genetically and biochemically with cytoplasmic RNA processing bodies (P-bodies) in glutamatergic motor neurons in a *Drosophila* FXS model. FMRP-containing P-bodies (FMRP/P-bodies) have also been identified in mammalian neurons and traffic to synapses in response to stimuli normally associated with long-term plasticity. P-bodies are highly conserved ribonucleoprotein particles (RNPs) that are involved in mRNA deadenylation followed by translational repression or decapping and 5' to 3' decay. Interactions between FMRP and P-bodies suggest that FMRP-mediated deadenylation and decay may represent an uncharacterized regulatory mechanism in neurons. Here, we examine the relationship between FMRP and P-bodies in additional detail. We find that FMRP interacts genetically with genes encoding for conserved P-body proteins to control synaptic growth at the larval neuromuscular junction (NMJ). FMRP forms punctae in motoneuron cell bodies and these RNPs traffic in axons projecting to the NMJ. Finally, we show that FMRP-containing particles are highly dynamic structures and that conserved RNA binding domains within FMRP influence dynamics as well as interactions with P-body components. Together, our findings begin to shed light on an important but novel function for FMRP in neurons. **Keywords:** Fragile X Syndrome, FMRP, ribonucleoprotein particles, RNA processing bodies

## 20) Development of a *Drosophila* Vps54 model for motor neuron disease

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Vacuolar sorting protein 54 (Vps54) is a subunit of a heterotetrameric tethering factor called the Golgi-associated retrograde protein (GARP) complex. The GARP complex is associated with the trans-Golgi network (TGN) and functions as a tethering factor that is involved in endosome-to-TGN transport. A hypomorphic mutation in the Vps54 gene is the underlying cause for the wobbler mouse model for human motor neuron disease. The wobbler mouse shares clinical features with Amyotrophic lateral sclerosis (ALS) including the progressive neurodegeneration of both upper and lower motor neurons. The wobbler mouse also share many cytological hallmarks with ALS including Golgi fragmentation, mitochondrial dysfunction, axon transport defects, neurofilament accumulation, and TDP-43 (TAR DNA binding protein 43) aggregation. Here, we demonstrate that *Drosophila* Vps54 has a presynaptic function in the control of synaptic development at the glutamatergic larval neuromuscular junction (NMJ). Vps54 localization in larval motoneurons overlaps with markers for both the trans-Golgi network and early endosomes. Interestingly, Vps54 loss-of-function leads to Golgi fragmentation, a preclinical phenotype observed in motor neurons in the wobbler mouse and ALS model systems. Vps54 loss-of-function also results in the accumulation of neuronal RNA processing bodies (P-bodies) in the soma. In wild-type animals, these highly conserved ribonucleoprotein particles (RNPs) are actively transported in motoneuron axons that project to the NMJ. Finally, Vps54 homozygous mutant adults are male sterile, have a significantly reduced lifespan, and show phenotypes consistent with motor defects. Similarly, mice homozygous for the homozygous wobbler mutation are infertile and die prematurely with progressive motor impairments. Collectively, these data are beginning to suggest that *Drosophila* Vps54 mutants recapitulate wobbler mouse phenotypes. We hope to take advantage of the power of fly genetics to explore the relationship between Vps54, vesicle trafficking pathways, and ALS. **Keywords:** Vps54, GARP complex, vesicle trafficking, *Drosophila*, P-bodies, ALS

## 21) Coordinated regulation of translation by FMRP and the miRNA pathway

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Fragile X syndrome (FXS) is caused by the inability of the FMR1 gene to produce the Fragile X Mental Retardation (FMRP) protein in affected individuals. FMRP is an RNA-binding protein and is widely believed to repress translation of target mRNAs through a mechanism involving either translational elongation or initiation. In axons and dendrites, FMRP localizes to ribonucleoprotein particles (RNPs) that are actively transported towards the synapse. Interestingly, these RNPs also contain miRNAs and conserved components of the miRNA-containing RNA-induced silencing complex (miRISC). It has been shown that FMRP interacts biochemically and genetically with RISC

proteins to control synaptic development. The RISC regulates translation by targeting mRNAs for deadenylation followed by repression or 5' to 3' exonucleolytic decay (and does not repress at the level of initiation or elongation). Interaction between FMRP and the miRISC suggests that FMRP might be regulating an important set of neuronal transcripts via this mechanism. Here, we use a *Drosophila* FXS model system to examine coordinated regulation of translation by FMRP and the miRNA pathway. We have used a novel reporter assay to show that FMRP-mediated repression requires components of the miRISC. Moreover, we demonstrate that repression of the reporter by a miRNA requires FMRP binding. In vivo, FMRP colocalizes with the miRISC and deadenylation machinery in the larval ventral ganglion. FMRP also interacts genetically with genes encoding for miRISC proteins and deadenylation enzymes to control synaptic development at the glutamatergic larval neuromuscular junction (NMJ). Collectively, these data support our model where FMRP is controlling the expression of important neuronal mRNAs involved in synaptic growth via miRNA-mediated deadenylation. We predict that these studies will provide important additional insight into the molecular basis of mental retardation in FXS patients. **Keywords:** Fragile X Syndrome, ribonucleoprotein particles, miRNA pathway, *Drosophila*

## 22) A role of presenilin in the developing visual circuit of *Xenopus* tadpole

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Presenilin (PS) is an interesting molecule that was first identified, and named, in the context of Alzheimer's disease, but is now known to carry out a myriad of functions that are important during development. As the catalytic component of  $\gamma$ -secretase, PS is responsible for cleaving a wide range of substrates that are crucial for many phases of nervous system development, including neurogenesis, differentiation, and axon guidance. This suggests a global and multifaceted role for this molecule in the development of neural circuits. Here, to provide a comprehensive understanding of the roles PS plays in circuit development we use the *Xenopus* tadpole retinotectal projection as our model. This projection is the major component of the amphibian visual system. This model system allows for the function of a protein to be characterized across all stages of neural circuit development at the cell, circuit, and behavioral levels. First, western blot studies confirmed that PS is expressed in the tadpole optic tectum during the time when the retinotectal circuit is forming. To test the role of PS during the development of this circuit, PS function was inhibited globally by adding the PS blocker L685,458 (5 $\mu$ M) to the tadpoles' rearing solution during development, or by electroporating a PS morpholino into the tectum to knock down PS expression specifically in the postsynaptic tectal neurons. We found that blocking PS function using either of these approaches significantly compromised visual avoidance behavior, which was quantified using an established moving dot test (control: 65.6%  $\pm$  5.9%, n=25; PS morpholino: 33.3%  $\pm$  4.9%, n=30). This suggests deficits in visual system function. To further identify the underlying pathology at the circuit level, we performed in-vivo whole cell electrophysiological recordings from PS-inhibited neurons. We found that PS morpholino-transfected neurons displayed significantly decreased peak current amplitudes in response to light-activated RGC input (control: 72.07  $\pm$  11.01 pA, n=15; PS morpholino: 28.87 $\pm$ 3.43 pA, n=16) while passive electrical properties such as resting membrane potential, input resistance, and capacitance were unchanged compared to control. This indicates that the decreased light responses could be due to compromised synaptic transmission. Thus far, our results suggest a role for PS in the normal development and function of the tadpole visual system.

## DISORDERS OF THE NERVOUS SYSTEM

## 23) Identifying genes potentially common to Schizophrenia pathways based on correlated gene expression analysis

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Schizophrenia (SCZ) is a severe psychiatric disorder affecting 0.7% of the population.[1] When inadequately treated, subjects with SCZ experience symptoms that render them dysfunctional and unable to discern aspects of reality. A large genome-wide association study (GWAS) recently pinpointed 108 significant loci within the human genome that contribute to SCZ pathogenesis.[5] While some loci include genes that have been previously implicated in SCZ, the majority, due to the unbiased nature of the genetic investigation, include genes with unknown relevance to SCZ. This investigation is based on the premise that: 1) at least one of the genes at the 108 loci contribute to SCZ etiology; 2) some of the genes contributing to SCZ etiology are in a common pathway; and 3) some genes in a common pathway will have correlated gene expression. Gene expression data available in the gene expression omnibus (GEO) was used to identify correlated expression among the 369 genes (853 isoforms) found at the 108 loci associated with SCZ. Expression data came from bone marrow CD34+ selected cells isolated from 66 individuals (GSE4619). First, correlation among genes related to the DRD2 pathway was analyzed to test the hypothesis that some SCZ genes are in a common pathway and have correlated expression. Then, two pathways were generated based on correlated expression of genes at the 108 loci. One pathway consisted of the largest number of genes with correlated expression (56) and included four genes from the DRD2 pathway and seven of

the 33 genes that were previously implicated in SCZ. The second pathway, a novel pathway of 12 genes, was constructed by excluding both the 33 genes that were previously implicated in SCZ and other genes that exhibited significantly correlated expression with these 33 genes. Correlated expression analysis among SCZ-associated genes at the 108 loci provides evidence implicating those genes with correlated expression in SCZ pathogenesis. In addition, these analyses will facilitate pathway identification creating starting points for targeted experiments to verify or refute the hypothetical pathways generated here. Ultimately identifying the genes and pathways at the 108 loci involved in SCZ genesis will inform novel pharmaceutical development for treatment and prevention of SCZ.

**Keywords:** Schizophrenia, transcriptomics, antipsychotic, DRD2, genome-wide association study, genomics, gene expression, gene pathway analysis

## 24) Chronic vs. acute effects of subthalamic nucleus deep brain stimulation on olfactory bulb volume in patients with Parkinson's disease

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Olfactory deficits are an overlooked non-motor symptom of many neurodegenerative diseases, such as Parkinson's Disease (PD). It is often the first non-motor symptom that can be observed, and unlike motor symptoms, olfaction is a deficit that has shown no improvement with dopamine agonists such as L-Dopa, a common treatment for PD patients. However, there have been observable improvements in olfaction with subthalamic nucleus (STN) deep brain stimulation (DBS), a secondary treatment modality for PD. The aim of this study was to investigate differences in measurements of cortical structures, olfactory bulb and olfactory sulcus at different time points in PD patients that have undergone bilateral DBS. MRI datasets of 18 PD patients that have undergone DBS were obtained and analyzed, along with 5 ET patients who served as controls. Given that we cannot use a normal control group, we included Essential Tremor (ET) patients treated with DBS, which would allow comparison of a DBS-treated movement disorder population with no known olfactory deficits. Using Statistical Parametric Mapping (SPM 12) in Matlab, all DICOMs were converted to NIFTI files, after which gray and white matter were segmented using voxel based morphometry. Thereafter, cortical and subcortical segmentation analyses were conducted using FreeSurfer, and olfactory bulbs were manually traced using ITK-SNAP. We hypothesize that PD patients that have undergone longer periods of STN stimulation will have increased olfactory bulb volumes, compared to PD patients with shorter stimulation. These results will build upon previous work that has demonstrated a correlation between olfactory bulb volume and disease-induced changes in olfactory function. Specifically, amelioration in PD-related olfactory deficits following STN-DBS will correlate with changes in olfactory bulb volume, providing a clinometric phenotype for olfactory recovery following STN-DBS in PD. **Keywords:** deep brain stimulation, olfaction, Parkinson's disease, movement disorder

## 25) Cortical mitochondria from R6/2 Huntington's disease mice have elevated iron and altered proteomic and functional markers

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Huntington's disease (HD) is a progressive autosomal dominant disorder caused by an expanded CAG repeat in exon 1 of the huntingtin gene. Dysregulation of iron homeostasis and energetic dysfunction are consistent features in HD mouse models. However, it is unclear if there is a connection between iron accumulation and energetic dysfunction in HD. The present study aimed to assess the relationship between mitochondria and iron dysregulation in R6/2 HD mice. Studies were completed in 12-week-old HD mice that had advanced HD and wild-type (WT) litter-mates. Inductively-coupled-plasma mass spectrometry (ICP-MS) analysis of iron levels in purified mitochondria revealed a 51.6% increase in HD mice ( $p=0.0020$ ) compared to controls. We used a number of outcomes to characterize mitochondrial state. Mitochondrial membrane potential and ATP level were decreased by HD ( $p=0.0086$  and  $0.0120$ , respectively). Two-dimensional electrophoresis with matrix-assisted-laser-desorption-ionization (MALDI) time-of-flight (TOF)/TOF was used to identify differentially expressed mitochondrial proteins. Preliminary analysis has identified seventeen proteins including peroxiredoxin 3, DJ-1, ATP synthase sub-unit  $\beta$  and isocitrate dehydrogenase 3. These proteins have functions linked with energy metabolism, carbohydrate metabolism, redox cycling, protein folding, the ubiquitin proteasome system and apoptosis. We conclude that elevations of iron in HD brain mitochondria are consistent with preferential accumulation in this organelle. Findings demonstrate co-localization of iron dysregulation and measures of mitochondrial dysfunction in R6/2 HD brain. **Keywords:** Mitochondrial proteomics

## 26) Dietary docosaheptaenoic acid alleviates autistic-like behaviors resulting from maternal immune activation in mice

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The prevalence of autism spectrum disorders over the last several decades has risen at an alarming rate. Factors such as broadened clinical definitions and increased parental age only partially account for this precipitous

increase, suggesting that recent changes in environmental factors may also be responsible. One such factor could be the dramatic decrease in consumption of anti-inflammatory dietary omega-3 (n-3) polyunsaturated fatty acids (PUFAs) relative to the amount of pro-inflammatory omega-6 (n-3) PUFAs and saturated fats in the Western diet. Docosahexaenoic acid (DHA) is the principle n-3 PUFA found in neural tissue and is important for optimal brain development, especially during late gestation when DHA rapidly and preferentially accumulates in the brain. In this study, we tested whether dietary DHA supplementation throughout development could improve measures related to autism in a mouse model of maternal immune activation. We found that dietary DHA protected offspring from the deleterious effects of gestational exposure to the viral mimetic polyriboinosinic-polyribocytidilic acid on behavioral measures of autism and subsequent adulthood immune system reactivity. These data suggest that optimal dietary levels of DHA, especially during pregnancy and nursing, may help protect normal neurodevelopment from the potentially adverse consequences of environmental insults like maternal infection.

## 27) Contributions of brain-derived neurotrophic factor to exercise-induced attenuation of methamphetamine-induced neurotoxicity

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Abuse of methamphetamine (METH) in the United States has increased significantly in the past 15 years, and use is now endemic in the Western states. Colorado currently ranks 7th in the nation for total number of METH users over the age of 25. Overall, the economic cost of drug abuse is high. METH abuse alone costs the U.S. \$23.4 billion annually. In addition to the known health risks associated with psychostimulant abuse, METH use carries the additional danger of permanent brain injury. One well-known animal model of METH abuse utilizes binge METH administration, where repeated doses of METH are given to rats in a single day. This dosing regimen has been shown to cause long-lasting damage to dopaminergic nerve terminals in the striatum and serotonergic nerve terminals in the prefrontal cortex similar to that seen in human METH abusers. In humans, it has been suggested that METH-induced monoaminergic damage may lead to the development of Parkinson's disease. Exercise is a non-pharmacological treatment, known for its beneficial physiological effects and cognition-enhancing properties, being explored for use in treating Parkinson's disease. Recently, this work has been extended to the study of METH-induced monoaminergic neurotoxicity. It has been shown that when rats exercised for 3 weeks before and 3 weeks after a binge treatment of METH, this exercise significantly attenuated METH-induced decreases in striatal dopamine. Interestingly, if the exercise regimen was limited to only 3 weeks before a binge treatment of METH, it did not protect against striatal dopamine damage, suggesting that pre-METH exercise does not help with prevention of neurotoxicity, but perhaps post-METH exercise aids in recovery. Recently, we've shown that 3 weeks of exercise after a METH binge resulted in significant attenuation of neurotoxicity, suggesting that exercise may provide a novel, non-pharmacological treatment for METH-induced neurotoxicity. In an effort to identify a potential mechanism for this attenuation, we've begun examining the contributions of the neurotrophic factors BDNF (brain-derived neurotrophic factor). Voluntary exercise is known to induce production of neurotrophic factors and an extensive literature details the beneficial role of neurotrophins in neurodegenerative disease. The study presented herein examined not only the expression levels of BDNF, but also the correlation between BDNF expression and attenuation of neurotoxicity.

## 28) Local and use-dependent effects of $\beta$ -Amyloid oligomers on NMDA receptor function revealed by optical quantal analysis

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Beta amyloid ( $A\beta$ ) triggers elimination of excitatory synaptic connections in the central nervous system, an early manifestation of Alzheimer's disease. Oligomeric assemblies of  $A\beta$  peptide associate with excitatory synapses resulting in synapse elimination through a process that requires NMDA-type glutamate receptor activation. Whether  $A\beta$  directly impacts synaptic NMDA receptor function, whether  $A\beta$  acts locally at bound synapses and whether synaptic activity influences  $A\beta$  synaptic binding and synaptotoxicity have remained fundamental questions. Here we used an optical  $Ca^{2+}$  reporter to visualize NMDA receptor function at thousands of individual synapses before and after  $A\beta$  application.  $A\beta$  triggered a robust impairment of NMDA receptor function at a large fraction, but not all synapses. NMDA receptor function was more severely impaired at highly active synapses and synapses with bound  $A\beta$ , but activity was not required for  $A\beta$  binding at synaptic sites. Pharmacologically blocking NMDA receptors during  $A\beta$  exposure completely blocked  $A\beta$ -mediated impairment. Thus,  $A\beta$  binding triggers local impairment of synaptic NMDA receptors in a use-dependent manner. **Keywords:** Beta amyloid, NMDA Receptor, Live Cell  $Ca^{2+}$  Imaging

## 29) Stressor controllability is not protective in female rats

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Adverse life events are an important etiological factor for a variety of psychiatric disorders. The degree of behavioral control over some aspect of a stressor is one of the most potent variables in modulating the outcome of a stressful

event. When a controlling response is provided (rats to humans) many of the behavioral and neurochemical sequelae of adverse events are blunted. Prior research from our laboratory and others have shown that uncontrollable, relative to controllable, stressors activate the serotonergic dorsal raphe nucleus (DRN), a key structure in the production of behavioral stress outcomes. However, when behavioral control is detected, the medial prefrontal cortex (mPFC) exerts top-down inhibitory control over DRN serotonergic activity, thereby reducing the impact of the stressor. While this line of research is critical for understanding how resilience is inculcated, all prior experiments have been conducted in male rats. Here we test whether or not behavioral control is protective in females and whether or not it engages the same neural circuitry as described in males. Women are more susceptible than men to stress-related psychiatric disorders. Therefore, understanding the relevance of stressor controllability across the sexes is a research imperative in addressing the biological basis of stress-related clinical phenomena. Here we demonstrate that controllability in females does not modulate the neurochemical and behavioral outcomes of stress. This suggests significant sexual dimorphism in the layout and usage of the relevant neural pathways that will be critical to understand in future experiments. **Keywords:** Stress resilience, anxiety, prefrontal cortex, serotonin, sex, neurobiology

### 30) Hypothalamic POMC neuron involvement in an activity-based anorexia rodent model

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Poopediomelanocortin (POMC) neurons in the arcuate nucleus of the hypothalamus are critical regulators of energy balance. Perturbations in POMC neurons lead to diseases of energy homeostasis including obesity and anorexia. However, the mechanism by which alterations in POMC neurons contribute to disorders of energy regulation, especially in regard to anorexia, is not fully understood. Previous work has shown that POMC mRNA levels rise transiently in rodents subjected to activity-based anorexia (ABA). ABA is a commonly-used behavioral paradigm in which food restriction paired with voluntary wheel running produces an anorexic phenotype. Whether a transient rise in POMC is necessary for the development of ABA remains to be determined. To address this question, POMC neurons were silenced during ABA via the inhibitory hM4Di Designer Receptor Exclusively Activated by Designer Drug (DREADD). The inducible cre-lox system was used to selectively express the inhibitory DREADD only in POMC cells following activation of cre-recombinase with Tamoxifen. Female mice were 4 weeks old when cre-recombinase was activated. Behavioral experiments took place when animals were 7-8 weeks of age. Wheel running activity, food intake, and bodyweight were measured throughout the study. Additional ABA experiments were also performed on wildtype mice prior to the DREADD experiments to verify that reliable ABA behavior can be elicited. Following behavioral experiments, presence of the inhibitory DREADD in the arcuate nucleus of the hypothalamus was evaluated using confocal microscopy. Mice displayed increased wheel running activity as well as decreases in bodyweight in response to 3 days of food restriction. Food anticipatory activity (FAA), a hallmark of ABA, was also observed in mice exposed to both food restriction and voluntary wheel activity. Confocal microscopy revealed the presence of the inhibitory DREADD within the arcuate nucleus of the hypothalamus. The results from this study will indicate the role of POMC neuron activity in the onset of anorexia. **Keywords:** animal behavior, DREADD, confocal microscopy

### 31) Characterization of multiple adeno-associated virus (AAV) serotypes for gene expression in neurons and astrocytes in vivo and in vitro

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The non-pathogenic parvovirus, adeno-associated virus (AAV), is an efficient gene expression vector in mammalian cells that has shown promising results for monogenic disorder treatments in clinical trials. With the rise in experimental and therapeutic use of AAVs for brain disorders, additional studies are necessary to characterize and identify the tropism of different AAV serotypes throughout the CNS. Currently, there are more than 100 AAV serotypes identified, which differ in the binding capacity of capsid proteins to specific cell surface receptors and thereby effect transduction efficiency in different CNS cell types and brain regions. In the current study, a library of AAV serotypes expressing a GFP reporter (AAV1, AAV2/1, AAVDJ, AAV8, AAVDJ8, AAV9, AAVDJ9) were screened for their transduction efficiency in both primary murine astrocyte and neuronal cell cultures via immunofluorescence analysis. Based on the in vitro results from both cell types, AAV2/1, AAVDJ8, and AAV9 were selected for further investigation of their tropism throughout different brain regions and cell types. Each AAV was administered to P0-neonatal mice via intracerebralventricular injections (ICV); mice were then aged for 3 or 6 weeks before brain tissue collection. Brain regions of the olfactory bulb, striatum, cortex, hippocampus, substantia nigra (SN), and cerebellum were isolated by cryo-sectioning and analyzed for intrinsic AAV-GFP expression within both astrocytes and neurons by immunofluorescent (IF) co-labeling. Stereological cell counting demonstrated that AAV2/1 infections were more prevalent in the cortical layers, but less penetrable to the midbrain areas compared to AAVDJ8 and AAV9. Additionally, there were viral infection differences observed with comparing 3 to 6 weeks post infection. In the SN, AAV9 and AAVDJ8 infection significantly increased between 3 to 6 weeks, and AAV2/1 showed minimal AAV

infection during both time points post-infection. AAVDJ8 also displayed more tropism in astrocytes compared to AAV9 in the SN region. As a result of this study, we can conclude which specific AAV serotypes are required to deliver transgenes of interest to different brain regions in both astrocytes and neurons for further experimental and potential therapeutic use. AAVDJ8 and AAV9, in particular, may be useful for targeting the SN for gene delivery in studies modeling Parkinson's disease and related disorders. **Keywords:** AAVs, primary cell culture, immunofluorescence

### 32) Automated dopaminergic cell counting in a viral induced Parkinson's disease CD-1 mouse model

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Parkinson's disease (PD) is the second most common neurodegenerative disorder, characterized by loss of voluntary motor control, degeneration of dopaminergic neurons of the substantia nigra pars compacta (SNpc), alpha-synuclein aggregation and gliosis. Lack of appropriate animal models and a shortage of quantitative histological methodologies has limited our understanding of PD pathogenesis. Most commonly used MPTP and Rotenone based PD animal models allow for SNpc DA neuronal loss but lack many key hallmarks of the disease. Previous research has shown that intranasal inoculation with a recombinant firefly luciferase mosquito-borne alphavirus, Western equine encephalitis virus (WEEV), in an outbred CD-1 mouse resulted in musculoskeletal abnormalities, rapid propagation to the basal ganglion, excessive activation of glia, minor loss of dopaminergic neurons, and morbidity within four days. To mimic the pathology and increase dopaminergic cell loss, CD-1 outbred mice were intranasally infected with recombinant firefly luciferase WEEV and treated with monoclonal antibodies to the WEEV E1 viroporin. Eight weeks after infection, brain tissue was fixed and cryosectioned for immunofluorescent staining of DA neuronal cell bodies. Additionally, to assess the accuracy and utility of two different immunofluorescent-based cell counting techniques, a total number of dopaminergic neurons in the SNpc were determined by traditional design-based 3D stereology and a more rapid based 2D automated cell counting method. Both cell counting techniques revealed statistically significant loss of dopaminergic neurons in the infected group compared to the uninfected group. In summary, this study provides a new PD animal model that closely replicates the enigmatic pathogenesis of PD. Furthermore, automated dopaminergic cell counting provided similar accuracy, sensitivity, and reproducibility to traditional design based 3D stereology but in more than half the time. Together, this viral PD animal model, along with rapid image-based stereology, provides an exceptionally quick system for future disease modeling and drug discovery. **Keywords:** Parkinson's disease, animal models, automated stereological methods for tissue cell counting

### 33) Mutant huntingtin alters the response of microglial cells to lipopolysaccharide stimulation

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Huntington's disease (HD) is an inherited neurological disease that results in degeneration of brain regions controlling movement. HD is an autosomal dominant disease caused by a polyglutamine expansion in the huntingtin gene. This mutation leads to production of mutant huntingtin protein that is detrimental to many cell types. Neuroinflammation is a feature of HD characterized by activation of microglial cells, the resident immune cells of the brain. The cause of neuroinflammation is largely unknown and may be a result of dysfunctional microglia. The goal of this study is to determine if mutant huntingtin expression in microglial cells alters their response to lipopolysaccharide (LPS) challenge. We used the EOC-20 microglial cell line to study mutant huntingtin-induced dysfunction. Cells exposed to LPS have changes in nitric oxide and production of the cytokine interleukin-6 (IL-6). We determined that mutant huntingtin expression in cultured microglial cells alters these parameters. **Keywords:** neuroinflammation, microglial cells, cytokines, Huntington's disease

### 34) Increased mortality of Huntington's disease mice with *Toxoplasma gondii* infection: a possible role of elevated indoleamine-2,3-dioxygenase

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Upregulation of the kynurenine pathway of tryptophan metabolism is a feature of both Huntington's disease (HD), a progressive neurodegenerative disease, and *Toxoplasma gondii* (T. gondii) infection, a common neuroinvasive pathogen. Indoleamine-2,3-dioxygenase (IDO) catalyzes the oxidation of tryptophan to kynurenine, the first and rate-limiting step in the kynurenine pathway. We tested the thinking that an interaction via IDO exists between these two brain diseases by infecting HD mice with T. gondii before phenotypic onset of HD. We demonstrate that T. gondii infection results in significantly earlier death of HD mice compared with wild-type infected and non-infected HD mice. At a timepoint just before death, we measured a specific increase in cerebral cortical IDO activity in infected HD mice. At this timepoint, we also measured a significant increase in T. gondii parasite load and an altered immune response to the infection in HD mice. Together, these data demonstrate a novel interaction between HD, a neurodegenerative disorder, and T. gondii, a neuroinvasive protozoan. Further, we think increased

IDO activity may mediate this interaction leading to an altered response to the parasite in HD mice. Our data is relevant to understanding human HD and how neuroinflammation and neurotropic pathogens may act as an environmental influence on progression of neurodegenerative diseases. **Keywords:** neuroinflammation, Huntington's disease, *Toxoplasma gondii*, neuroimmunology

### 35) Determining the role of PrPC-mediated signaling during prion-induced neurodegeneration

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The pathogenic mechanism of prion-induced neurotoxicity is not well defined; it is postulated that either the loss of cellular prion protein (PrPC) function or the gain of toxic function of PrPC and/or PrP<sup>Sc</sup> (infectious PrP) plays a significant role. PrPC function is linked to both neuronal maturation and neurotoxicity, therefore, it is reasonable that PrPC-mediated signal transduction has a central role in controlling neuronal viability. In this study, we examine the role of PrPC in neurogenesis as well as the contribution of PrPC-mediated Fyn activation to the pathogenesis of prion disease. Fyn, a nonreceptor tyrosine kinase, is an important regulator of neurogenesis and PrPC-mediated Fyn activation can promote neuritogenesis upon binding of neural cell adhesion molecule (NCAM) to PrPC. This study attempts to link both the normal physiological function of PrPC and the potential gain of toxic function of PrPC through the Fyn signaling pathway in prion disease. We investigated PrPC function and signaling using olfactory sensory neurons (OSNs), which undergo continual renewal in adulthood, both during infection and in transgenic mice expressing altered levels of PrPC. OSN integration into the existing neural network is necessary for olfactory function, and our preliminary findings indicate that OSN axon targeting to glomeruli in the olfactory bulb (OB) is altered during prion infection. We investigated the effect of this structural change in the neural network on synaptic loss and neuronal death by quantifying OSNs in the olfactory epithelium as well as synapse activity in the OB. Proliferation and survival of newborn neurons was quantified, and the neuronal maturation status was determined at each stage of differentiation during prion infection. Our studies show that prion infection is impacting normal neuronal maturation and axon integration, resulting in an OSN population shift toward an immature neuron status. These developmental alterations may help decipher how Fyn activation modifies cellular pathways contributing to neurodegeneration. To examine the PrPC-mediated signaling pathway, we will measure the direct interaction of NCAM and PrPC and quantified activated Fyn during prion infection. Together, these studies inform on the role of PrPC and Fyn activation on normal physiological function, and in toxicity during prion infection. **Keywords:** prion disease, olfactory system, neurogenesis

### 36) Unexpected early proteomic changes in Alzheimer's disease model mice synaptosomes

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We have employed label-free quantitative proteomics of wild-type and Alzheimer's disease model mice synaptosomes to investigate proteomic changes occurring during Alzheimer's disease progression as a prelude to analysis in humans. We present methods and the analysis of more than 4000 proteins using multiple analysis tools and statistical criteria. The data demonstrate that a large number of changes occur in the proteome very early relative to the onset of both traditional disease markers such as amyloid accumulation, tau phosphorylation and cognitive dysfunction. These results reinforce the importance of mechanistic investigations in early disease progression long before the classical markers of Alzheimer's disease are present. Most strikingly, we observe significant and early changes in the number of synapses as well as early changes in the onco-proteome suggesting an important proteomic overlap between neurodegeneration and oncogenesis that correlates with the well-established inverse comorbidity of cancer and neurodegenerative disease and that may provide insight into the biology behind this epidemiology.

### 37) Quantitative measures of brain MRI as a potential predictive factor of cognitive outcomes after Subthalamic Nucleus Deep Brain Stimulation for Parkinson's disease

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**BACKGROUND:** Subthalamic nucleus Deep Brain Stimulation (STN-DBS) is a proven and effective treatment for the motor symptoms of Parkinson's disease (PD). Nonetheless, cognitive decline, an adverse effect of this surgery, can be seen in a select population of patients. After STN-DBS surgery, cognitive impairments in verbal memory and verbal fluency are often observable. All DBS candidates undergo a systematic pre-surgical evaluation to carefully consider the risk-to-benefit ratio. Two of the most important factors in the assessment are MRI of the brain and neuropsychological (NP) evaluation. Interestingly, among PD patients, cognitive declines have been shown to be associated with a greater burden of T2-hyperintense white matter lesions (WML) on MRI. Currently, the relationship between WML volume and cognitive declines post-DBS surgery is not known, and the strongest predictive factor of post-DBS cognitive outcomes is pre-surgical cognitive status. **OBJECTIVE:** The aim of this study was to determine

whether WMLs, measured quantitatively on MRI of the brain, predict a change in cognition after DBS surgery. METHODS: The University of Colorado Hospital neuropsychology database was retrospectively screened for PD patients who had STN-DBS surgery from Jan 2011-June 2016. Patients with pre-operative and  $\geq 6$  mo post-operative NP testing, as well as pre-operative brain MRI were included. 45 patients met these inclusion criteria. NP evaluation scores were recorded and T2-FLAIR and 3D T1-weighted MR images were processed to obtain lesion volume and total brain volume. PRELIMINARY RESULTS: Patients completed post-operative NP evaluation an average of 14.6 mo ( $\pm 6.5$ ) after surgery. Results of NP data show statistically significant declines on measures of executive function, verbal fluency and working memory, suggesting that our population experienced impairments consistent with those reported in other studies. Next steps will involve correlating the degree of WMLs and change in performance on NP tests. Secondary analyses will include correlation between total brain volume and change in performance score on NP tests. CONCLUSIONS: Results from this study will provide important information regarding the impact of the existing burden of WMLs on the cognitive outcomes after STN-DBS surgery, thereby, equipping future DBS teams with an important clinical tool enabling more precise determination of the risk-to-benefit ratio.

### 38) Voluntary exercise attenuates methamphetamine-induced monoaminergic neurotoxicity

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Methamphetamine (METH) abuse continues to be a major public health concern. As many as 60 million people worldwide report using amphetamine-type stimulants, especially METH. Use is endemic in the western United States; Colorado currently ranks 7th nationally in METH use among people over the age of 25. The use of METH is highly problematic, not only due to the acute effects of the drug which can include psychosis and aggressive behavior, but also due to the well documented long-term consequences of the drug on the structure and function of the central nervous system, and concomitant cognitive deficits. METH-induced toxicity to central monoamine systems has been modeled in numerous species. In rodents, partial monoamine loss has been reported to exist for at least 6 months and is associated with impaired cognitive function. Imaging studies in humans show similar long-lasting decreases in markers of dopamine (DA) innervation in the caudate-putamen of METH abusers. In fact, recent studies have shown that METH abusers are more likely to develop Parkinson's disease, suggesting enduring and possibly progressive DA loss as a consequence of METH abuse. Exercise is well known to have myriad positive effects on the CNS. Studies using rodent models of Parkinson's disease have demonstrated a beneficial role of exercise on neurochemical and behavioral outcomes. Recently, this work has been extended to the study of METH neurotoxicity; with data showing that wheel running ameliorates METH-induced monoaminergic loss. Importantly, that study employed an exercise regimen consisting of both pre- and post-METH exercise. While these results are encouraging, the study was not designed to elucidate whether this effect was the result of protection against the neurotoxic insult, or was due to accelerating the known neurochemical recovery seen after METH administration. Here we show that 3 weeks of post-METH exercise significantly attenuates monoaminergic neurotoxicity. Having established that voluntary exercise beginning immediately post-METH attenuates drug-induced monoamine neurotoxicity, we now turn our attention to the timing of this intervention. By delaying the start of exercise for 7 or 30 days post-METH, we can target the therapy to a time when the bulk of the neurotoxicity has already taken place. As a result, we can begin to investigate whether post-METH exercise is disrupting the mechanisms driving neurotoxicity or, rather, is reversing the neurotoxic effects post-hoc. **Keywords:** methamphetamine, exercise, neurotoxicity

### 39) Intermittent imaging of cultured hippocampal slices during long term incubation

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Two major methods are widely used for long term culture of brain slices: culturing on membranes at the air liquid-interface or culturing on coverslips in sealed tubes allowed to rotate in a roller incubator to provide aeration. Neither of these methods is conducive to repetitive microscopic observations of the same slices over long-term periods (weeks/months) of treatments. Here we develop a closed culture tube method that overcomes these limitations. Hippocampal slices (250-300  $\mu$ m) are prepared from day P5 mouse pups and are adhered to a glass coverslip (12 x 22 mm) that was previously coated with 3-aminopropyltriethoxysilane to introduce amino groups on the glass surface. The slices were adhered using a drop of chicken plasma treated with thrombin. After the plasma clotted, the coverslips were affixed to a flat sided plastic culture tube with a 6 mm drilled hole around which is a strip of Secure Seal with an aligned hole. The hippocampal slice embedded in the plasma clot was secured facing into the tube. The position of the hole was carefully positioned from the bottom of the tube such that 0.8 ml of culture medium covers the slice when the tube is at a 50 angle, the angle in the roller culture incubator; the slice is bathed in medium once every rotation (5 min). After affixing the slice, the tubes are flushed with 5% CO<sub>2</sub>/95% air and the screw cap is tightened. Slices are generally cultured for 7-10 days before use to allow recovery from the slicing. During this time, usually after a week, the medium is supplemented overnight with 0.0025 units/ml of active plasmin to dissolve the clot, which improves the imaging. Slices have been infected with viruses for expression of

proteins of interest. We have made a special stage adapter for holding these tubes for imaging by confocal microscopy and representative images will be presented. Our long-term goals are to use these slices for studying formation and reversal of cofilin-actin rods in response to glutamate excitotoxicity, anoxia, amyloid- $\beta$ , proinflammatory cytokines, and other neuronal stress agents. This new culturing and imaging technique will allow significant progress to be made studying the role of cofilin/actin rods in stroke, neuroinflammation and Alzheimer's Disease. (Supported by NIH grant AG049668 and funding from the CSU Microscope Imaging Network). **Keywords:** Brain slice culture, confocal microscopy

## NEURAL EXCITABILITY, SYNAPSES, AND GLIA

### 40) Somatostatin not parvalbumin interneurons mediate feedforward inhibition in the basolateral amygdala

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The basolateral amygdala (BLA) is a brain region that plays a vital role in associating specific environmental stimuli with emotionally salient valence information. Excitatory principal neurons (PNs) encode this integrated sensory-valence information (Herry et al, 2008; Paton et al, 2006; Shabel & Janak, 2009). However, local BLA inhibitory interneurons (INs) gate the activity and plasticity of the PNs via feedforward inhibition (Bissière et al, 2003; Ehrlich et al, 2009; Lang & Paré, 1997). One major source of feedforward inhibition to the BLA is the lateral entorhinal cortex (Brothers & Finch, 1985; Mouly & Di Scala, 2006), a cortical region associated with sensory object representation (Keene et al, 2016; Tsao et al, 2013; Xu & Wilson, 2012). We hypothesized that entorhinal afferents to the BLA would target distinct populations of INs to drive feedforward inhibition of BLA PNs. To test our hypothesis, we performed whole-cell electrophysiology in horizontal slices of adult mice. To determine the role of entorhinal input in modulating BLA circuitry, we stimulated the lateral entorhinal cortex while recording from BLA neurons. We show that these afferents synapse onto somatostatin (SST) and parvalbumin (PV) positive INs in addition to BLA PNs. To elucidate the role of the different INs in feedforward inhibition, we expressed the inhibitory chemogenetic protein hM4Di in SST and PV INs. These experiments revealed that CNO mediated inactivation of SST but not PV INs decreased feedforward inhibition onto BLA PNs (median percent of control feedforward IPSC following inactivation of SST INs: 55.3% with 46.6-66.2% interquartile range,  $p < 0.01$  Wilcoxon signed rank test,  $n = 8$  cells, 4 mice; PV: 90.5% with 61.2-108.2% interquartile range,  $p = 0.31$  Wilcoxon signed rank test,  $n = 8$  cells, 5 mice). In the BLA, SST INs provide feedforward inhibition to PNs via putative dendritic targeting inhibition. This is in marked contrast to other brain regions, where somatic targeting PV INs provide this function. **Keywords:** basolateral amygdala, inhibition, interneuron, somatostatin, parvalbumin, neural circuits

### 41) Membrane insertion by both C2 domains of the calcium sensor, synaptotagmin, are critical for neurotransmitter release

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Calcium-induced vesicular fusion is a critical step in synaptic transmission. This process relies on the synaptic vesicle protein, synaptotagmin, to detect elevated presynaptic calcium concentrations following neuronal depolarization. Membrane interactions mediated by the calcium-binding domains of synaptotagmin, C2A and C2B, couple  $\text{Ca}^{2+}$  influx with vesicle fusion. Hydrophobic residues on the distal tips of the C2 domains penetrate into the membranes in a  $\text{Ca}^{2+}$ -dependent manner and this mechanism is hypothesized to promote vesicular fusion following calcium binding. However, the relative importance of the two domains has been controversial. A point mutation in the C2B domain that disrupts this interaction completely blocks synaptic transmission, while the homologous mutation in C2A only impaired transmission by 50%. In order to directly test the role of C2A, both of these hydrophobic residues in the C2A domain (M222 and F284) were mutated in isolation and in tandem to the polar and hydrophilic amino acid, glutamic acid. Each mutation cut evoked neurotransmitter release in half when expressed in isolation. Interestingly, the two mutations had a summative effect and nearly abolished all neurotransmitter release when expressed in tandem. This is the only case where a mutation in the C2A domain, normally assumed to have a less critical role, results in a nearly complete abolishment of vesicular fusion. These results demonstrate that these hydrophobic residues are required for vesicular fusion and indicate that membrane penetration by C2A is necessary to couple  $\text{Ca}^{2+}$  influx to neurotransmitter release. Thus, C2A plays a more active role in synaptic transmission than previously understood. **Keywords:** Drosophila, electrophysiology

### 42) Role of NFAT in the Inactivity-Dependent Regulation of Kv4 Channels

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Synaptic homeostasis plays a pivotal role in the stabilization and protection of neurons from over- and under-activity. We have previously reported that inhibition of synaptic activity mediated by nicotinic acetylcholine receptors (nAChRs) results in an increase in synaptic strength due to a selective increase in the Drosophila  $\alpha 7$  ( $\text{D}\alpha 7$ ) nAChR. We also revealed a subsequent response, an increase in the voltage-dependent A-type Kv4 channel, which appears to be a

secondary homeostatic control mechanism. We showed that this inactivity-induced increase in Kv4 channels is dependent on  $\text{D}\alpha 7$  and  $\text{Ca}^{2+}$  influx, and blocked by inhibitors of transcription. Here, we investigate the molecular mechanisms underlying the inactivity-induced increase in Kv4 channels in vivo. We blocked activity using a temperature-sensitive choline acetyltransferase (ChAT) allele, *Chats*, that exhibits reduced ChAT enzymatic activity and therefore, decreased ACh synthesis. We show that heat-shock indeed leads to an 18% increase in Kv4 protein levels that persists for at least 4 hours and that this inactivity-induced increase in Kv4 protein is dependent on  $\text{D}\alpha 7$  nAChRs, similar to our previous study. To examine if suppression of cholinergic neurotransmission induces an increase in Kv4 gene expression, we performed real-time quantitative PCR (RT-qPCR) and indeed found a transient increase in Kv4 mRNA. Since our previous study also showed the increase in Kv4 to be dependent on  $\text{Ca}^{2+}$ , we investigated whether the  $\text{Ca}^{2+}$ /calcineurin transcriptional activator, Nuclear Factor of Activated T-cells (NFAT), might be involved. We used a null mutant for NFAT in combination with *Chats*. We found that in the absence of NFAT, blockade of synaptic activity was unable to induce an increase in Kv4 mRNA or protein. Our results suggest that NFAT is a key mediator in the inactivity-induced up-regulation of Kv4. Next steps will be to test if NFAT directly regulates the Kv4 promoter, and to identify and test putative NFAT target sites in the Kv4 locus in vivo.

#### 43) Synaptic Homeostasis Contributes to $\text{A}\beta 42$ -Induced Changes in Cholinergic Neural Activity

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Alzheimer's disease (AD) is the most prevalent form of dementia in the elderly population, with one in eight over 65 affected (~5.4 million). It is widely believed that the generation of  $\beta$ -amyloid ( $\text{A}\beta$ ) peptides in the brain is a primary event leading to AD. Research in the last decade has shown that the toxic  $\text{A}\beta 42$  species induces an alteration in neuronal activity that is likely to contribute to aberrant signaling, and other downstream pathologies. Interestingly, these changes include both increases and decreases in neural activity, especially in cholinergic regions of the brain. And this has caused some controversy in the field. One hypothesis is that early increases in cholinergic activity trigger endogenous homeostatic mechanisms that initially protect neural stability, but eventually lead to a decrease in activity at later stages. Here, we use primary neurons from the predominantly cholinergic CNS of *Drosophila* to study the effects of  $\text{A}\beta 42$  on nicotinic acetylcholine receptor (nAChR)-mediated synaptic activity. We use both wild-type neurons exposed to exogenously applied  $\text{A}\beta 42$ , as well as neurons from a transgenic *Drosophila* model that over-expresses a secreted human  $\text{A}\beta 42$  peptide. We show that  $\text{A}\beta 42$  induces an initial increase in cholinergic synaptic activity that is followed by synaptic depression, and that this sequence of events occurs in the intact brain as well. Since these changes parallel the changes in cholinergic activity reported in mammalian models, our system offers a model in which to investigate the molecular mechanisms underlying these changes in cholinergic activity. We show that the early increase in synaptic activity is likely due to extracellular  $\text{A}\beta 42$  acting on pre-synaptic  $\alpha 7$  nAChRs. We further show that increasing synaptic activity at early stages in wild-type does indeed lead to a homeostatic decrease in activity at later stages, suggesting that synaptic homeostasis contributes to the sequential  $\text{A}\beta 42$ -induced changes in neural activity. Understanding how  $\text{A}\beta 42$  induces opposing changes in cholinergic activity is likely to give important insight into the progression of downstream pathologies. **Keywords:** homeostasis, Alzheimer's disease, *Drosophila*, cholinergic synapse

#### 44) Potential neuroprotective role of *slo2* during over-excitation

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*Slo2* encodes a  $\text{Na}^{+}$ -Activated  $\text{K}^{+}$  channel and recent studies suggest it is specifically activated by the persistent sodium current component of the voltage-gated  $\text{Na}^{+}$  channel. Although the biophysical properties of this channel have been characterized, little is known about its physiological role in the nervous system. Since *slo2* channels are activated by  $\text{Na}^{+}$  and repolarize membrane potentials when activated, they likely act in a homeostatic manner. Using *Drosophila melanogaster* as a model, we test the hypothesis that *slo2* channels protect neurons from over-excitation. Specifically, we have generated a functional null mutant of *slo2* (*slo2*<sup>-/-</sup>) using the CRISPR/cas9 system. We have also utilized a transgenic fly line that allows for tissue-specific overexpression of the endogenous *slo2* gene. To test whether overexpression of *slo2* can protect against over-excitation, we used a background line containing a knock-in mutation in the *Drosophila*  $\text{Na}^{+}$  channel gene, *para*, that is homologous to a mutation in *SCN1A* that causes the epileptic disorder Generalized Epilepsy with Febrile Seizures Plus (GEFS+). The GEFS+ mutation is temperature-sensitive, such that increased temperatures shift the deactivation threshold of the persistent  $\text{Na}^{+}$  current to more negative potentials, but leave the transient component unaffected. The heat-induced seizure phenotype associated with the GEFS+ mutation is similar in both humans and flies. Indeed, we found that during heat exposure, the probability of seizing in the GEFS+ line is 39%, whereas the GEFS+ line overexpressing *slo2* only has a 15% probability of seizing. This suggests that *slo2* may play a neuroprotective role when confronted with conditions of over-excitation, perhaps especially when caused by increased  $\text{Na}^{+}$  influx. Consistent with a role in tempering cell excitability, the *slo2*<sup>-/-</sup> null mutants exhibit an enhanced sensitivity to mechanical stimulation. When larvae were mechanically stimulated with 54mN of force, the likelihood of *slo2*<sup>-/-</sup> reacting was 62% whereas the wild-type line was only 34% likely to react. Conversely, preliminary results suggest

that overexpression of slo2 leads to a decreased sensitivity to mechanical stimulation. Together these results implicate slo2 in the modulation of neuronal excitability, in both physiological sensory responsiveness and pathological over-excitation. **Keywords:** *Drosophila*, epilepsy, ion channels

#### 45) Local synaptic activity dynamically regulates recycling endosome cargo trafficking

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The processes by which synaptic connections are strengthened or weakened in response to varying patterns of neuronal activity are broadly referred to as "synaptic plasticity". Many forms of synaptic plasticity important in learning and memory modify synaptic strength through the addition or removal of neurotransmitter receptors at the postsynaptic membrane. Although an individual neuron may have thousands of tightly spaced synaptic connections, plasticity can take place locally at individual synapses. Such spatially-restricted postsynaptic changes are critical for associative learning; however, how such "input-specific" alterations occur remains a fundamental question. We hypothesized that local alterations to synapses are mediated by regulated trafficking of postsynaptic proteins through organelles called recycling endosomes (REs), which act as reservoirs for important postsynaptic molecules. REs are housed within a large fraction of dendritic spines, the major postsynaptic sites of excitatory connectivity, and are thus well-poised to rapidly respond to changes in local activity to modulate synaptic structure and function. Using optical techniques coupled with local synapse activation and inactivation, we show that the rate of RE cargo trafficking bidirectionally scales with activity at individual synaptic sites situated on the same dendritic arbor. Additionally, we show that RE cargo trafficking is coupled to synaptic activity by NMDA receptors and extracellular calcium. Future experiments will test the hypothesis that local synaptic activity mediates input-specific postsynaptic changes by regulating RE content and dynamics. Mechanistic insights into RE cargo trafficking at synaptic sites may lead to an enhanced understanding of the activity-induced changes underlying central cognitive functions. **Keywords:** glutamate uncaging, recycling endosome, AMPA receptor, synaptic plasticity, membrane trafficking

#### 46) Illuminating the opioid epidemic: opioids inhibit retinal cells responsible for the photoentrainment of circadian rhythm

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There is an epidemic of opioid abuse in the United States that is positively associated with increasing rates of accidental death due to overdose as well as heroin initiation. Chronic opioid users often suffer side effects such as altered circadian rhythm characterized by increased sleepiness during the day and insomnia at night, regardless of the impetus for opioid use. Such circadian pathology not only confers a poor quality of life, but has strong negative impact on the outcome of opioid abuse treatments. The body's master clock, located in the suprachiasmatic nucleus (SCN), is synchronized to environmental light cycles (photoentrainment) exclusively by a subset of retinal ganglion cells, the melanopsin-expressing, intrinsically photosensitive retinal ganglion cells (ipRGCs) that process and carry ambient light information to the SCN. We have shown that ipRGCs express  $\mu$ -opioid receptors (MORs) and that MOR specific agonists strongly attenuate light-evoked firing of ipRGCs. The molecular events underlying the effect of MOR specific agonists are unknown. K<sup>+</sup> channel opening and resultant neuronal hyperpolarization is an important inhibitory mechanism for opioid-induced anti-nociception. Thus, we hypothesized that MOR specific agonists affects K<sup>+</sup> current (I<sub>LK</sub>) in ipRGCs. To test this hypothesis, we enzymatically dissociated ipRGCs from the retina of a genetically engineered mouse line, in which the promoter of the melanopsin gene (*Opn4*) drives the expression of green fluorescent protein (*Opn4::EGFP*), so that dissociated ipRGCs can be identified based on green fluorescence. Then, using patch clamp electrophysiology in combination with pharmacological tools, we dissected the effects of DAMGO, a MOR specific agonist, on depolarization-evoked firing and I<sub>LK</sub> of ipRGCs. We found that DAMGO-induced inhibition of ipRGC excitability is consistent with DAMGO-mediated increase in I<sub>LK</sub> at the activation threshold of voltage-gated Na<sup>+</sup> channels, thereby delaying the Na<sup>+</sup>-mediated depolarization of ipRGCs. This mechanism underlies opioid-induced attenuation of light evoked firing of ipRGCs. As ipRGCs are exclusively responsible for photoentrainment of the sleep-wake cycle, further elucidation of opioid-induced inhibitory effects on ipRGCs may have significant impact on future therapeutic mediation of circadian rhythm pathology and thereby treatment of the current opioid epidemic. **Keywords:** Opioids, mu opioid receptor, retina, melanopsin, ganglion cells, circadian, potassium channel, electrophysiology

#### 47) Requirement of AKAP79/150 palmitoylation in synaptic plasticity

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Lipid modifications, such as palmitoylation, are important for protein localization, including targeting to the synaptic membrane and recycling endosomes (REs). Palmitoylation is a reversible lipidation of cysteine residues that is emerging as an important regulator of synaptic plasticity through its ability to control trafficking and function of a number of postsynaptic proteins. A-Kinase Anchoring Protein 79/150 (AKAP79/150, human/rodent) is a

postsynaptic scaffolding protein that anchors kinases (PKA, PKC) and phosphatases (Calcineurin/PP2B) that control AMPAR trafficking. Previous work in the lab using a knockdown/replacement strategy in rat neurons showed that AKAP79/150 is palmitoylated and when this lipid modification is prevented, AKAP79/150 localization to dendritic REs is lost, activity-induced RE exocytosis is impaired, and subsequent delivery of the AKAP and AMPARs to synapses during LTP is prevented. In my poster, I will test the hypothesis that AKAP79/150 palmitoylation is required for synaptic plasticity. Our lab has generated a palmitoylation-dead knock-in mutant of AKAP150, the first animal to our knowledge with such a mutation, where the two palmitoylated cysteines in the polybasic N-terminal domain of AKAP are mutated to serines (AKAPCS). **Keywords:** Palmitoylation, fractionation, synaptic plasticity, field electrophysiology, whole-cell electrophysiology, AKAP79/150, super resolution microscopy

#### 48) Influence of perineuronal nets on the firing properties of neurons within the prefrontal cortex after exposure to cocaine

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Repeated drug use creates persistent drug-related memories, which contributes to chronic relapse in drug addicts. Our laboratory is interested in studying how the extracellular matrix and associated proteins contribute to the development and persistence of drug memories. Perineuronal nets (PNNs) are specialized extracellular matrix structures that primarily surround the soma and proximal neurites of inhibitory parvalbumin-containing interneurons. However, a small percentage of pyramidal cells (~20-25%) also are surrounded by PNNs. PNNs provide protection from oxidative stress, help regulate the ionic microenvironment, and play a significant role in synaptic stabilization. Previous work by our collaborator, Dr. Sorg, has shown that removal of PNNs within the medial prefrontal cortex (mPFC) disrupts cocaine-induced reinstatement. In addition, work by us and others have shown that PNNs influence the firing properties of cells. This work looks to expand upon our previous findings and systematically define the dynamic changes in intrinsic excitability and synaptic transmission from neurons with and without PNNs within the prelimbic PFC (PL-PFC) following cocaine exposure. To characterize the electrophysiological properties of cells within the PL-PFC brain slices from male Sprague Dawley rats (PND60) were prepared and whole-cell recordings were performed. PNN positive cells were identified by Wisteria floribunda agglutinin (WFA)-induced fluorescence. A subset of WFA+ pyramidal cells (slow-adapting regular spiking group II) displayed a significant reduction in their firing pattern in response to depolarizing current pulses under basal conditions relative to WFA- neurons. A single cocaine injection (12mg/kg i.p.) did not significantly alter the firing pattern of WFA+ or WFA- pyramidal neurons relative to saline controls. Future studies are looking at repeated cocaine exposure to determine whether this influences firing properties of WFA+ and WFA- negative neurons as previous work by our collaborators has shown that repeated cocaine exposure increases the intensity of PNNs and may render neurons resistant to plasticity. Through this work we hope to identify the functional consequences of cocaine-induced PNN adaptation, which may lead to novel therapeutics for the treatment of drug addiction.

#### 49) Exposure to a high-fat diet attenuates perineuronal net intensity in the prefrontal cortex

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A key factor to the development of obesity is the overconsumption of foods calorically high in fat, which not only elicits weight gain but promotes plasticity within the reward circuitry of the brain. Our previous work shows that exposure to food calorically high in fat induces structural plasticity within the medial prefrontal cortex (mPFC). Specifically, we see a decrease in dendritic spine density on pyramidal cells within the infralimbic prefrontal cortex (IL-PFC). Relative to drugs of abuse little is known about food-induced neuronal plasticity within the reward circuit of the brain, which may facilitate maladaptive food seeking behaviors. Of particular interest to our lab and our collaborators is the role of perineuronal nets (PNNs) in mediating experience-dependent plasticity. PNNs are specialized extracellular matrix structures that surround, primarily, the soma and proximal neurites of inhibitory parvalbumin-containing interneurons. PNNs contribute to synaptic stabilization, provide protection from oxidative stress, and help regulate the ionic microenvironment within cells. Recent work by our collaborator Dr. Sorg has shown that exposure to cocaine results in modification of the PNN intensity within the mPFC. We set out to determine whether exposure to a diet high in fat (60%) would alter the presence and/or intensity of PNNs in the PFC. To test this, we placed rats on one of three dietary conditions: ad libitum chow, ad libitum 60% high-fat, or restricted 60% high-fat for three weeks and subsequently quantified PNN density and intensity in the IL-PFC, prelimbic prefrontal cortex (PL-PFC), and orbitofrontal cortex (OFC). Our results demonstrate that fat exposure induces a significant reduction in PNN intensity in both the PL-PFC and OFC and a decrease in PNN density in the OFC. Interestingly, no changes were observed in the IL-PFC, suggesting that high-fat consumption may alter excitatory and inhibitory structures in a regionally specific manner. **Keywords:** prefrontal cortex, perineuronal net, high-fat

## 50) Somato-dendritic mu opioid receptors inhibit the activity of pro-opiomelanocortin neurons in the arcuate nucleus of the hypothalamus through multiple effector pathways

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The excitability of pro-opiomelanocortin (POMC) neurons of the arcuate nucleus of the hypothalamus is regulated by mu opioid receptors (MORs) in two distinct compartments; axon terminals pre-synaptic to POMC neurons where opioid receptors inhibit synaptic release and do not undergo acute desensitization, and the somato-dendritic region post-synaptic to upstream inputs where opioid receptors hyperpolarize the cell by activating a G-protein-coupled inward rectifier potassium (GIRK) conductance which desensitizes by ~50% within minutes following maximal activation by opioid agonists. We hypothesized that the differential desensitization of the MOR would result in a dynamic evolution of POMC excitability during the first few minutes of opioid receptor activation which would eventually reach a steady-state after post-synaptic MORs had fully desensitized. Using a combination of extracellular action potential (AP) firing recordings and genetically encoded calcium indicator (GCaMP6F) recordings in acute hypothalamic brain slices, we found that the inhibition of AP firing and Ca<sup>2+</sup> activity by maximal activation of MORs did not desensitize acutely during a 10-minute drug application. Furthermore, blockade of GIRK channels with 100  $\mu$ M Ba<sup>2+</sup> only resulted in a 2-fold rightward shift of the EC<sub>50</sub> of inhibition of Ca<sup>2+</sup> activity by the opioid agonist [Met<sup>5</sup>]-Enkephalin (ME), from 150 nM to 300 nM, indicating that an effector other than GIRK channels was mediating the inhibition. Thus the inhibition of POMC activity by activation of MORs is achieved through multiple effector pathways and this appears to obscure the effects of receptor desensitization due to the robust inhibition achieved by each of the effector pathways. **Keywords:** brain slice, GCaMP6F, opioid receptors, hypothalamus, POMC

## 51) AgRP neurons do not contribute tonic GABAergic inhibition onto POMC cells

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Critical to the regulation of homeostatic energy balance are the orexigenic agouti-related peptide (AgRP) neurons and the anorexigenic proopiomelanocortin (POMC) neurons located within the arcuate nucleus of the hypothalamus. AgRP neurons are predominately inhibitory projection neurons and release two inhibitory neuropeptides, neuropeptide Y and AgRP. Additionally, AgRP neurons can exert pronounced physiological and behavioral effects through the release of GABA onto efferent targets. Despite what is known about the downstream activity of AgRP cells, the GABAergic connectivity between AgRP and POMC cells remains to be fully elucidated. Further, while POMC cells receive substantial GABAergic input, the afferent origin of these signals is not completely understood. Therefore, we employed transgenic, electrophysiological and pharmacological techniques to probe the physiological contribution of AgRP to POMC GABAergic connectivity in mouse brain slices. To make initial measurements of this circuit we transgenically deleted the vesicular GABA transporter (VGAT) in AgRP neurons. The frequency of spontaneous IPSCs (sIPSCs) recorded from visually identified POMC cells was similar in hypothalamic slices from AgRP VGAT KO animals relative to wild type (WT) controls (WT:  $5.8 \pm 0.74$  Hz; VGAT KO:  $6.2 \pm 1.29$  Hz,  $p = 0.77$ ). Further, fasting the mice overnight resulted in an increase in sIPSCs onto POMC cells, an effect that was not blocked by AgRP VGAT KO. To limit the potential contribution of compensatory mechanisms arising from constitutive deletion of GABA from AgRP cells we employed a strategy wherein mu opioid receptors (MOR) were deleted from AgRP neurons and inhibition of presynaptic GABA release onto POMC neurons following bath application of the MOR selective agonist DAMGO was assessed. 10  $\mu$ M DAMGO produced similar inhibition of sIPSC frequency in both WT (from  $6.2 \pm 0.96$  Hz to  $1.65 \pm 0.83$  Hz) and AgRP MOR KO mice (from  $7.07 \pm 1.48$  to  $2.49 \pm 0.72$ ). Collectively, these data suggest that tonic inhibitory modulation of POMC cells can be attributed primarily to activity of non-AgRP neurons. **Keywords:** hypothalamus, electrophysiology, channelrhodopsin, knock out, GABA

## NEUROENDOCRINE

## 52) Effects of chronic caffeine exposure on rat brain serotonergic systems

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Chronic caffeine exposure during adolescence has been shown to induce persistent maladaptive anxiety-like behavioral responses into adulthood in rats. It is possible that these maladaptive responses are mediated by the serotonergic system. In this study, we investigated the effects of chronic adolescent caffeine exposure on the rat brain serotonin (5-hydroxytryptamine; 5-HT) system. Specifically, we analyzed serotonergic neuron gene expression and activation in subregions of the dorsal raphe nucleus (DRN), a brainstem region with abundant serotonergic neurons. After a week of acclimatization, rats were randomly divided into four groups in a two-by-two experimental design. Two groups received chronic caffeine (CC) administration in drinking water (0.3 g/L) from postnatal day 28 to postnatal day 56 while the other two groups received drinking water (NC) alone during the same developmental time period. After 28 days of caffeine or control treatment and a 24-hour washout period, rats

received an i.p. injection of either 30 mg/kg caffeine (C) or 0.9% sterile saline (S) vehicle, were then replaced in their home cages, and were euthanized 90 minutes following treatment for immunohistochemistry experiments and 4 hours following treatment for in situ hybridization histochemistry experiments. This was a 2 x 2 design with four treatment groups, NCS, NCC, CCS, and CCC. Using in situ hybridization histochemistry data caffeine has profound and unexpected decreases in DRN-wide expression following treatment. The changes of expression for SLC6a4, 5ht1a, and OCT3 mRNA were more moderate and region specific. Using a double immunostaining technique we quantified the immunoreactivity for the acute activation marker c-Fos and tryptophan hydroxylase 2 (Tph2) as a marker of serotonergic neurons. NCC rats, relative to NCS and CCC groups, had higher activation of 5-HT neurons in the rostral-dorsal portion of dorsal raphe (rDRD) and caudal-dorsal portion of the dorsal raphe (cDRD), ventral part of the dorsal raphe nucleus (DRV), caudal portion of the dorsal raphe (DRC), and intrafascicular portion of the dorsal raphe (DRI). These data are consistent with the hypothesis that the DRN is a key structure in promoting the adult pro-anxiety behavioral phenotype following adolescent caffeine exposure. **Keywords:** Serotonergic, 5-HT, caffeine, dorsal raphe nucleus, immunohistochemistry, in situ hybridization

### 53) The effect of Fgfr3 deficiency on HPG axis function

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The hypothalamic-pituitary-gonadal (HPG) axis coordinates communication between the brain and the gonad to initiate the onset of puberty and reproductive function in mammals. Defects in this axis have significant implications for the ability of mammals to reproduce. An example, hypogonadotropic hypogonadism, is a condition in which the hypothalamus or pituitary harbors a defect in the ability to secrete the hypophysiotropic neurohormone gonadotropin-releasing hormone (GnRH) or gonadotropins (FSH and LH), respectively. Neurons that secrete GnRH express two of the four receptors of the fibroblast growth factor (Fgf) signaling family, Fgfr1 and Fgfr3. Previously, Fgfr1 has been shown to be required for the proper birth and specification of GnRH neurons during prenatal development, but Fgfr3 does not appear to be required prenatally. Instead, it is hypothesized that Fgfr3 functions to maintain the GnRH neuron population postnatally. The goal of this work is to examine the function of the HPG axis in transgenic mice harboring a global heterozygote knockout of Fgfr3 (Fgfr3<sup>+/-</sup> mice) at postnatal day (PN) 30, 60, and 120. To assess hypothalamic function, GnRH neuron numbers and relative expression of GnRH mRNA are quantified in wildtype (WT) and Fgfr3<sup>+/-</sup> mice. Concentrations of FSH and LH in the pituitary and plasma of WT and Fgfr3<sup>+/-</sup> mice are quantified to assess the function of the pituitary, and the gonadal function is explored via immunohistochemistry for cleaved caspase-3 within the ovary of WT and Fgfr3<sup>+/-</sup> mice. Previous findings show a significant decrease (43%) in GnRH neuron number in Fgfr3<sup>+/-</sup> mice compared to WT at PN60. However, current data shows no significant difference in GnRH mRNA expression at PN60 or PN120, suggesting that the GnRH system may compensate for a deficit in GnRH neuron number by upregulating GnRH transcript levels. (This work is supported by NIH R01 HD042634). **Keywords:** GnRH, fertility, transgenic mouse, HPG axis, Fgf signaling, Fgfr3

### 54) Compensatory mechanisms for GnRH production in Fgf8-deficient mice

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GnRH (gonadotropin-releasing hormone) is a peptide hormone produced by neurons from the brain and is indispensable for the onset and maintenance of vertebrate reproduction. The development of GnRH neurons relies greatly on fibroblast growth factor (Fgf) signaling. In fact, it has been shown that in fibroblast growth factor 8-deficient (F8 Het) mice, the number of GnRH neurons is reduced by about 50%. Interestingly, F8 Het males and females appear to compensate for this reduction by undergoing normal puberty and producing normal levels of the GnRH peptide before 60 days of age. However, the mechanisms for this compensation are unknown. We hypothesized that F8 Het mice may compensate for a defected GnRH system by increasing the production of transcripts for: (1) GnRH, (2) two GnRH prohormone processing enzymes, CPE and PCSK2, and (3) KiSS1, an upstream stimulator of GnRH release and neuronal activity. Accordingly, the goal of this project was to use quantitative polymerase chain-reaction (qPCR) to investigate if genes involved in these three levels of GnRH system control were upregulated in F8 Het mice. Our results suggest that none of mechanisms proposed were responsible for the plasticity observed. In fact, F8 Het mice harbored significant defects in both GnRH and KiSS1 expression. Our results highlight the complex levels of control that drive the function of the GnRH system and suggest other compensatory mechanisms that we have not yet identified are at play. **Keywords:** GnRH, Fgf signaling, puberty, transgenic mice, Fgf8, KiSS1, GnRH prohormone

### 55) Multicellular signaling in the gut: linguistic convergence?

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Signaling in the intestine involves communication among commensal bacteria, immune cells, and neural components using numerous shared secretory products. Peptides such as gonadotropin releasing hormone (GnRH), calcitonin gene related peptide (CGRP), corticotropin releasing hormone (CRH), galanin, and the

monoamine serotonin are often secreted by multiple cell types and bacteria (Grenham et al., 2011). Chemical signaling between enteroendocrine cells and enteric neurons occurs, and both cell types can communicate with enteric glia (Bohorquez & Liddle, 2015). In addition, some receptor types such as toll-like receptors, are expressed on enteric neuronal, immune, and epithelial cells, and exhibit altered expression in the presence of certain bacteria (Hormann et al., 2014). Studying these secreted factors and their impact on gut function and health requires models, many of which lack some of the cell types and/or bacteria present in vivo, and struggle to maintain tissue health beyond 24h ex vivo. Using an organotypic slice model, 250  $\mu$ m thick intestinal slices are generated from transgenic mice expressing yellow fluorescent protein driven selectively by the Thy-1 promoter, allowing visualization of enteric neurons in healthy tissue for up to 6 days ex vivo (Schwerdtfeger et al., 2016). Enteric neuronal projections in these slices show movements that change speed and distance traveled over the course of 2h after treatment with lipopolysaccharide, a component of bacterial cell walls. The slice model can be used to extract luminal fluid for analysis as demonstrated by the detection of serotonin after 48h ex vivo. Immunohistochemistry demonstrated abundant GnRH immunoreactive varicosities surrounding enteric submucosal ganglia. CGRP and CRH immunoreactivity was seen in enteric fibers throughout the myenteric and submucosal regions, and galanin immunoreactivity was restricted in the myenteric region. Finally, S100B immunoreactive enteric glia were located throughout the myenteric and submucosal plexuses. These results set the stage for further dissection of peptide signaling networks amongst enteric neuro-immune-bacterial systems in a model that can be manipulated parametrically in controlled environments ex vivo. **Keywords:** organotypic, intestine, signaling, peptides

## 56) Effects of acute systemic corticosterone (CORT) treatment on clock gene expression in the male rat brain

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Daily cycles in clock gene expression, or circadian clocks, exist in cells throughout the body. These clocks consist of positive arm genes *Bmal1* and *Clock*, whose protein products induce transcription of negative arm genes *Per* and *Cry*. PER and CRY proteins then feedback to inhibit the positive arm, creating a molecular oscillation with a period of ~24h. In mammals, light is transduced into cellular clock gene expression by a brain region called the hypothalamic suprachiasmatic nucleus (SCN). Serving as a master circadian pacemaker, the SCN regulates diurnal release of adrenal glucocorticoid hormones (CORT), which in turn entrain circadian clocks in many peripheral cells. The clock gene *Per1* has a CORT receptor response element in its promoter, a potential mechanism for such entrainment. This process aligns peripheral cell functions to the solar day. It is generally believed that extra-SCN brain clocks may also depend on CORT as a critical circadian entraining factor, but few studies have actually tested whether acute CORT can induce *Per1* expression in brain tissue. Presented here are three experiments examining whether acute systemic CORT injection is sufficient to induce *Per1* mRNA expression in the male rat brain. Our results align with our past work showing that 30 min of acute restraint stress rapidly increases *Per1* mRNA in the rat hypothalamus and neocortex, but that this induction is abrogated by ADX only in the hypothalamus. These findings suggest that acute stress may induce *Per1* expression differently in different brain regions, through both CORT-dependent and CORT-independent mechanisms. **Keywords:** stress, glucocorticoids, clock genes, circadian rhythms, *Per1*

## 57) Chronic variable stress reduces oxytocin and fos immunoreactivity in the paraventricular nucleus (PVN) of the female mouse

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While oxytocin is primarily associated with social bonding and reproductive function, this hormone has more recently been implicated in anxiolysis. Oxytocin levels in plasma and in the paraventricular nucleus (PVN) are elevated following acute stress, and microinfusion of oxytocin into the PVN decreases anxiety-like behavior in the rodent. Oxytocin's effects on anxiety-like behavior likely result, in part, from this hormone's mediation of the hypothalamo-pituitary-adrenal (HPA) axis. Intracerebroventricular (i.c.v.) oxytocin infusion decreases PVN corticotropin releasing hormone (CRH) mRNA following restraint stress, while i.c.v. administration of an oxytocin antagonist increases plasma corticosterone levels. Despite the known effects of acute stress on oxytocin, the effects of chronic variable stress (CVS) on oxytocin neurons are not well understood. One study investigating CVS in the male rat found a mild increase in oxytocin mRNA and immunoreactivity (ir) within the PVN. Additionally, while PVN fos expression is decreased following CVS in the male rat, it has not been assessed in the female mouse. In the current experiment, female C57BL/6J mice exposed to six weeks of CVS and age-matched controls underwent twenty minutes of immobilization stress on the afternoon of diestrus. 90 minutes after stressor onset subjects were transcardially perfused, and brains were examined for fos-ir and oxytocin-ir using immunofluorescence. In a separate group of subjects, brains of CVS-treated females and age-matched controls were flash frozen, and the PVN was isolated by micro punching and analyzed for corticotropin releasing hormone (CRH) mRNA using digital droplet PCR. Within the PVN, immunohistochemistry results indicated a decrease in both oxytocin-ir ( $p < 0.05$ ) and fos-ir ( $p < 0.01$ ) in CVS-exposed animals. The percentage of activated oxytocin cells were not altered following CVS

exposure. Finally, we report alterations in HPA axis activity following CVS, indicated by an increase in adrenal weight, a blunted corticosterone response to acute stress, and an elevation in CRH mRNA within the PVN. These findings demonstrate a downregulation in both oxytocin-containing neurons and stress-induced neuronal activation in response to CVS in the female mouse, indicating an additional mechanism by which CVS may negatively impact rodent behavior and neuroendocrine response.

#### 58) Cortisol responses to stress are blunted among infants delivered by Cesarean section

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Background: Cesarean section (CS) birth has been shown to have long-term consequences on offspring health later in life such as an increased risk for obesity, asthma, and diabetes. Given that nearly one third of infants are born by CS, it is important to understand the mechanism by which CS impacts health outcomes. It is possible that the hypothalamic-pituitary-adrenal (HPA) axis is one potential mechanism for this relation. Infant HPA axis functioning has been shown to differ by mode of delivery such that infants born via CS have lower cortisol levels at birth and at eight weeks postpartum. It is unclear how long this difference persists. Understanding the implications that mode of delivery has on the infant HPA axis is important given the role it plays in health outcomes. Methods: The current study evaluated the association between mode of delivery and infant cortisol response to inoculation at 6 months of age in 138 infants (74 male). Results: A repeated measures ANOVA showed that cortisol concentrations increased from baseline in response to the inoculation challenge,  $p < .001$ . Infants delivered via CS had significantly lower cortisol levels at baseline and in response to inoculation than infants delivered vaginally,  $p < .05$ . Discussion: These results indicate that mode of delivery is associated with the infant cortisol response to stress. It is possible that mode of delivery programs the development of the HPA axis. These data suggest that alterations in HPA axis functioning may be one of the mechanisms by which Cesarean delivery has long-term health consequences as altered HPA axis functioning early in life has been linked to later risk of metabolic disease.

#### 59) Corticotropin-releasing hormone (CRH) regulation by acute glucocorticoid receptor activation and restraint stress

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Activation of the hypothalamic pituitary adrenal (HPA) axis enables homeostatic responses to environmental changes by increasing glucocorticoid (GC) production. Yet, chronic HPA activation alters behaviors in rodents and increases risk for neuropsychiatric disorders in humans, emphasizing the importance of understanding its regulation. The principle regulator of the HPA axis is CRH, a GC regulated neuropeptide synthesized and secreted by neurons of the hypothalamic paraventricular nucleus (PVN). Largely through binding to the glucocorticoid receptor (GR), GCs directly down-regulate PVN crh to maintain stress-induced HPA activity within homeostatic limits. Despite their significance, the molecular mechanisms underlying GC negative regulation of crh remain poorly understood. Thus, using immunohistochemistry on CRH-cre:tdTomato (Ai14) mice in which CRH neurons are permanently tagged with a tdTomato fluorophore, we initially demonstrated expression of GR in virtually all CRH neurons of the PVN. To then determine if GRs are involved in the effects of acute GC treatment on HPA activity and CRH expression we utilized digital droplet PCR (ddPCR) to allow us to measure, with a high degree of sensitivity and accuracy, absolute levels of CRH mRNA and primary transcript (heterologous nuclear RNA; hnRNA) in micropunched PVN. 48 hrs after adrenalectomy (ADX), male C57b15/J mice were injected with RU28362 (0.4 mg/kg BW; a selective GR agonist) or Vehicle and then challenged with a 20-minute restraint stress. Mice were sacrificed immediately at the end of restraint (stressed mice) or after removal from their homecage (unstressed mice). Brains were frozen, thick coronal sections were taken, and the PVN were micropunched. Absolute levels of CRH mRNA and CRH hnRNA were measured using ddPCR. Results show that RU28362 treatment decreases CRH hnRNA compared to vehicle treated controls in non-stressed animals ( $P < 0.05$ ). Following the 20' restraint stress, we also observed a significant decrease in CRH mRNA ( $P < 0.01$ ) and hnRNA ( $P < 0.01$ ), which was potentiated by RU28362. These data indicate that GCs can act through GR to rapidly suppress HPA activity; and, moreover, that restraint stress can also rapidly reduce CRH transcription. Our results ultimately suggest that GR plays a role in down-regulating PVN CRH in a context dependent manner. **Keywords:** ddPCR

#### 60) Alternative mechanisms for HPA axis regulation following selective paraventricular nucleus (PVN) deletion of estrogen receptor beta 3rd exon

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The PVN is the main integratory node of the Hypothalamo-Pituitary-Adrenal (HPA) axis and it expresses estrogen receptor beta (ER $\beta$ ) at high levels; activation of which has been shown to decrease HPA axis response to stress. In this study, we aimed to elucidate the actions of ER $\beta$  in the PVN in male and female mice. For this, we used a Sim1-Cre transgenic mouse crossed to a reporter line where loxP flanked the ER $\beta$  3rd exon to target the deletion of the 3rd exon of ER $\beta$  to Sim1-Cre-expressing neurons, which are densely present in the PVN. Immunohistochemistry of

these mice (ERbCKO) showed complete knockout of ERb in the PVN, but not in other brain areas that express Sim1. Interestingly, although the ER $\beta$  3rd exon codes for the downstream half of the DNA binding domain utilized in classical estrogen response element (ERE) signaling pathways, treatment of mice with the ER $\beta$  selective agonist, R-DPN (1 mg/kg BW for 4 days), still reduced the corticosterone (CORT) to restraint stress, albeit with slightly less efficacy in the ERbCKO mice compared to WT. These data suggest that the DNA binding domain is not required for ER $\beta$  signaling within the PVN, at least in the control of HPA axis function. Furthermore, deletion of ER $\beta$  3rd exon resulted in an increase in exon 4-8 transcripts which corresponds with the ability of the 3rd Exon deletion variant to utilize an activator complex-1 (AP-1) mediated signaling pathway rather than ERE-dependent signaling in vitro. Alternatively, the PVN receives inputs from the bed nucleus of the stria terminalis (BnST), a region that serves as a major information hub, to inhibit the HPA axis. Using a CRH-cre mouse crossed to a loxP-STOP-loxP-TdTomato reporter strain (Ai14), we found a large cluster of CRH neurons in the BnST. IHC using the Z8P ab against ERb showed that over 23% of BnST CRH neurons expressed ERb. Moreover, in the mouse PVN, 31% of CRH neurons also express ERb. Thus, BnST may serve as a limbic-PVN bridge, integrating excitatory signals from upstream brain sites. In turn, the BnST uses GABAergic or CRH projections to the medial parvocellular PVN, to regulate the HPA axis. These findings suggest a potential ERb-ergic circuit involving BnST and PVN CRH neurons, and also give insight to an alternative ER $\beta$  signaling pathway that may rely on AP-1 mediated transcriptional activation, potentially through the recruitment of ER $\beta$  splice variants encoded by exons downstream of the 3rd exon. **Keywords:** CLARITY, imaging, Imaris

## SENSORY AND MOTOR SYSTEMS

### 61) Representation of calls in the activity of neurons in the songbird premotor nucleus HVC

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Calls are a vocalization produced by both male and female songbirds that are shorter in duration than songs and have a less complex acoustic structure. Some parts of the call vocalization have been shown to be learned. Lesion and electrophysiological studies indicate that the nuclei in the song motor pathway, HVC and RA, are necessary for call vocalizations. This study investigated the role of HVCINT and HVCX neurons in both production and perception of call vocalizations. Individual HVCX or HVCINT neurons were recorded in awake and freely behaving adult male Bengalese finches (*Lonchura striata domestica*) using a miniature motorized microdrive. Neurons were identified through bipolar antidromic stimulation from Area X. To determine the activity of cells during call production and perception, calls were recorded through a microphone and played back through a speaker. A majority of HVCX neurons recorded were active in association with auditory playback of the birds own call (BOC). This result suggests that the song learning pathway does receive auditory-related activity that is associated with calls, supporting the idea that the song system is no longer involved in just song production and learning, but instead is a vocal communication system including songs and calls. Analyses of the spectral content of BOC that elicited activity in HVCX neurons are ongoing in addition to studies investigating the response selectivity of HVCX neurons to other call stimuli such as heterospecific calls or conspecific female calls. All HVCINT sampled were active prior to call production. This finding could indicate that either HVCINT neurons are active in driving the vocalization of calls (e.g. through precise regulation of HVCRA neurons) or HVCINT neurons are relaying a motor copy (e.g. corollary discharge) of the call from the HVCRA neurons to a sensorimotor network. These results indicate that call-related activity is present in HVCX and HVCINT neurons and support the role of the song system in representing the sounds used communication that include both songs and calls. **Keywords:** Awake electrophysiological recordings from freely behaving animals

### 62) Identification of metabolite-sensing muscle afferents in vivo using GCaMP6s

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Although many chronic pain conditions are musculoskeletal in nature, the sensory inflow from muscles under different metabolic states is poorly understood. Recently, two populations of muscle afferents were shown to respond to different concentrations of muscle metabolites in reduced preparations (Light et al., J Neurophys 100: 1184, 2008; Jankowski et al., J Neurophys 109: 2374, 2013); metaboreceptors responded best to lower levels found in muscle following moderate exercise and may contribute to the sense of fatigue, whereas metabonociceptors responded best to higher levels found after strenuous and/or ischemic contractions and may contribute to pain (Pollak et al., Exp Physiol 99:368, 2014). To better understand the properties of metabolite-sensing muscle afferents in vivo, we imaged population responses of these cells in GCaMP mice. Briefly, mice with GCaMP6s expression in all cells were anesthetized, L3-5 DRGs exposed, and DRG cells imaged while infusing the gastrocnemius with different metabolite solutions [control: 300nM ATP, 1mM lactate, pH 7.4; low: 1 $\mu$ M ATP, 15mM lactate, pH 7.0; high: 5 $\mu$ M ATP, 50mM lactate, pH 6.6; N=6]. To date, 40 DRG cells that responded to infusions have been characterized. A few (n=6) responded equally well to control and metabolite infusions and were presumably chemically-

insensitive mechanoreceptors. However, most in our sample ( $n=34$ ) responded robustly to elevated metabolite levels and could be divided into two subpopulations. Half responded best to high metabolite levels ( $17.03 \pm 3.35 \Delta F/F$ ,  $n=17$ ,  $p<0.01$ , ANOVA w/ Tukey's) and were presumably metabonociceptors, whereas the rest responded best to low metabolite levels ( $16.61 \pm 2.68 \Delta F/F$ ,  $n=17$ ,  $p<0.05$ ) and thus identified as metaboreceptors. Interestingly, the cell bodies of most metaboreceptors were small ( $76\% \leq 27 \mu\text{m}$ ) whereas the majority of metabonociceptors had medium-to-large diameter somata (60% between 28–43  $\mu\text{m}$ ), further suggesting these are distinct populations. Overall, these findings confirm two populations of metabolite-sensing muscle afferents in vivo under normal conditions and suggest that the majority of metaboreceptors exhibit fine-diameter afferent fibers that are selective for metabolites. Further studies using GCaMP to examine plasticity of these afferents in vivo may provide valuable insight into the development of chronic musculoskeletal pain. **Keywords:** GCaMP, muscle nociceptors

### 63) A role for glycine in altered excitation and inhibition in the auditory brainstem of fragile X mice

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The sound localization pathway in the auditory brainstem helps us to make sense of a conversation in situations where distracting background sounds are present, and forms the neural basis for our cognitive ability to focus on the sound source of interest. Being unable to localize the source of a sound, and to focus on a conversation when distracting noises are present, is a cardinal symptom in autistic patients. This autism related auditory dysfunction is most noticeable as impairments in communication skills, social difficulties and sound localization. A recent theory posits that autism spectrum disorders may be caused by an imbalance in the ratio of excitation to inhibition, particularly in sensory systems. Since sound localization relies heavily upon the synaptic ratio of excitation and inhibition (E/I ratio) in the auditory brainstem, we hypothesized that these neural circuits may be altered in a mouse model of autism, the Fragile X mouse (Fmr1<sup>-/-</sup>).

We investigated differences in presynaptic markers for the neurotransmitters glutamate, glycine and GABA in the nuclei of the mammalian sound localization pathway, specifically the medial nucleus of the trapezoid body (MNTB), anterior ventral cochlear nucleus (AVCN), ventral nucleus of the trapezoid body (VNTB) and the lateral superior olive (LSO). These centers receive substantial excitatory and inhibitory inputs and relay sound information to each other for different types of processing and sound sources.

Recently, it has been shown that there are more presynaptic GABAergic synapses in the MNTB of Fmr1<sup>-/-</sup> mice as indicated by vesicular GABA transporter (VGAT). This study, however, did not investigate the effect of glycine, which, in the MNTB, becomes the primary inhibitory neurotransmitter in adulthood. The main reason why glycine has not been studied in the context of Fragile X is that the current E/I model of Fragile X assumes most changes occur in GABAergic inhibition. Here we address the role of glycine in Fmr1<sup>-/-</sup> mice by anatomical studies examining changes in number and organization of glycinergic neurons and synapses in the MNTB. Our results suggest that all three: glycine, glutamate and GABA are altered in Fmr1<sup>-/-</sup> mice, suggesting that not only GABAergic but also glycinergic inhibition may play an important role in auditory impairments seen in Fragile X. In addition changes in inhibition and excitation may lead to impairments in auditory processing and sound localization difficulties. **Keywords:** Optogenetics, anatomy, behavior

### 64) A comparison of autism-spectrum quotient (AQ) factors in non-clinical populations using mismatch negativity

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Autism Spectrum Disorder (ASD) is known to present atypical responses to different sensory stimuli. Humans typically recognize auditory patterns through an inherent measurement of time. Therefore, individuals with ASD may demonstrate abnormal responses to auditory stimuli in regards to temporal processing. The present study investigated the Event Related Potential (ERP) specifically known as Mismatch Negativity (MMN) within individuals suggested to be exhibiting symptoms of high-functioning ASD (HFASD). This ERP has frequently been proposed as an objective method to index auditory sensory memory, in other clinical populations, but is understudied in HFASD. To assess possible HFASD traits in participants, The Autism Spectrum Quotient (AQ) survey was administered. The AQ measures five specific factors of ASD: social skills, attention to detail, attention switching, communication skills, and imagination. Participants ( $N=68$ ) who scored above a 26 were categorized as symptomatic of HFASD ( $n=31$ ) and below a 26 were categorized as controls ( $n=37$ ). Brain activity was recorded using the EEG 10-20 system for 30 minutes while participants listened to 2880 samples (120 cycles of 24 samples) of randomized standard and a deviant tone that differed in duration (Standard = 500 ms; Deviant = 250 ms). A correlation analysis of the ASD factors revealed a significant negative correlation between the social skill factor and MMN amplitude at the Fz, Cz, and Pz electrode locations. This data may suggest dMMN as a useful tool for identifying symptoms of high-functioning ASD. **Keywords:** Autism Spectrum Disorder (ASD), Mismatch Negativity (MMN), EEG, temporal processing

## 65) Manual and automated approaches for quantification of fungiform papillae on the tongue

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The overarching goal of our project is to develop an auditory substitution device that can translate auditory input into an electrical signal on the tongue, which can then be recognized and interpreted through practice as useful language information, much like learning Braille. Successful development of this novel device would provide an inexpensive alternative for individuals affected by auditory defects who aren't well suited for currently available options such as hearing aids, cochlear, or brainstem implants. The electrotactile device we are developing stimulates mechanosensory fibers, which are distributed throughout the tongue, both within connective tissue structures called fungiform papillae (FP), and in regions devoid of papillae. The exact distribution of mechanosensory fibers within and between papillae is unclear, although it is known that people have different densities of fungiform papillae. Currently, we are interested in determining whether papillae density correlates with differences in electrotactile sensitivity and discrimination ability. If a correlation exists, the distribution and number of papillae could be used as a model for predicting a particular participant's sensitivity to electrotactile stimulation (ETS). To determine whether or not there is a correlation between location and density of papillae and ETS sensitivity, participants' tongues were stained with blue food dye and photographed. Then two different researchers manually counted the papillae based on specific parameters. Initial counts varied widely between researchers, and we are now exploring methods to improve quantification. For the studies presented here, we compared the results of manual FP counts using the Denver Papillae Protocol (DPP) to counts obtained from a custom program written in MatLab, which uses image segmentation techniques to isolate and count the papillae. Results indicate that using strict criteria and the DPP for manual papillae quantification brought researcher counts to within 10%, allowing us to combine them for a statistically significant mean. Furthermore, initial data indicates that our custom MatLab program is able to detect fungiform papillae with the same accuracy as manual counts, if the image is high enough quality. However, more image segmentation techniques, such as k-means clustering, need to be explored in order to determine the efficacy of the program for long-term data analysis.

## 66) An analysis of cortical and subcortical white and gray matter volume in patients with movement disorders prior to deep brain stimulation treatment

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Subthalamic nucleus (STN) deep brain stimulation (DBS) is used to treat Parkinson's disease (PD) patients that do not respond to medication. STN-DBS is highly efficacious with a low-side effect profile. Treatment with STN-DBS often occurs in the advanced stages of PD. Given the variability in the neurodegenerative progression experienced by PD patients, there are no quantitative measures for predicting when to use STN-DBS and whom will benefit. In this study, we sought to determine whether PD disease duration correlated with changes in gray white matter structure and connectivity, in patients undergoing STN-DBS. Subcortical segmentation and total cortical parcellation was conducted using a combination of FreeSurfer, Statistical Parametric Mapping (SPM12), and ITK SNAP. Initially, it was postulated that basal ganglia structures would show reduced volumetric measurements in PD patients with longer disease duration because PD is a known neurodegenerative disease. In addition, as a control population, we included Essential Tremor (ET) patients undergoing ventral-intermediate thalamus (VIM) DBS. Volumetric measurements may not be able to identify subtle changes in neuroanatomy. Therefore, further research will analyze regional connectivity to better understand the underlying neurocircuitry of these two populations of DBS patients. **Keywords:** Deep brain stimulation, structural MRI, cortical volume

## 67) Temporal processing in college students indicating high-anxiety

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Temporal processing (TP) refers to the underlying processes that allow individuals to understand time. Accurate timing is an essential attribute for overall functionality because timing allows individuals to understand speech, initiate precise motor functions, respond to environmental warning signals, and is also related to planning and decision-making abilities. Deficits in TP are often related to psychopathology and can be quantified using an event-related potential paradigm known as mismatch negativity (MMN). MMN is a negative post-stimulus response waveform that occurs when the regularity of auditory tones is disrupted by the presence of a deviant tone. Literature has found that compared to controls, patients with disorders (e.g. schizophrenia, psychosis, dyslexia) have significantly attenuated MMN amplitudes and therefore, argue for MMN as a potential biomarker. The present study aims to support this claim in relating MMN amplitudes to scores on the state-trait anxiety inventory (STAI) in a healthy population. The hypothesis was that those who scored high on the STAI would correlate with attenuated MMN amplitudes. Participants (N = 70) were students at a large university, who took a large survey asking information regarding the following: demographics, brain injury, previous diagnoses, and family medical history. Participants also were administered the STAI to collect information regarding anxiety. Scores on the STAI can range from 20 to 80. Within this data set the range was 29-65. The mean score on the STAI was 45.2 (SD = 8.40). Brain activity was recorded using EEG at the Fz, Cz, and Pz electrode sites while participants passively listened

to 2880 samples (120 cycles of 24 samples) of randomized tones that differed in duration (Standard = 500 ms; Deviant = 250 ms). Results indicated that there was no significant correlation between electrode locations Cz or Fz and the STAI; however, Pz demonstrated a significant correlation ( $R^2 = .07$ ). Following correlation analyses, a regression was run to examine the relationship between Pz and STAI and significance was found ( $F(1,68) = 5.16$ ,  $p = .03$ ). Since this information was collected in populations without a diagnosis of anxiety and a significant effect was still found, this further supports MMN use as a biomarker for identifying those who may be more likely to develop psychopathology. **Keywords:** timing, temporal processing, electrophysiology, anxiety, event-related potentials, EEG, psychopathology

#### **68) Fungiform papillae density across the human tongue correlates with perceived intensity and discrimination ability during electrotactile stimulation for sensory substitution**

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Current treatments for hearing loss include assistive hearing aids for partial hearing loss, and cochlear implants which are invasive and only help those with peripheral auditory system damage. The overall goal of our research is to develop a sensory substitution device that transmits auditory information into a pattern of electrodes that stimulate somatosensory fibers on the tongue. Following a training period, a hearing-impaired person would be able to translate these patterns into auditory information. Sensitivity and discrimination ability for electrotactile lingual stimulation (ETS) varies substantially between individuals, complicating the creation of an optimal electrode array design for our device. The purpose of the current study is to determine whether specific neuroanatomical features correlate with the ability to perceive electrotactile stimulation. Specifically, we tested two hypotheses. The first was the hypothesis that people who can detect propylthiouracil (PROP) are better able to perceive electrotactile stimulation, and the second was that individuals with higher fungiform papillae (FP) density are better able to perceive and discriminate active electrodes. To test these questions, human participants were tested for propylthiouracil detection and their FP density determined following staining of the tongue with a 10% solution of food-grade blue dye. Electrotactile testing using a protocol that randomly activated electrodes across a 4cm by 4cm area of the tongue was then done to determine perceived intensity of the stimulus and two point discrimination ability. The PROP results, FP density and ETS data were then analyzed and compared to determine whether there was a correlation between ETS perception and PROP status and/or fungiform papillae density. Preliminary data indicate that there is no correlation between PROP taster status and ETS perception, however there does appear to be a correlation between FP density and perceived ETS intensity and discrimination ability. Participants had a higher FP density towards the most anterior portion of the tongue, and there was also greater perceived ETS intensity and two point discrimination in this region. **Keywords:** sensory substitution, electrotactile stimulation, tongue, fungiform papillae

#### **69) The relationship between cortical resource allocation, behavior, and neurocognitive function in adults with hearing loss (withdrawn)**

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Hearing loss is the 3rd most common chronic health condition facing older adults in the United States, affecting more than 30% of Americans ages 65-74 and approximately 55% of Americans over the age of 75. Perhaps equally alarming is the statistic that most adults wait over a decade following initial diagnosis before obtaining their first set of hearing aids. More recent research has shown a high correlation between hearing loss and neurocognitive consequences, including working memory and executive function deficits. Hearing loss has also been linked to increased dementia risk, such that for every 10-decibel increase in average hearing threshold, the risk for all-cause dementia increased by 20%. Current hypotheses underlying the relationship between hearing loss and cognitive decline include a common link in the aging process, social isolation, and increased cognitive load. Previous research studies in our laboratory have demonstrated that even mild hearing loss may induce changes in cortical resource allocation, including the recruitment of frontal cortex for auditory processing, and cross-modal recruitment of auditory cortex for visual and somatosensory processing. However, it remains unclear how these cortical brain changes relate to behavior and/or neurocognitive function. The purpose of this study is to examine changes in cortical resource allocation in adult hearing aid users using high-density EEG, and to correlate these changes with auditory and auditory-visual speech perception performance; self-reported scales of listening effort, depression, and social isolation; and behavioral measures of neurocognitive function. **Keywords:** high-density EEG, hearing loss, cortical resource allocation, cross-modal cortical plasticity, cognition

## OTHER TOPICS

**70) Spectral analysis of EEG activity during weekend recovery sleep**

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Millions of people worldwide suffer from insufficient sleep schedules to accommodate social and work demands of modern society. Therefore, the habit of receiving insufficient sleep during the work week and attempting to make up for this with extra weekend recovery sleep is common. Previous findings show EEG changes in response to short sleep durations and total sleep deprivation (TSD). However, the impact of ad libitum weekend recovery sleep on EEG has yet to be investigated. The aim of the current analysis was to investigate the effects of weekend recovery sleep after a simulated work week of short sleep on EEG. Sleep was assessed with standard sleep staging and quantitative EEG power spectral analyses. 36 participants (18 females) aged 25.5±4.7y (mean±SD) were randomized into one of three study conditions: 1) control received 9h sleep/night; 2) sleep restriction received 5h sleep/night; and 3) weekend recovery received 5h sleep/night for a 5 day simulated work week, then two days of ad libitum weekend recovery sleep with a minimum of 10h time in bed. Each condition began with 3 baseline nights of 9h sleep/night. Total sleep time was similar for conditions on baseline nights 2 and 3 (~8.0h) and was reduced during sleep restriction (~4.6h) on nights 4 and 5, as designed. Total sleep time for the ad libitum weekend recovery condition was significantly higher than the control or sleep restriction conditions on night 8 (~10.0h). Significant interactions between night and hour of the sleep opportunity such that delta and theta activity were significantly higher in the sleep restriction and weekend recovery conditions compared to baseline. Delta and theta power were consistently increased during sleep restriction and weekend recovery in the 1st hour of sleep. Delta and theta power were increased in the 1st and 9th hours of sleep on weekend recovery days. Beta power was significantly reduced in the sleep restriction condition after one week of insufficient sleep. Increases in lower frequency delta and theta power and the decreases in higher frequency beta power during sleep restriction and/or weekend recovery are consistent with the notion that higher homeostatic sleep pressure under these conditions is reflected by changes in multiple EEG frequencies beyond the traditionally examined delta band. **Keywords:** electroencephalogram (EEG), weekend recovery sleep

**71) Culturing primary neurons on patterned adhesive substrate allows for the separation of pre and post synaptic neuronal components**

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Cellular localization plays a key role in the function of proteins, especially within highly compartmentalized neurons. For example, several G-protein coupled receptors have been shown to desensitize within postsynaptic neuronal compartments, but not within presynaptic compartments (Pennock & Hentges, 2012). To further investigate this phenomenon, it is useful to understand if differential protein modifications or differential protein-protein interactions account for desensitization differences between pre and postsynaptic receptors. However, to do this efficiently it is necessary to physically separate axonal and somatodendritic regions for western blotting and immunohistochemistry, a task that is difficult in brain slices or in normal primary neuron culture. To overcome this difficulty, the current study focused on establishing a system in which axons from primary neurons could be harvested separately from cell bodies and dendrites. Using soft photolithography and microcontact printing, cell-adhesive Poly-D-Lysine (PDL) was patterned onto cell culture surfaces. Silicone molds were fabricated using negative photoresist, and flexible silicone stamps were cast from these molds. These stamps were used to print PDL patterns onto cell culture surfaces, which consisted of two rectangular domains with 10µm-wide lines connecting them. Using a stencil, dissociated neurons were seeded onto one rectangle, and the stencil was removed 1 day later to allow access to the lines. By 10 days in vitro, neurons had sprouted axons that followed the lines to the second PDL coated rectangle. Keeping the PDL lines below 10µm prevented cell bodies from invading the lined region, and increasing the length of the lines allowed axons to grow into the second PDL coated rectangle while excluding the shorter dendrites. By culturing neurons onto coverslips that had been pre-etched across the PDL coated lines, the coverslips could be severed so that axons were physically separated from cell bodies and dendrites. This system will be used to study whether inhibitory G-protein coupled receptors show functional differences between axonal and somatodendritic regions due to differential protein interactions or differential post-translational modifications. However, this system allows for the separation of any cellular component localized in the axon from cell bodies and dendrites, providing improved resolution to study a host of processes specific to neuronal compartments. **Keywords:** photolithography, microcontact printing, cell culture

## 72) Increased c-fos regulation in neocortical subregions in response to social interaction in young and adult female rats

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This study examined c-fos mRNA expression in the prefrontal cortex (PFC), basolateral nucleus of the stria terminalis (BNST), hypothalamic periventricular nucleus (PVN) and barrel fields of young adult (3 months) and older adult (18 months) female Sprague Dawley rats. Rats in each age group were divided into three experimental conditions: home cage control (HCC), novel context (CXT), or novel context with 10 minutes of social interaction (SI). Rats were killed 30 min after exposure to their respective experimental condition. Brains were removed and flash frozen. In-situ hybridization was used to measure mRNA expression at the time of death. Exposure to novel context produced a large increase in c-fos mRNA in all brain regions examined of both young and older female rats. In some brain regions social interaction during the last 10 min of novel context exposure produced an even greater increase in c-fos mRNA. This was evident in all neocortical subregions and the lateral septum, but not in some subregions of the BNST or PVN. This added effect of social interaction on c-fos mRNA was also more consistently evident in young compared to older female rats. These results suggest that novelty induced neural activity (as assessed by c-fos expression) in neocortex, but not some subcortical brain regions, is sensitive to an additional social component of the experience. Furthermore, the attenuated neural response to social interaction seen in older female rats is consistent with the impaired social interaction behaviors previously reported in female rats of this age when compared to 3 month old female rats.

## 73) Machine learning classification of lifestyle intervention outcomes on diffusion imaging data in older adults

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White matter (WM) integrity in the brain degenerates with age, even in neurologically healthy older adults. Exercise is one of the candidate lifestyle factors that can have protective benefits for the aging WM (Burzynska et al., 2013). However, one intervention study that investigated the effects of 1-year exercise on WM microstructure found no differences between aerobic walking and non-aerobic stretching and toning (Voss et al., 2013). One reason for this negative finding may be restricting the analyses to large WM regions (whole lobes) and focusing on center-of tract WM. This approach may not be sensitive to spatially restricted and scattered patterns of WM change resulting from lifestyle changes. To address this limitation, we explored diffusion imaging data from an exercise randomized clinical study (NCT01472744) using machine learning (ML). ML has been used with success to distinguish mild cognitive impairment from dementia based on structural brain images (Sun et al., 2009). However, it has never been applied to predict outcomes of interventions in healthy aging. Here, we aimed to find new patterns in the whole-brain voxel-wise data, not addressed in earlier regional analyses. 247 healthy adults of age 60 –79 were randomized into 6-month interventions: aerobic walking, aerobic walking + nutrition, dance, and stretching-toning control. 162 had good quality data pre- and post-intervention. We carried out unsupervised multivariate ML classification with SpaceNet penalty Graph-net or TV-L1 on two indices of WM integrity: fractional anisotropy (FA) and mean diffusivity (MD). The only information given to the model was the time point (pre- and post) and the intervention group. The 3D maps of change in WM integrity were calculated voxel-wise as post-minus-pre. The accuracies of classification were 65% for control vs. dance, 60% for control and walking/control and walking+nutrition, with chance equal to 50%. Classification prediction accuracy was tested using cross-validation. These preliminary findings suggest that whole-brain ML analyses may identify novel patterns of effects of lifestyle interventions on the aging WM. Future analyses will aim to improve classification by adding independent canonical analysis as part of data pre-processing, as well as adding regional brain volume, change in objective measures of aerobic fitness, and physical activity into the model. **Keywords:** aging, machine learning, MRI, SpaceNet, DTI, randomized clinical trial, aerobic fitness

## 74) Agonist dependent alterations of mu opioid receptor mobility

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Measuring the activity of a G-protein coupled receptors (GPCRs) generally requires the measurement of the activation or inhibition of downstream effectors that the receptors couple to. It is possible that desensitization or potentiation of downstream effectors can occur independent of the receptor of interest, thus complicating measurements of receptor activation or desensitization. In the present study single particle tracking of FLAG-tagged mu opioid receptors (MOPr) stably expressed in AtT20 cells is employed to measure receptor diffusivity before and after treatment with an agonist, thus providing a measurement of receptor activation that does not rely on downstream effectors. FLAG-MOPrs were labeled using a biotinylated anti-FLAG antibody that was subsequently conjugated to streptavidin-Qdot 565. Labeled receptors were imaged on a spinning disk confocal microscope at a rate of 20 frames/s. Videos were taken under basal conditions, and again after 10 minutes in the presence of the full

MOP agonist DAMGO. Labeled receptors were then tracked and their diffusivity analyzed before and after treatment with DAMGO. Before DAMGO application FLAG-MOPs existed in two populations, one with high mobility and another with low mobility. Activation of the receptors with DAMGO resulted in a reduction in the number of surface receptors as well as a higher fraction of the receptors being located in a low mobility state. Because a 10 min treatment with DAMGO is sufficient to cause desensitization and internalization to reach a steady, we hypothesize that the less mobile state of the FLAG-MOPr represents actively signaling receptors. Characterizing the diffusion patterns of inactive and active MOPs provides a direct measure of receptor activation that bypasses complications introduced by using the output of a given effector as a proxy for receptor activity, and may also be used to measure compartment specific differences in receptor activation that are difficult to perform using electrophysiological or biochemical techniques. **Keywords:** GPCR, single particle tracking, opioid receptor pharmacology

## 75) Role of KChIP in the stability of Kv4 channels in neurons

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K<sup>+</sup> Channel Interacting Proteins, known as KChIPs, are Ca<sup>2+</sup> binding proteins that have been shown to modulate the function and trafficking of voltage-dependent Kv4 channels. The goal of this study is to examine how a deletion of the KChIP gene affects Kv4 channels in vivo, using *Drosophila melanogaster* as a model system. In order to create a KChIP mutant, we employed a genetic strategy using PiggyBac transposable insertions that flank the KChIP gene. Each of the PiggyBac insertions contained FRT sites, oriented such that targeting by a FLP recombinase could result in deletion of the intervening sequence. In flies containing both PiggyBac elements, we induced FLP expression, and subjected individual lines to a three-step PCR screen to identify line(s) that underwent recombination and removal of the KChIP gene. We examined 120 lines, and found 5 candidate mutant lines; DNA sequencing of one of these candidates definitively confirmed the deletion of KChIP. Immunoblot analyses were implemented to analyze relative protein levels of Kv4 in the KChIP<sup>-/-</sup> mutant compared to wild-type. In both 3 and 10 day-old flies, we found a significant increase in Kv4 protein in KChIP<sup>-/-</sup> mutant flies when compared to age-matched wild-type flies. We hypothesize that KChIP is required for the trafficking of Kv4 channels from the endoplasmic reticulum (ER) to the plasma membrane, and that loss of KChIP may lead to an accumulation of Kv4 protein in the ER, thereby resulting in an increase in total Kv4 protein levels. To test this hypothesis, we will immunostain primary neurons from wild-type and KChIP<sup>-/-</sup> mutants to examine the subcellular localization of accumulated Kv4. Eventually, we would like to relate the molecular role of KChIP in neurons to behavioral consequences in vivo. **Keywords:** K<sup>+</sup> Channel Interacting Proteins (KChIP), Kv4 Channels

## 76) Altered encoding of motivational stimuli in the basolateral and central amygdala in cocaine-experienced rats

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The reinforcing properties of cocaine act via dopamine-related signaling in the nucleus accumbens (NAc). Consequently, our lab and others have shown that chronic experience with cocaine self-administration alters neural signaling properties in the NAc to the extent to which subjects experience a variety of behavioral deficits in motivated learning that normally depend on NAc processing. However, the NAc is part of a network involved in reward-related learning and receives projections from other nuclei in this circuit including a direct glutamatergic connection from the basolateral amygdala (BLA), and possible indirect connections from the central nucleus of the amygdala (CN) via the ventral tegmental area (VTA). In our lab cocaine-experienced rats display both impoverished neural encoding and abnormal phasic dopamine (DA) signals in the NAc. However it is not known whether this is due to neuroadaptations at the site of cocaine action, or whether drug experience alters associative encoding in afferent regions like the BLA and CN. Rats were assigned to either self-administer iv cocaine (Cocaine), receive passive iv infusions of cocaine (Yoked) or self-administer water to a food receptacle (Control) for 2h sessions over 14d. Following 30d of abstinence, we recorded neural activity from electrodes aimed at the BLA and CN neurons while subjects learned a first-order Pavlovian discrimination (FOC; CS+/food, CS-/nothing) followed by a second-order discrimination (SOC; SOC+/CS+, SOC-/CS-). Cocaine-experienced rats (both Cocaine and Yoked) showed greater conditioned approach during FOC sessions than Controls, but failed to show appropriate learning during SOC sessions. At the neural level, Cocaine groups showed altered neural signaling to task stimuli relative to Controls. During FOC, peak signaling for cue neurons was similar between Cocaine and Controls, but the proportion of cue-selective cells in Cocaine rats was reliably lower. Further, reward encoding in the BLA was enhanced in Cocaine groups. In contrast, CN neurons displayed both fewer cue-selective neurons and significantly lower peak activity following cue onset. During SOC sessions, both BLA and CN neurons failed to appropriately signal information about the SOC cues. These findings argue that repeated cocaine experience alters important limbic inputs to the NAc and may thus contribute to persistent neural and motivational impairments well after the cessation of drug taking activities. **Keywords:** Cocaine, neural coding, amygdala

**77) Serum GFAP levels as a predictor of prion related neurodegeneration.**

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Recent advances in bioassays have revealed serum levels of glial fibrillary acidic protein (GFAP), an intermediate filament protein expressed by astrocytes, to be a reliable indicator of suspected traumatic brain injury and concussion. Transmissible spongiform encephalopathies are infectious diseases of the brain caused by prions, misfolded isoforms of the PrP protein abundant in lymphoid and neurological tissues. Since encephalitis can be confirmed by upregulated GFAP visible via immunohistochemistry as a hallmark of end stage prion disease, we decided to test serum from terminal mice infected with prions for increased GFAP levels. Using enzyme-linked immunosorbent assay, we have observed increasing concentrations of serum GFAP levels at progressive time points in a murine model of prion disease at 20, 40, 60, 80, 100, 120 and 140 days post-inoculation. Implications for these findings include an early diagnostic for prion diseases, as well as other proteinopathies such as Alzheimer's disease. **Keywords:** clinical neurology, medicine

**78) Neuromorphology of gigantopyramidal cells across artiodactyls, perissodactyls, feliformia, caniformia, primates, a rodent, a lagomorpha, and a diprodontia**

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Although the basic morphological characteristics of gigantopyramidal (Betz) neurons have been documented in a limited number of species, the quantitative characteristics of these neurons across different taxa remain unexplored. To this end, the present study seeks to both qualitatively and quantitatively investigate gigantopyramidal neurons in the motor cortices of nineteen different species across eight phylogenetic taxa: artiodactyls (giraffe, kudu, blue wildebeest), perissodactyls (plains zebra, mountain zebra), feliformia (caracal, lion, clouded leopard, mongoose, Siberian tiger), caniformia (domestic dog, African wild dog), primates (baboon, human, golden lion tamarin, ring-tailed lemur), a rodent (rat), a lagomorpha (rabbit), and a diprotodontia (wallaby). For comparative purposes, three types of pyramidal neurons (i.e., superficial pyramidal, deep pyramidal, and gigantopyramidal; N= 617) were stained with a modified rapid Golgi technique and quantified on a computer-assisted microscopy system. Qualitatively, gigantopyramidal neurons varied considerably between species. Compared to other taxa, perissodactyls and artiodactyls demonstrated widely bifurcating V-shaped apical dendrites. Quantitatively, gigantopyramidal neurons were substantially larger than deep and superficial pyramidal neurons and exhibited more numerous primary basilar dendrites extending circumferentially from the soma. Feliformia exhibited the largest gigantopyramidal neurons, particularly of genus *Panthera*, consistent with Brodmann's (1909) observation of exceptionally large gigantopyramidal neurons in carnivores.