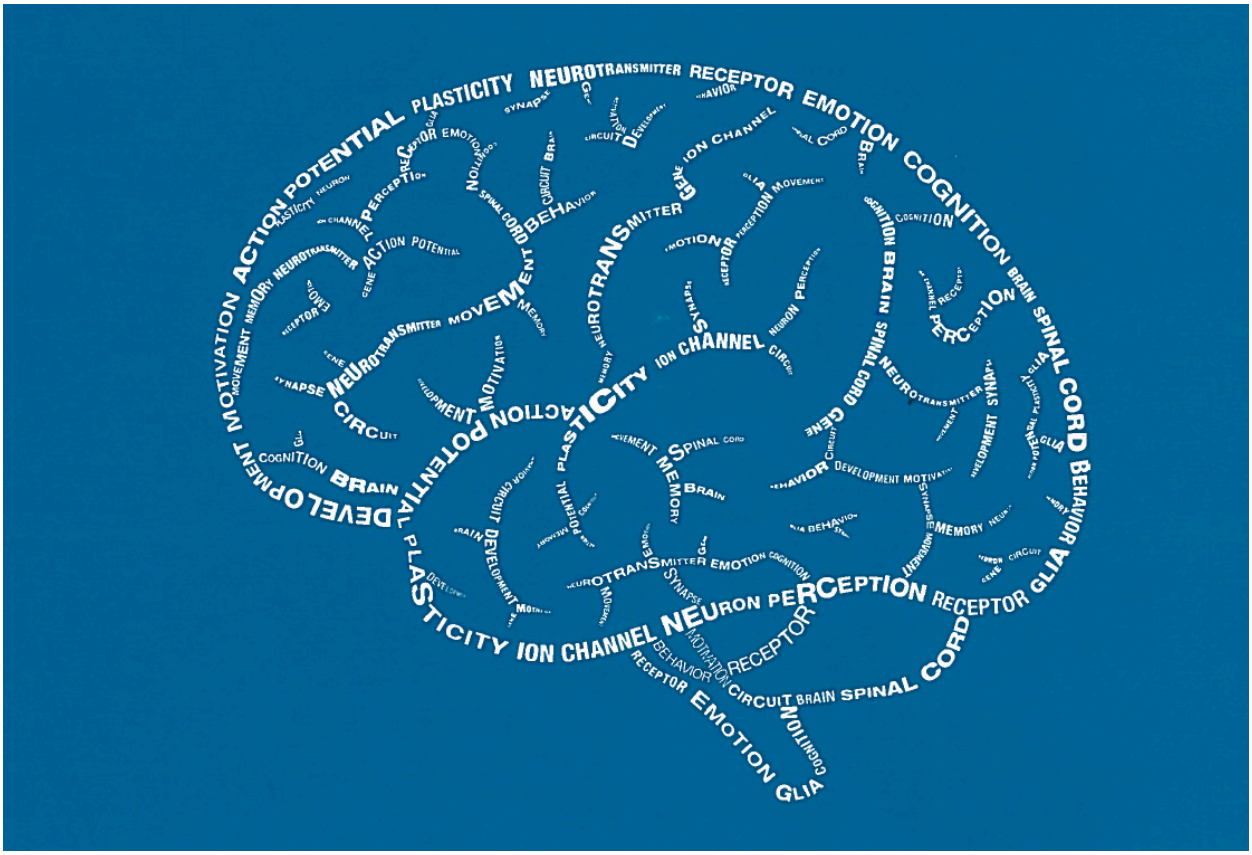
Western Massachusetts Chapter of the Society for Neuroscience

2017 Meeting

Friday, March 24, 2017

Life Sciences Laboratory Building, Conference Center
University of Massachusetts, Amherst, MA



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Institutions Represented (as of noon 3/22/2017)

Amherst College	(1)
Baypath University	(1)
Baystate Health	(1)
Keene State College	(2)
Merrimack College	(1)
Mt. Holyoke College	(10)
Quinnipiac University	(2)
Smith College	(4)
Stonehill College	(3)
Sunovoin Pharmaceuticals, Inc.	(1)
Tufts University Cummings School of Veterinary Medicine	(1)
University of Massachusetts, Amherst	(33)
University of Massachusetts Medical School, Worcester	(15)
Williams College	(2)
Worcester Polytechnic Institute	(2)
Total of 15 Institutions	(79)

SCHEDULE of EVENTS

Western Massachusetts Chapter of the Society for Neuroscience - 2017 Meeting

Life Sciences Laboratory (LSL 330S), UMass Amherst, March 24, 2017

12:15 - 12:45 pm	**Check-in and Registration**
12:45 - 1:00 pm	**Welcome and Vision for the Western Massachusetts Chapter** Speaker: Peter Reinhart, UMass Amherst
1:00 - 2:15 pm	**Symposium 1: Manipulation of Neuronal Circuit Activity and Behavior** Chair: Bekki Spencer, UMass Amherst **Matt Carter**, Williams College “Interplay between appetite-stimulating and appetite-suppressing brain systems.” **Christelle Anaclet**, UMass Medical School "Chemogenetic manipulation of sleep-wake behavior" **Elena Vazey**, UMass Amherst “Selective manipulation of locus coeruleus circuits *in vivo*”
2:15 - 2:30 pm	**Coffee Break**
2:30 - 3:45 pm	**Symposium 2: Neuroscience of Social Behavior** Chair: Luke Remage-Healey, UMass Amherst **Annaliese Beery**, Smith College “Social Neuroscience: models and methods” **Jiyong Park**, UMass Amherst “Cultural moderation of threat: Event-related brain potential (ERP) investigations” **Ben Nephew**, Tufts Cummings School of Veterinary Medicine “Peripartum pitocin and postpartum depression/anxiety and transgenerational effects of intranasal oxytocin and vasopressin in rats”
3:45 - 4:00 pm	**Business Meeting, Break.** Dave Weaver and Peter Reinhart
4:00 - 4:30 pm	**Datablitz,** Chair: Mike Francis, UMass Medical School. 1 slide, 1 minute previews of delivered by the poster presenters.
4:30 - 5:30 pm	**Poster Session. Refreshments served.**
5:30 - 6:00 pm	**Professional Development Roundtable** Panelists are PhD-holders representing different employment sectors Lauri Kurdziel, Ph.D., Merrimack College Carrie Blum, MD, Ph.D., Sunovion Pharmaceuticals, Inc. David Moorman, Ph.D., UMass Amherst

Organizing Committee for the 2017 Chapter Meeting

Co-Chairs:
Peter Reinhart
Dave Weaver

Faculty
Mike Francis
Kenny Futai (absent)
Youngbin Kwak (absent)
David Moorman
Catalina Ruiz-Canada
Rebecca Spencer

Post-docs
Ratna Chaturvedi
Bethany Jones

Grad student
Rita Fagan
John Hernandez
Carolyn Sweeney
Maggie Ugolini

Undergraduates
Nick Blauch
Hadiya Williams (absent)

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Institute of Applied Life Sciences, UMass Amherst

List of Posters

Presenting Author, Local Institution(s). Career Stage. Datablitz status,
Poster Title

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Loss of Neurofibromin Function Leads to Increased Metabolic Expenditure in *Drosophila*

2 **Sarah Heissenberger,** Keene State College, Undergrad. DataBlitz+
Exploring the Neurodevelopmental Effects of Sublethal Exposure to the Priority PAH Pyrene in the Amphibian Model *Xenopus laevis*

3 **Vincent van der Vinne**, UMass Med School. Postdoc. DataBlitz+
A mouse model of internal desynchrony between circadian clocks in brain and periphery

4 **Amanda DePasquale**, Stonehill College. Undergrad. DataBlitz+
The Role of Sleep Spindles in Memory Consolidation: An Optogenetic Approach in Mice

5 **Daniel M. Vahaba,** UMass Amherst, Grad student. DataBlitz No
Developmental and estrogenic effects on auditory neurophysiology in juvenile male songbirds

6 **Catherine de Bournonville,** UMass Amherst, Postdoc. DataBlitz No
Testosterone fluctuations in the female zebra finch auditory forebrain in response to song

7 **Amanda Krentzel,** UMass Amherst, Grad student. DataBlitz No
Characterization of estrogen-producing and estrogen-responsive neurons in the songbird forebrain

8 **Matthew LaClair**, UMass Amherst. Grad student. DataBlitz+
Sex differences in cognition, emotional reactivity, and motor ability in middle-aged marmosets (*Callithrix jacchus*).

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Inflammatory Alterations and Maternal Behavior after Maternal Separation Stress in Rodents

10 **Irio Schiano,** Quinnipiac University, Grad student. DataBlitz No
Oral Riluzole Alters Inflammatory Markers and Glutamate Transporters in Rodent Hippocampus Following Chronic Unpredictable Stress

11 **Ellen M. Rodberg,** UMass Amherst, UG/Other. DataBlitz+
Stress facilitates the development of cognitive dysfunction after chronic ethanol exposure

12 **Nicholas Blauch**, UMass Amherst. Undergrad. DataBlitz+
On cortical modularity: insight from simulations of 2 deep convolutional neural networks

13 **Brooke Martineau**, Baypath University. Undergrad. DataBlitz+
Not so Fast: Video Game Training Alters Response Time on Cognitive Tasks

14 **Tian Zhou**, UMass Amherst. Grad student. DataBlitz+
Discovering Discriminative Motifs on Brain Networks

15 **Daniil Frolov**, UMass Amherst & Amherst College. Grad student. DataBlitz+
Spike train recovery from adaptation suggests two independent mechanisms for vesicle pool replenishment in zebrafish lateral line hair cells.

16 **Daniel A. Gutierrez**, UMass Med School. Grad student. DataBlitz+
Visualizing lactate efflux

17 **Kyra Burnett,** Worcester Polytechnic Institute, Grad Student. DataBlitz no
Understanding the Effects of Butyl Acetate on Sensory Level Variability in *C. elegans* Using Whole Brain Imaging

18 **Ross Lagoy,** Worcester Polytechnic Institute, Grad Student. DataBlitz+
Functional Screening of Neuromodulators for *C. elegans* Models of Human Calcium Channelopathies

19 **Carolyn Sweeney**, UMass Med School. Grad student. DataBlitz+
Dopamine transporter amino- and carboxy-termini synergistically mediate Ack1-dependent endocytosis

20 **Rita Fagan**, UMass Med School. Grad student. DataBlitz No
Using *Drosophila melanogaster* to Study the Impact of Regulated Dopamine Transporter Trafficking on DA-dependent Behaviors

21 **Trisha Zintel**, UMass Amherst. Grad student. DataBlitz No
Differential gene expression in the visual cortex of primate species

22 **Jonathan Isenstein**, UMass Amherst. Undergrad. DataBlitz No
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Abstracts appear on the following pages

1

Loss of Neurofibromin Function Leads to Increased Metabolic Expenditure in *Drosophila*

Valentina Botero [1], Keith R. Murphy [2], Kenneth J. Colodner [1], William W. Ja [2], and Seth M. Tomchik [2]

[1] Neuroscience & Behavior, Mount Holyoke College.
[2] Department of Neuroscience, The Scripps Research Institute

Neurofibromatosis type 1 is an autosomal dominant genetic disorder resulting in tumor formation and predisposes individuals to cognitive and behavioral dysfunction. The fruit fly, *Drosophila melanogaster*, which contains a conserved *nf1*-encoded neurofibromin protein (Nf1), has been used as a model of the disease. *Drosophila nf1* mutants are smaller and exhibit elevated levels of spontaneous grooming, but the extent to which these phenotypes are related to alterations in metabolism and energy expenditure is unclear. To determine if loss of Nf1 function affects metabolism in flies, we used a feeding assay and compared respiration in *nf1* mutants and wild type flies. We found that RNAi-mediated knockdown of Nf1 in neurons results in increased feeding and metabolism, and provide evidence suggesting that this effect is mediated by specific subpopulations of neurons.

Support: Marilyn Dawson Sarles Science Internship Fund, Harap Scholarship Fund, NIH/NIMH R00MH092294, Whitehall Foundation, and the Elise M. Besthoff Charitable Foundation

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2

Exploring the Neurodevelopmental Effects of Sublethal Exposure to the Priority PAH Pyrene in the Amphibian Model *Xenopus laevis*

Sarah Heissenberger, Anna McFarlin, Robert Tocci, and Susan Whittemore

Keene State College, Keene NH

Polycyclic aromatic hydrocarbons (PAHs) are a diverse group of pollutants resulting from combustion of cigarettes, wood, oil, diesel fuel, garbage, and gas. This study focused on the behavioral effects of developmental exposure to the priority PAH pyrene (PYR), using the larvae (stage 49, day 12) of the African clawed frog, *Xenopus laevis*. Parameters included activity, distance traveled, spatial use of the arena, and speed. We found that larvae exposed to the highest dose (2.5 μM) of pyrene were on average 30% more active and traveled 73% farther. These animals also demonstrated stunted growth which could result from spending more energy swimming and/or less time feeding.

Funding: NH-INBRE and KSC BEST programs

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3

A mouse model of internal desynchrony between circadian clocks in brain and periphery

Vincent van der Vinne and David R. Weaver

Department of Neurobiology, UMass Medical School, Worcester, MA

Circadian clocks control daily rhythms in physiology and behavior and allow organisms to anticipate daily environmental changes. In humans, disruptions of circadian rhythms by shift work are associated with higher incidence of diseases such as obesity, depression, cardiovascular diseases and cancer. The causal mechanisms underlying the adverse consequences of shift work are unknown but internal phase desynchrony between the main clock in the brain (SCN) and oscillators in peripheral tissues (e.g. liver, kidney) as a result of repeated phase shifting associated with shift work has been hypothesized to result in adverse health consequences. In order to test this hypothesis, we want to develop a mouse line that maintains a permanent state of internal desynchrony between brain and periphery. A GABA-cell specific Cre-driver allows us to alter the intrinsic period of clocks in the brain while leaving the periphery unaltered (Vgat-Cre^{+}; CK1Delta$^{flox/flox}$; CK1Epsilon$^{flox/+}$). In these mice, the SCN has an intrinsic period of ~27h while peripheral tissues maintain an intrinsic period of ~24h as determined by PER2::LUC bioluminescence recording in vitro. The long period of the SCN results in similarly long periods (~27h) in locomotor and body temperature rhythms in vivo, which do not entrain to 24h (12L:12D) lighting cycles but do entrain to 27h light-dark cycles (13.5L:13.5D). *In vivo* measurement of PER2::LUC bioluminescence in anesthetized mice shows that peripheral oscillators are entrained to the long behavioral period with an advanced phase (5-6h), revealing internal desynchrony between clocks in the brain and peripheral oscillations.

Funding: NIH ES024684

DataBlitz: Yes / Postdoc / Vincent.vanderVinne@umassmed.edu

4

The Role of Sleep Spindles in Memory Consolidation: An Optogenetic Approach in Mice

Amanda DePasquale [1], Fumi Katsuki [2], James T. McKenna [2], Robert E. Strecker [2], Robert W. McCarley [2] and John G. McCoy [1]

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[2] Department of Psychiatry, VA Boston Healthcare System and Harvard Medical School, West Roxbury, MA

Memory consolidation has been shown to correlate with sleep spindles occurring during NREM sleep. Abnormalities in spindles have also been linked to memory impairment in patients with schizophrenia. However, the specific cellular mechanisms controlling spindles and associated cognitive function are still unclear. Here, we applied an optogenetic approach in mice to test whether inhibition of parvalbumin (PV) containing GABAergic neurons in the thalamic reticular nucleus (TRN), known to be abnormal in the schizophrenia patients, during sleep following learning, would impair memory performance. The novel object recognition (NOR) task and the object place recognition (OPR) task measure recognition memory based on the mice's natural tendency to investigate novelty. In the familiarization phase, the mouse explored two identical objects. In the recall phase, the mouse again explored the objects but one of the objects was replaced by a new object for NOR or moved to a different location for OPR. To manipulate spindles, optogenetic inhibition of TRN-PV neurons was performed by laser illumination (1-min on, 4-min off) for four hours in between these two phases. Behavioral performance was compared between laser-on and control conditions. In both control conditions for the NOR and OPR recall phase, the mice were able to recall the object presented in the familiarization phase. However, following inhibition of TRN-PV neurons, the mice in both memory tasks showed a significant decrease in being able to recall objects from the familiarization phase, indicating memory impairment. These results indicate the possible role of sleep spindles controlled by TRN-PV neurons in memory.

Funding: VA Merit 1I01BX001356, VA Merit 1I01BX002774, VA CDA 1IK2BX002130, T32HL007901, MH039683, HL095491, Stonehill SURE Program

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5

Developmental and estrogenic effects on auditory neurophysiology in juvenile male songbirds

Daniel M. Vahaba, Matheus Macedo-Lima, Luke Remage-Healey

Neuroscience & Behavior Graduate Program, Center for Neuroendocrine Studies, and Psychological and Brain Sciences, University of Massachusetts, Amherst MA

Brain-derived hormones can act as neuromodulators of sensory coding. Specifically, 17β-estradiol (E_2; a centrally synthesized neuroestrogen) enhances auditory-evoked activity in a higher-order sensory area of adult songbirds (caudomedial nidopallium; NCM). NCM is functionally homologous to mammalian secondary auditory cortex, and is implicated in auditory learning in adult and developing zebra finches. Further, NCM contains a significant population of aromatase-positive neurons, expresses membrane-bound estrogen receptors, and shows dynamic E_2 fluctuation in adult and developing songbirds. However, it is unclear how E_2 impacts auditory-evoked neuronal activity in NCM during the critical period for song learning. Song learning is achieved across two phases: sensory and sensorimotor. In the sensory phase, non-singing birds create an auditory memory of their father's song. The sensorimotor phase is marked by birds beginning to match their own burgeoning vocalizations to the tutor memory. Therefore, it is possible that the effect of E_2 on NCM is phase-dependent. We found that sensory-aged (20 – 35 days post-hatch; DPH) male zebra finches exhibited stronger baseline auditory-evoked neural activity compared to older juveniles (40 - 95 DPH). Further, E_2 produced an age- and hemisphere-dependent change in auditory-evoked firing and auditory encoding in NCM. In sensory subjects, left NCM was unaffected by E_2, whereas E_2 decreased classification accuracy in right NCM. In sensorimotor subjects, E_2 increased stimulus-evoked firing in left NCM, and increased the spontaneous firing in right NCM, without affected classification accuracy. These data extend our understanding of development shifts in auditory processing, and suggests E_2 modulation can be lateralized and age-dependent.

Funding: NSF IOS1354906

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6

Testosterone fluctuations in the female zebra finch auditory forebrain in response to song

Catherine de Bournonville and Luke Remage-Healey

Department of Psychological and Brain Sciences, Center for Neuroendocrine Studies, University of Massachusetts, Amherst, MA

Steroids can be synthesized in the brain and act as neuromodulators to regulate major biological functions such as reproduction, cognition and auditory processing. In zebra finches, estradiol is rapidly synthesized in a secondary auditory region (caudomedial nidopallium; NCM) in response to conspecific songs. Estradiol is produced in the brain via testosterone aromatization, an enzyme densely expressed in NCM. This local increase in estradiol quickly enhances auditory response of NCM neurons and has downstream consequences on song processing. However, the mechanisms by which estradiol elevation occurs in NCM remain unknown. Here, we hypothesize that local estradiol rises during song exposure via an increase in local level of the substrate, testosterone. 3β-HSD, the enzyme that produces testosterone, is highly expressed in the female NCM and its activity can be acutely regulated by environmental stimuli, unlike males. In this study, we measured testosterone fluctuation in the female brain during song exposure using in vivo microdialysis and enzymatic immunoassays. Results show that testosterone did not fluctuate significantly in the female NCM during song. However, a massive (>650%) song-evoked increase in testosterone can be observed when the local production of estradiol is blocked by the aromatase inhibitor fadrozole. Therefore, this experiment suggests that the NCM estradiol rise needed for song processing is mediated by an increase in testosterone. In ongoing experiments, brain dialysates and blood samples will be collected in the same conditions while infusing trilostane, a 3β-HSD inhibitor in order to determine whether this testosterone rise occurs locally or comes from the periphery.

Funding: NIH R01NS082179

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7

Characterization of estrogen-producing and estrogen-responsive neurons in the songbird forebrain

Amanda Krentzel [1,3], Maaya Z. Ikeda [2,3], Tessa J. Oliver [3], Garrett B. Scarpa [3], and Luke Remage-Healey [1,2,3]

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[2] Molecular and Cellular Biology Program,
[3] Psychological and Brain Sciences,
University of Massachusetts Amherst, Amherst, MA 01002

The enzyme aromatase converts testosterone to estradiol which can act locally and rapidly in discrete brain regions. Songbirds have robust aromatase expression in the forebrain, particularly in regions involved in audition. A membrane-bound estrogen receptor (GPER1), is thought to mediate some of the rapid neuromodulatory effects of estradiol observed in aromatase rich brain regions. This study directly examines the identity of both aromatase and GPER1 expressing cells in the auditory forebrain. Previous work indicates a role for interneurons in auditory responsiveness, and that estradiol rapidly enhances the auditory-evoked activity of forebrain neurons, so parvalbumin (PV) and calbindin (CALB) were used to determine the extent of interneuron cell identity for aromatase and GPER1. We co-labeled aromatase and GPER1 with PV and CALB in adult male and female zebra finches using immunofluorescence labeling and imaged with confocal microscopy. We quantified expression in representative subregions of several brain nuclei including the caudal nidopallium, HVC shelf, caudomedial mesopallium, and the hippocampus. Aromatase cells in all regions were either PV-positive or single labeled, and aromatase was not co-expressed with CALB. Up to 15% of aromatase cells are parvalbumin-positive depending on region. Preliminary findings indicate that GPER1-positive cells do not co-express either interneuron marker but may be co-expressed with aromatase. Aromatase tended to cluster with other aromatase+ cells and the interneuron subtypes, suggesting a role for coordinated communication. Overall, neuroestrogen signaling is supported by the organization of cells in the auditory forebrain, and characterization of aromatase cells gives further evidence to these distinct auditory brain areas.

Funding: NIH R01NS082179

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8

Sex differences in cognition, emotional reactivity, and motor ability in middle-aged marmosets (*Callithrix jacchus*).

Matthew LaClair [1,2], Nicole Gervais [2,3], Katy Workman [3], and Agnès Lacreuse [1,2,3]

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[2] Center for Neuroendocrine Studies, University of Massachusetts, Amherst, MA
[3] Psychological and Brain Sciences, University of Massachusetts, Amherst, MA

Sex differences in cognition are well documented. Women outperform men on measures of perceptual speed and verbal abilities, while men outperform women on tests of spatial processing. Robust sex differences also exist in stress responses. However, it is unclear how these sex differences change over time and whether males and females follow different trajectories of age-related cognitive decline. Studies in nonhuman primate models can help resolve this issue. The common marmoset (*Callithrix jacchus*) is a New World primate with a short lifespan that can perform complex cognitive tasks in computerized settings that are comparable to those used with humans. The present study is part of a longitudinal project aimed at determining whether males and females follow different trajectories of cognitive aging. This report focuses on sex differences at study entry. Twenty two marmosets (11 females), aged 4-6 years were tested on a comprehensive battery of tasks assessing cognitive function, motor skills and emotional reactivity. For cognition, monkeys performed a reversal learning task and a set shifting task using the Cambridge Neuropsychological Test Automated Battery (CANTAB). They also performed the Hill-and-Valley task as a measure of fine motor skills. To assess emotional reactivity, each marmoset was separated from their colony for 7 hours. Behavioral assessments, which involved recording the occurrence of approximately 25 behaviors, occurred a total of 6 times: immediately before separation, 3 times during separation, immediately after separation, and 24-hr later. No sex difference was found for simple discrimination, but males tended to perform better than females on the reversal learning task. No sex difference was observed in motor skills. During separation from the colony, females were more reactive than males, as indicated by more agitated locomotion, and vocalizations. Together, these findings expand upon previous studies and demonstrate sex differences in reversal learning and emotional reactivity in gonadally-intact middle-aged marmosets. As the study progresses, we should be able to determine the neural correlates of these sex differences and how they may change with aging.

Funding: NIH R01AG046266

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9

Inflammatory Alterations and Maternal Behavior after Maternal Separation Stress in Rodents

Kezzia S. Jones, L. Teliska, R. Rotolo, C. Little, T. Strange, T. Medwid and A.J. Betz

Center for Behavioral Neuroscience, Quinnipiac University, Hamden CT

Maternal separation (MatSep) in rodents is a widely-used animal model used to induce early-life stress. This model has reliably demonstrated an increased risk of depressive-like behavior later in life and has been shown to alter brain structure and physiology. Two regions of the hippocampus, the dorsal and the ventral, are suggested to be functionally different and susceptible to microglial activation and pro-inflammatory factor release. This study examines the inflammatory alterations in animals exposed to MatSep and maternal behavior after separation stress. In the present study, Sprague Dawley male pups (n=20) were separated from their dam from PND 2 to PND 16 for 3 hours a day. A control condition of non-separated pups was maintained. Maternal care behavior was also recorded for all dams on PND 10 and PND 16 for after 3-hr separation events. Depressive/anxious behavior in offspring were evaluated using the elevated plus maze during adolescence. Alterations in hippocampal Iba1, CD11b, NF-kB, histone modification and cytokine expression were observed and may provide insight as to the molecular mechanisms responsible for Major Depressive Disorder pathogenesis and possible therapeutic remedies.

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10

Oral Riluzole Alters Inflammatory Markers and Glutamate Transporters in Rodent Hippocampus Following Chronic Unpredictable Stress

Irio Schiano, T. Strange, L.Teliska, L. Fruehauf, A. Roselund, A. Najjar, M. Szdhaj, T. Medwid, and A.J. Betz

Quinnipiac University, Hamden CT

Studies have shown that glutamate activity during stress is associated with causing atrophy of the hippocampus that may be implicated in major depressive disorder (MDD). Macrophages called microglia remove this excess glutamate from the synapse in order to decrease the damage caused by this deterioration. Understanding the correlation between glutamate and MDD introduces potential novel therapeutics for depression. Riluzole, a glutamatergic antagonist, is used experimentally as an antidepressant in order to control glutamate transmission. In this experiment, we investigated how EAAT1, the glutamate transporter found on glial cells, and CD11b, a glial inflammatory marker, were both altered in the hippocampus of rats given oral riluzole following chronic unpredictable stress (CUS). The stress model used creates anxiety and depressive-like behavior in rats and has been shown to closely resemble symptoms of MDD. We found that EAAT1 increased expression in the dorsal hippocampus in CUS rats when given oral riluzole. However CD11b was found to decrease expression in the ventral hippocampus when given a low dosage of riluzole, but increase expression in the dorsal hippocampus when given a high dosage of riluzole. These changes in glial expression between the dorsal and ventral hippocampus suggests different roles in MDD pathogenesis. Both the dorsal and ventral regions of the hippocampus are functionally different as the dorsal is involved in cognitive function while the ventral is involved in emotional function. Knowing these functional differences and seeing structural changes during a stress response suggests a relationship between section of the hippocampus and glutamate expression following stress.

Funding: Quinnipiac University and Brain and Behavior Research Foundation

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11

Stress facilitates the development of cognitive dysfunction after chronic ethanol exposure

Ellen M. Rodberg [1], Carolina R. den Hartog [1], Rachel A. Anderson [2], Howard Becker [2], David E. Moorman [3], and Elena M. Vazey [1]

[1] Department of Biology, University of Massachusetts, Amherst MA
[2] Medical University of South Carolina, Charleston SC
[3] Department of Psychological and Brain Sciences, University of Massachusetts Amherst MA.

Chronic exposure to stress or alcohol can drive neuroadaptations that alter cognition. Alterations in cognition may contribute to alcohol use disorders by reducing cognitive control over drinking and maintenance of abstinence. Here we examined effects of combined ethanol and stress exposure on prefrontal dependent cognition. Adult male C57BL/6J mice were trained to drink ethanol (15%, v/v) on a 1hr/day 1-bottle schedule. Once stable, mice were exposed to cycles of chronic intermittent ethanol (CIE) or air-control vapor exposure (Air), followed by test cycles of 1hr/day ethanol drinking. During test drinking mice receive no-stress (NS) or 10 minutes of forced swim stress (FSS) 4 hours before each test. This schedule produced four experimental groups: control, Air/NS; ethanol-dependent no stress, CIE/NS; non-dependent stress, Air/FSS; or ethanol-dependent stress, CIE/FSS. After two cycles of CIE and FSS exposure we assessed prefrontal dependent cognition using object/context recognition and attentional set shifting. At the end of the study mice were perfused and brains collected for c-Fos activity in prefrontal cortex and locus coeruleus. CIE/FSS mice escalated ethanol intake faster than CIE/NS and consumed more ethanol than Air/NS across all test cycles. After two cycles of CIE/FSS, mice showed impairments in contextual learning and extra-dimensional set shifting relative to other groups. In addition to cognitive dysfunction, CIE/FSS mice demonstrated widespread reductions in c-fos activity within prefrontal cortex and locus coeruleus Together, these findings show that interactions between ethanol and stress exposure rapidly lead to disruptions in signaling across cognitive networks and impairments in prefrontal dependent cognitive function.

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12

On cortical modularity: insight from simulations of 2 deep convolutional neural networks

Nicholas Blauch [1,2], Elissa Aminoff [2,3] and Michael J. Tarr [2,4]

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[2] Dept. of Psychology, Fordham University, New York, NY
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[4] Center for the Neural Basis of Cognition, Pittsburgh PA

Preferential activation to faces in the brain's fusiform gyrus has led to the proposed existence of a face module termed the Fusiform Face Area (FFA) (Kanwisher et. al, 1997). However, arguments for distributed, topographical object-form representations in FFA and across visual cortex have been proposed to explain data showing that FFA activation patterns contain decodable information about non-face categories (Haxby et. al, 2001; Hanson & Schmidt, 2011). Using two deep convolutional neural network models able to perform human-level object and facial recognition, respectively, we demonstrate that both localized object category representations and a face module per se allow for similar decoding accuracy between non-preferred visual categories as between a preferred and non-preferred category. Thus, our results suggest that neuroimaging of a cortical face module should yield significant decodable information for non-face categories so long as representations within the module are activated by non-face stimuli.

Funding: NB was supported by the Summer Undergraduate Program in Neural Computation at Center for the Neural Basis of Cognition

DataBlitz: Yes / Undergraduate / *nblauch@umass.edu*

13

Not so Fast: Video Game Training Alters Response Time on Cognitive Tasks

Brooke Martineau [1], S. McCart [2], K. Rossi [2], and K. Bailey [2]

[1] Neuroscience Program, Science Department, Bay Path University
[2] Neuroscience Program, Department of Psychology, Ohio Wesleyan University

Video game training on Action Video Games (AVGs) has previously reduced response times in cognitive tasks. Real Time Strategy games (RTS) stretch attention over a field of play rewarding proactive control: an actively held goal in the forefront of the mind. This is in opposition to AVGs, which immerse the player in a more fast-paced situation that rewards reactive control: the reminder of a set goal by a stimulus in the environment. RTS games may be a more accurate comparison to AVGs when studying reaction times due to the similar immersive gameplay. Participants were put through 10 hours of training on either an AVG or a RTS. Reduced response times were not observed for all cognitive tasks. On some tasks, response times increased post-testing. Future studies should utilize electroencephalogram data with cognitive tasks to determine if neural activity changes after game training.

Funding: NSF 1560082

Datablitz: Yes / Undergraduate / bmartineau@baypath.edu

14

Discovering Discriminative Motifs on Brain Networks

Tian Zhou [1,2], Oliver Spiro [3], Lixin Gao [1]

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[2] Dept. of Computer Science and Technology, Xi'an Jiaotong University, China
[3] Dept. of Mathematics and Statistics, University of Massachusetts, Amherst, MA

Being able to capture temporal brain activities, functional Magnetic Resonance Imaging (fMRI) technology is widely used to describe the dynamic functional connectivity within a brain. It has been reported that many diseases affect the dynamic functional connectivities of patients' brains in some particular ways. Intrigued by this, researchers have used fMRI data for disease detection through approaches such as singular value decomposition and deep neural networks. In this paper, we model a brain as networks across different regions using the functional connectivity described by fMRI data and aim to identify a set of discriminative motifs in the networks. Identifying discriminative motifs is challenging since the number of possible motifs is exponential in term of the number of nodes in the brain network. We propose a novel search algorithm optimized for the discriminative scoring functions satisfying a simple bounded condition. The algorithm is able to shrink the search space into a tractable scale, which is shown to be less than 7 orders of magnitudes on ABIDE dataset with AAL atlas. Together with a shortest distance based signature technique, the workload of scanning the brain networks is reduced by 40% - 70%. Further, we implement the algorithm in a distributed environment, and show that the algorithm scales well with the increasing dataset size. Evaluated on four real fMRI datasets, our algorithm identifies about 90% patients with the precision of 55% - 70%. We find that some of the top discriminative motifs for Autism involve as many as 6 regions.

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Spike train recovery from adaptation suggests two independent mechanisms for vesicle pool replenishment in zebrafish lateral line hair cells.

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Sensory adaptation is an important neurological process that allows organisms to appropriately respond to sensory stimuli by filtering out static or unchanging stimulus information. Sensory systems with hair-cell receptors, such as vertebrate auditory systems and lateral-line systems in fish, adapt robustly to constant stimuli, yet the exact mechanisms and their contribution to adaptation remain poorly understood. In order to examine the molecular contributions to spike-rate adaptation in hair-cell systems, we mechanically stimulated hair cells of the zebrafish lateral line while recording action potentials (spikes) from individual afferent neurons. We observed substantial adaptation of both first spike latency (FSL) and overall spike rate in response to a constant, saturating stimulus. By determining the time courses of recovery from adaptation for both FSL and spike rate, we observed that FSL recovers more quickly than spike rate. The differential recovery rates of FSL and spike rate suggested that two distinct mechanisms may underlie these forms of adaptation, as a shared mechanism would presumably return both parameters to their non-adapted values within a similar time course. As a thought experiment, we considered possible features of hair-cell systems that would account for the observed difference in recovery rates of FSL and spike rate and propose that mechanisms at the ribbon synapse best account for the portion of spike-rate adaptation that remains following the rapid recovery of FSL adaptation. These findings provide preliminary insight into the contributions of known hair cell and afferent neuron mechanisms for adaptation of spike trains.

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Visualizing lactate efflux

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The still controversial astrocyte-neuron lactate shuttle hypothesis (ANLSH) demonstrates the need for the development of new biochemical tools in the field of neuroscience in order to address currently unobservable phenomena. The ANLSH states that during periods of prolonged neuronal firing of glutamatergic or other excitatory neurons, astrocytes provide lactate as the primary metabolic substrate to fuel and sustain neuronal activity, not glucose, as was previously assumed. However, *in vivo* and culture experiments noting increases of lactate upon neuronal stimulation have yet to identify the cellular source of lactate production. Thus, two methods are currently being developed in order to visualize lactate efflux. Our first method utilizes tetraacetylated N-azidoacetyl-D-mannosamine to reengineer the cells glycocalyx, followed by tris-Ni^{2+}-NTA-PEG4-DIBO click addition and binding of a recombinant 10X-his tagged FRET lactate sensor. Our second method utilizes the same FRET lactate sensor, but has been engineered to express and display on the extracellular surface for *in vivo* use. Future experiments will include quantitating lactate efflux upon neuronal firing *via* optogenetic activation in neuronal/astrocytic cultures, as well as utilization of the genetically engineered lactate FRET sensor *in vivo*.

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Understanding the Effects of Butyl Acetate on Sensory Level Variability in *C. elegans* Using Whole Brain Imaging

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Understanding complex information processing in the brain is a central goal of neuroscience. For decades, scientists have used *C. elegans* neural networks to advance research topics such as learning and memory, sleep, and development in higher organisms. Current instruments used to study these neuronal networks include three-dimensional microscopy techniques such as spinning disk confocal and structured illumination. These systems can acquire signals from multiple neurons but only for limited duration due to photobleaching and phototoxicity. Light sheet or selective plane illumination microscopy (SPIM) prevents these problems by capturing more emission light, but standard sensory stimulation methods are optically incompatible with this imaging system. Toward long-term, 3D, high resolution recording of complex neuronal networks in living animals, we have developed a hydrogel-based approach to optical and microfluidic stimulation compatible with SPIM. In preliminary studies, we have characterized the gelling capabilities of our optically index-matched material, polyethylene(glycol)diacrylate (PEGDA), and found that it provided a safe, long term environment for worms. Light-stimulated responses were made in multiple neuron types, with some experiments lasting up to 14hrs, compared with about 20mins maximum with prior methods. Thus, our methods can monitor neural changes during dynamic processes such as learning and sleep. Toward chemical stimulation, we are developing hydrogel-based microfluidic devices that are compatible with SPIM. Ultimately, this methodology will not only improve the understanding of information flow in *C. elegans* neural networks, but will also advance the understanding of dynamic processes in other well-studied organisms, such as zebrafish and *Drosophila*.

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Functional Screening of Neuromodulators for *C. elegans* Models of Human Calcium Channelopathies

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Mental health disorders, like autism, depression, and epilepsy, affect millions of people worldwide. Some of these illnesses are highly associated with channelopathies, or dysfunction in ion channels, that affect neural activity in the brain. Timothy syndrome (TS) is a well-studied disorder characterized by a missense mutation (G406R) in the human calcium channel gene CACNA1C which causes severe autism, arrhythmia, and developmental disorders. Cells derived from TS patients and other models show that this mutation causes decreased calcium channel inactivation. To further our understanding and discover treatments for these disorders, we need additional whole-organism models and screening methods. The organism *C. elegans* is genetically tractable, transparent, and amendable to high-throughput screening. Recently, we developed the first *C. elegans* model of TS using CRISPR-mediated homologus recombination in EGL-19/CACNA1C, which causes a severe developmental phenotype likely from prolonged calcium channel opening. Our other channelopathy models have altered channel kinetics, detectable using our methods of odor and light stimulation using genetically encoded calcium sensors (GCaMP) and optogenetics (Chrimson). To rapidly and cheaply screen many drugs in C. elegans, we developed two automated approaches. The first adapted microfluidic-based approach can expose animals to drugs from seconds to minutes while recording neural responses when stimulated by odor or light. The second is a 384-well plate-based screen that can expose animals to drugs for hours and record neural responses. We plan to screen hundreds of small-molecules and detect hits that can be used to restore normal calcium channel function in various disease models.

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Dopamine transporter amino- and carboxy-termini synergistically mediate Ack1-dependent endocytosis

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Synaptic dopamine levels are spatiotemporally constrained by presynaptic reuptake via the dopamine transporter (DAT). DAT function and surface expression is acutely regulated by protein kinase C (PKC). PKC activation results in rapid DAT internalization. Multiple reports independently implicate domains within both DAT intracellular N- and C-termini as required for PKC-stimulated DAT endocytosis. Whether independent mechanisms for regulated endocytosis exists at both N- and C-termini or one synergistic mechanism requiring both domains remains unknown. To test whether DAT N- and C-termini work synergistically to coordinate DAT endocytosis, we generated DAT/SERT chimeras in which we replaced DAT N-, C-, or both termini with those of SERT. DAT and SERT are homologous transporters, yet they share little sequence identity at their N- and C-termini. They both undergo PKC-stimulated endocytosis, but only DAT requires Ack1 inhibition, downstream of PKC activation, for this process. We tested internalization rates for each chimera in the presence of the PKC activator (PMA) or Ack1 inhibitor (Aim-100) to test whether the N- and C-termini synergistically mediate PKC-stimulated endocytosis. Substituting SERT's C- terminus alone onto DAT did not affect endocytic rates compared to WT DAT. Surprisingly, substitution of SERT's N-terminus onto DAT abolished PKC-stimulated endocytosis, but maintained enhanced rates following Ack1 inhibition. These results suggest that DAT may serve as a scaffold to localize proteins necessary for PKC dependent inactivation of Ack1. We predict that there is an N-terminal DAT binding protein(s) that inactivate Ack1 downstream of PKC activation, and we are currently investigating this line of questioning.

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Using *Drosophila melanogaster* to Study the Impact of Regulated Dopamine Transporter Trafficking on DA-dependent Behaviors

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Dopamine (DA) critically controls behaviors such as movement, sleep, and reward, as well as cognitive processes including mood, learning, and memory. Impaired DAergic neurotransmission is a common feature of neuropsychiatric diseases and disorders such as Parkinson's disease, schizophrenia, attention-deficit/hyperactivity disorder, autism spectrum disorder, and addiction. DA levels are controlled by the plasma membrane dopamine transporter (DAT), which maintains synaptic DA homeostasis by clearing released DA and replenishing presynaptic DAergic stores. DAT surface expression is dynamic. DAT constitutively internalizes from and recycles to the plasma membrane via endocytic trafficking. Protein kinase C (PKC) activation decreases DAT surface expression by enhancing DAT endocytosis. Our laboratory further determined that neuronal GTPase, Rin (RIT2), binds directly to DAT and is required for PKC-stimulated DAT endocytosis. Multiple *in vivo* studies support that DAT plays a central role in DA homeostasis. $DAT^{-/-}$ mice and Drosophila DAT (dDAT) null flies exhibit hyperactivity, sleep perturbation, and altered responses to psychostimulants. While it is clear that complete DAT loss perturbs DA homeostasis, the physiological relevance of regulated DAT endocytosis in vivo is still unknown. Here we demonstrate that dDAT is subject to PKC-stimulated functional downregulation, and that Ric is preliminarily required for this process. Further, overexpression of a constitutively active Ric (G68V) mutant also attenuates the PKC-mediated decrease in DA uptake by dDAT. Significant reductions in locomotor and sleep behavior were observed in *Drosophila* expressing the Ric G68V mutation in DA neurons. These results preliminary suggest that Ric activity is required for PKC-stimulated dDAT functional downregulation and DA-dependent behaviors.

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Differential gene expression in the visual cortex of primate species

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Despite high genetic conservation among primate species, there are significant phenotypic differences, particularly in the brain. These differences include those related to visual processing. Previous research has determined that interspecific phenotypic differences amongst primates are due, at least in part, to altered gene expression. In order to investigate species-specific functional differences in visual cortex gene expression across primate species, RNA-seq was performed on mRNA isolated from post-mortem tissues from the visual cortex of 8 primate species (*Homo sapiens, Pan troglodytes, Gorilla gorilla, Pongo abelli*, *Symphalangus syndactylus, Macaca mulatta, Macaca nemestrina*, and *Callithrax jacchus*). From these data, we determined differential expression at the level of genes as well as in categorical gene ontology. We found that when gene expression was compared across broad taxonomical categories (Hominoidea (apes) vs New/Old World Monkeys), 11.65% of the genes identified were significantly differentially expressed. Furthermore, upon comparing humans to each non-human species, differential expression was present in all comparisons at rates between 9.6%-21.2%. Across all comparisons, differentially expressed genes were enriched for both neural and metabolic processes.

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Stimulus-Evoked Turning Behavior in Lampreys

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In vertebrates, central pattern generators (CPGs) in the spinal cord produce basic patterns of muscle activity that generate locomotor behavior. A brainstem command system is responsible for initiating locomotion. Reticulospinal (RS) neurons extend from this command system and directly activate the CPGs. RS neurons can also modulate the function of the spinal locomotor networks to produce adaptive variations of locomotion, such as turning, acceleration, or deceleration. In the lamprey, a lower vertebrate, straight locomotion (swimming) is characterized by rhythmic and symmetrical left-right body undulations. In addition, lampreys can execute spontaneous turning maneuvers, in which movements and muscle burst activity are asymmetrical and the cycle time is elongated during the turn cycle. The purpose of the current study was to develop and characterize a method for stimulus-evoked turning. Larval sea lampreys (P. marinus) were anesthetized, and pairs of fine copper wire electrodes were inserted along the body musculature to record muscle burst activity. Additionally, stimulating electrodes were inserted into the left, lateral oral hood. During swimming, brief stimulation was applied to the oral hood at different phases (times) of the swim cycle. The perturbed cycle (cycle in which stimulation was applied) was compared to earlier cycles to determine which stimulus phases elicited turning-like behaviors. Preliminary results indicate that initiation of stimulus-evoked turning is dependent on when the stimulation is applied during the cycle time. Stimulation applied early in the perturbed cycle elicited turning-like muscle burst activity. Therefore, stimulus-evoked turning is a reliable experimental method for eliciting this variation of locomotor behavior.

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Lymphocytic infiltration and bacterial alterations of digestive system tissue after Chronic Unpredictable Stress exposure in rodents

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Chronic unpredictable stress (CUS) is an animal model of major depressive disorder (MDD), a complex psychological disease. It is well known that chronic stress paradigms in rodents induce structural and molecular changes within the central nervous system (CNS) that parallel those of humans. Recent studies have begun to examine the gut-brain axis (GBA) in relation to stress disorders such as MDD. This system is a bidirectional communication between the CNS and the enteric nervous system. Recent studies are shedding light on the importance of gut microbiota influencing behavior. Bacterial endotoxins are known to elicit anxiety-and depressive-like behaviors in rodents, increase pro-inflammatory cytokines in stress-sensitive brain regions and disturb microbial communities in the gastrointestinal tract. The aim of the current pilot study was to examine whether there is presence of gut bacteria in rats exposed to CUS. Further, we sought to determine the presence or absence of lymphocytes infiltrating the digestive system in neural innervations. We found disruption of bacteria and alterations in the presence of lymphocytes. Future studies will examine the type of bacteria and type lymphocytes found in CUS exposed animals. This data will help link emotional and cognitive centers of the brain with peripheral digestive function.

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