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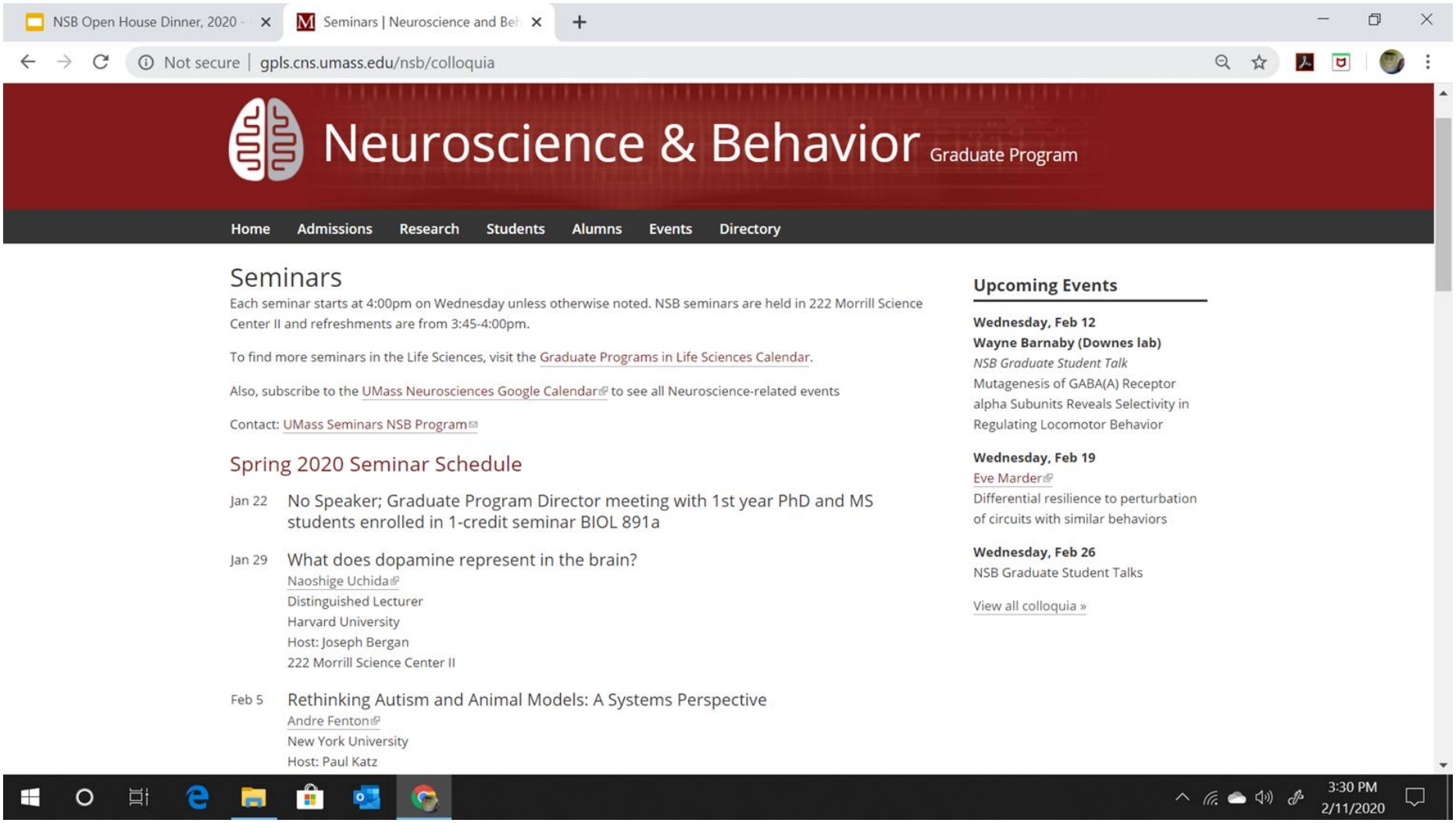
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Seminars | Neuroscience and Be
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Seminars
Each seminar starts at 4:00pm on Wednesday unless otherwise noted. NSB seminars are held in 222 Morrill Science Center II and refreshments are from 3:45-4:00pm.
To find more seminars in the Life Sciences, visit the Graduate Programs in Life Sciences Calendar.
Also, subscribe to the UMass Neurosciences Google Calendar to see all Neuroscience-related events
Contact: UMass Seminars NSB Program
Spring 2020 Seminar Schedule
Jan 22 No Speaker; Graduate Program Director meeting with 1st year PhD and MS students enrolled in 1-credit seminar BIOL 891a
Jan 29 What does dopamine represent in the brain?
Naoshige Uchida
Distinguished Lecturer
Harvard University
Host: Joseph Bergan
222 Morrill Science Center II
Feb 5 Rethinking Autism and Animal Models: A Systems Perspective
Andre Fenton
New York University
Host: Paul Katz
Upcoming Events
Wednesday, Feb 12
Wayne Barnaby (Downes lab)
NSB Graduate Student Talk
Mutagenesis of GABA(A) Receptor alpha Subunits Reveals Selectivity in Regulating Locomotor Behavior
Wednesday, Feb 19
Eve Marder
Differential resilience to perturbation of circuits with similar behaviors
Wednesday, Feb 26
NSB Graduate Student Talks
View all colloquia »
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Increased Catecholamine Levels Decrease Attention in a Sexually Dimorphic Manner

Emma S. Dauster, Kara M. Conlan, & Elena M. Vazey

Department of Biology, University of Massachusetts, Amherst MA

Introduction

Catecholamines act in the prefrontal cortex among other regions, and are critical in attention regulation. The Yerkes-Dodson Law outlines an inverted U shaped attention curve that can be related to dopamine (DA) and norepinephrine (NE) function, along with attention behavior (Yerkes, 1908, Berridge & Arnsten, 2013). Attention is known to be a sexually dimorphic behavior (Swanson et al., 1998).

Healthy individuals use catecholamine enhancing drugs as study aids and cognitive enhancers. An example is Methylphenidate (MPH), a DA and NE reuptake inhibitor known to have sexually dimorphic effects. Atomoxetine (ATM) is a NE reuptake inhibitor also used as a cognitive enhancer. It remains largely unknown if these drugs influence attention behavior in a sexually dimorphic manner.

We aim to better understand the role of catecholamines in both male and female attention. Thus, we characterized male and female rodent behavior in an operant two-alternative forced choice task under the influence of MPH or ATM.

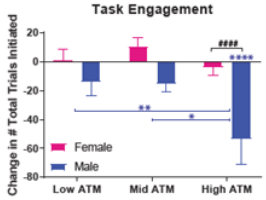
Hypothesis:
Catecholamine regulation of attention can differ between sexes.

Methods

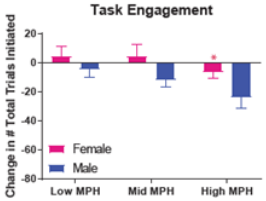
2AFC Paradigm to Measure Attention

Results

Atomoxetine



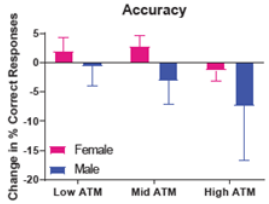
Methylphenidate

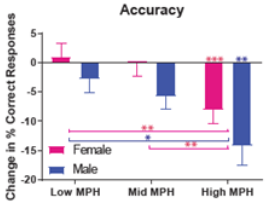


ATM decreases male engagement, and MPH for females.

ATM reduced task participation at high doses in males only. Effect of drug dose($p<0.0001$), sex ($p<0.0001$) and interaction($p=0.0028$).

MPH showed a main effect of drug dose ($p=0.005$) with females significantly decreasing trials after high dose MPH, relative to vehicle.



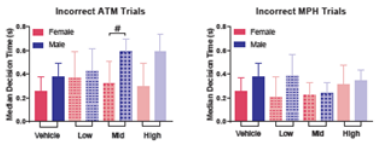


MPH decreases accuracy in males and more in females.

Performance accuracy after ATM showed a main effect

Accuracy after MPH show a main effect of sex ($p=0.037$)

Median Decision Times



ATM but not MPH increased decision time on incorrect trials.

Conclusions

ATM and MPH were not cognitive enhancers in average individuals performing the 2AFC task.

Males and females showed different responses to ATM and MPH in cognitive performance.

Neural Circuits for Social Behavior

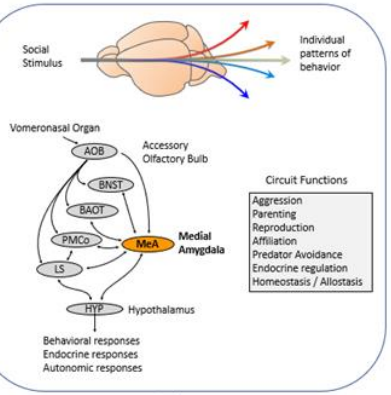
Jonathan Woodson, Addison Neimeyer, Diane Kelly, Prakruti Nanda, Tal Inbar, Joseph Dwyer, Marcelo Correia, Joseph Bergan

Background

Throughout the animal kingdom, dedicated signals allow individuals to identify and distinguish between members of their own species: songbirds attract mates during bouts of singing, cichlid fish communicate status by changing the coloration of their bodies, and rodents signal a wealth of social information through chemical cues. In turn, these sensory stimuli trigger instinctive behaviors such as mating, parenting, aggression, and defense that are relevant to an animal's environmental and physiological context. We want to understand how the neural circuits that organize species-specific instinctive behaviors are controlled by the brain and how they are modulated by factors such as an animal's age, sex, or physiological status.

Studies have revealed a molecular logic within the sensory epithelium of the VNO by which different receptors extract biological information about animals and stimuli in the immediate environment. This information is processed by subsequent nuclei of the vomeronasal system including the accessory olfactory bulb, medial amygdala, and hypothalamus. By analyzing this circuitry and recording the activity of single neurons in these structures we hope to understand:

- How social stimuli are represented in the brain
- How neural circuits produce social behavior
- How social circuits are specialized for the needs of individual animals



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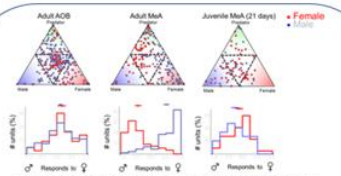
Isogai, Y., Si, S., Pont-Lezica, L., Tan, T., Kapoor, V., Murthy, V. N., & Dulac, C. (2011). Molecular organization of vomeronasal chemoreception. *Nature*, *478*(7368), 241-5. doi:10.1038/nature10437

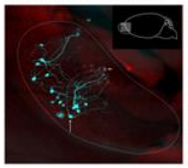
Watabe-Uchida, M., Zhu, L., Ogawa, S., Vamanrao, A, and Uchida, N, (2012). Whole-Brain Mapping of Direct Inputs to Midbrain Dopamine Neurons. Neuron:74(5):858-873.

Support for this work came from the US National Institutes of Health (MH115094-01A1), Institute of Applied Life Sciences, Mellon Mutual Mentoring Grant, Institute of Social Science Research, and the Armstrong Fund for Science.

Sex differences in circuit structure and function



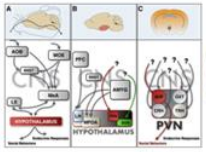
Response of neurons in the AOB and MeA to Predator, Male, or Female stimulus collected using electrophysiology. These results show a clear bias towards the opposite sex in the MeA, but not the AOB. Further experiments in juveniles show a lack of response.



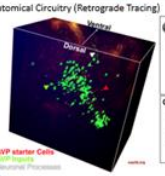
GFP-labeled neurons in the AOB (delineated by the white outline). The location of the image in the context of the brain is shown in the upper-right corner. The result of retrograde tracing from the MeA to the AOB using a g-deleted rabies virus (Watabe-Uchida, et al. 2012). This image shows lateralized expression with many more GFP-expressing neurons in the anterior as opposed to the posterior AOB.

Anatomical and Functional Contributions of AVP Neurons

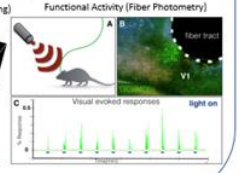
- **Arginine Vasopressin (AVP)** is a neuropeptide hormone that plays a key role in the **homeostasis** of the body.
- When **released** in the CNS it seems to play an important role in **social behavior, sexual motivation and pair bonding**
- Our aim is to explore the **functional role of AVP** within the social behavior circuit



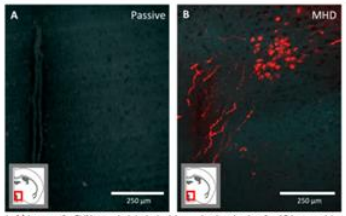
Anatomical Circuitry (Retrograde Tracing)



Functional Activity (Fiber Photometry)

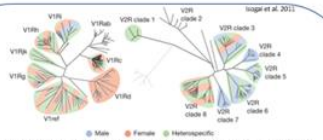


Antibody Labeling in intact tissue

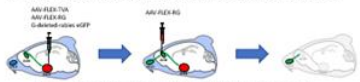


Left) Image of a PVN sample labeled with passive incubation for 12 hours with an oxytocin label (red). Right) Image of a PVN sample actively labeled using MHD with antibodies for oxytocin (red) with autofluorescence (cyan). Labeling is observed up to 1.4 mm into the tissue. Position of the labeled tissue chunk in an intact mouse brain (Bregma -0.8 mm) is shown in the lower-left of both images.

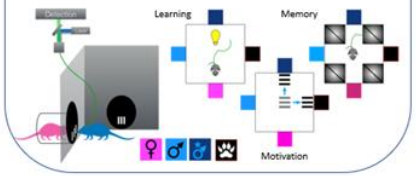
Future Directions



- We want to find the source of the sexual dimorphism in MeA response and the circuit as a whole
- One candidate is differential expression of VNO receptors in males and females
- Specifically, if more of one subtype of receptors innervate the dimorphic aromatase-positive neurons in the meA this might explain the differential activation observed in these neurons between males and females
- However, this requires tracing across two synapses (MeA to AOB to VNO)



Cell-type Specific Functional Activity within Behavioral Contexts



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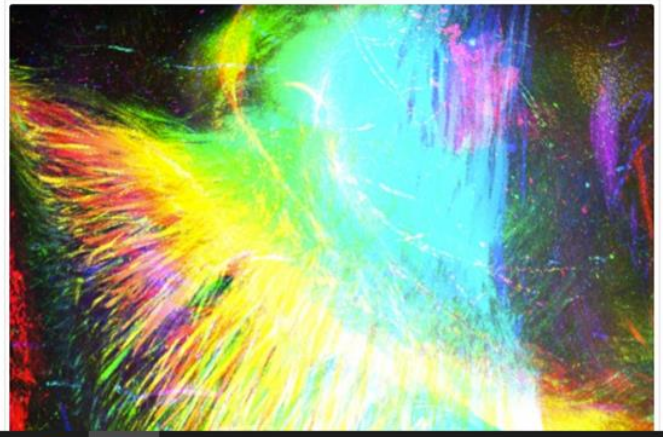

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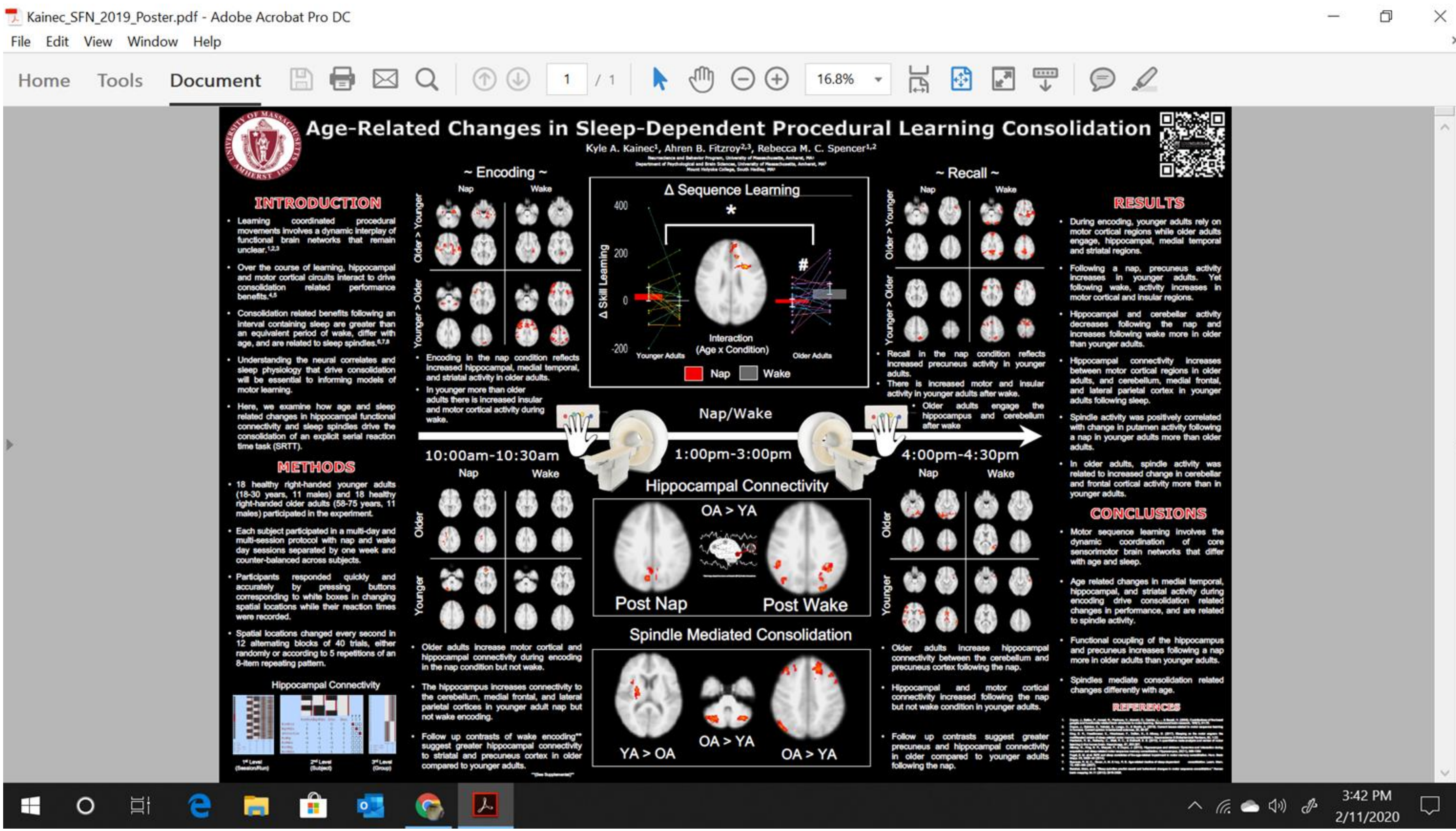
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Age-Related Changes in Sleep-Dependent Procedural Learning Consolidation
Kyle A. Kainec[1], Ahren B. Fitzroy[2,3], Rebecca M. C. Spencer[1,2]
INTRODUCTION
• Learning coordinated procedural movements involves a dynamic interplay of functional brain networks that remain unclear.[1,2,3]
• Over the course of learning, hippocampal and motor cortical circuits interact to drive consolidation related performance benefits.[4,5]
• Consolidation related benefits following an interval containing sleep are greater than an equivalent period of wake, differ with age, and are related to sleep spindles.[6,7,8]
• Understanding the neural correlates and sleep physiology that drive consolidation will be essential to informing models of motor learning.
• Here, we examine how age and sleep related changes in hippocampal functional connectivity and sleep spindles drive the consolidation of an explicit serial reaction time task (SRTT).
METHODS
• 18 healthy right-handed younger adults (18-30 years, 11 males) and 18 healthy right-handed older adults (58-75 years, 11 males) participated in the experiment.
• Each subject participated in a multi-day and multi-session protocol with nap and wake day sessions separated by one week and counter-balanced across subjects.
• Participants responded quickly and accurately by pressing buttons corresponding to white boxes in changing spatial locations while their reaction times were recorded.
• Spatial locations changed every second in 12 alternating blocks of 40 trials, either randomly or according to 5 repetitions of an 8-item repeating pattern.
Hippocampal Connectivity
1st Level (Session/Run)
2nd Level (Subject)
3rd Level (Group)
~ Encoding ~
Nap
Wake
Older > Younger
Younger > Older
• Encoding in the nap condition reflects increased hippocampal, medial temporal, and striatal activity in older adults.
• In younger more than older adults there is increased insular and motor cortical activity during wake.
Δ Sequence Learning
Δ Skill Learning
400
200
0
-200
*
#
Interaction (Age x Condition)
Younger Adults
Older Adults
Nap
Wake
Nap/Wake
10:00am-10:30am
1:00pm-3:00pm
4:00pm-4:30pm
Nap
Wake
Older
Younger
• Older adults increase motor cortical and hippocampal connectivity during encoding in the nap condition but not wake.
• The hippocampus increases connectivity to the cerebellum, medial frontal, and lateral parietal cortices in younger adult nap but not wake encoding.
• Follow up contrasts of wake encoding** suggest greater hippocampal connectivity to striatal and precuneus cortex in older compared to younger adults.
Hippocampal Connectivity
OA > YA
Post Nap
Post Wake
Spindle Mediated Consolidation
YA > OA
OA > YA
OA > YA
~ Recall ~
Nap
Wake
Older > Younger
Younger > Older
• Recall in the nap condition reflects increased precuneus activity in younger adults.
• There is increased motor and insular activity in younger adults after wake.
• Older adults engage the hippocampus and cerebellum after wake
Nap
Wake
Older
Younger
• Older adults increase hippocampal connectivity between the cerebellum and precuneus cortex following the nap.
• Hippocampal and motor cortical connectivity increased following the nap but not wake condition in younger adults.
• Follow up contrasts suggest greater precuneus and hippocampal connectivity in older compared to younger adults following the nap.
RESULTS
• During encoding, younger adults rely on motor cortical regions while older adults engage, hippocampal, medial temporal and striatal regions.
• Following a nap, precuneus activity increases in younger adults. Yet following wake, activity increases in motor cortical and insular regions.
• Hippocampal and cerebellar activity decreases following the nap and increases following wake more in older than younger adults.
• Hippocampal connectivity increases between motor cortical regions in older adults, and cerebellum, medial frontal, and lateral parietal cortex in younger adults following sleep.
• Spindle activity was positively correlated with change in putamen activity following a nap in younger adults more than older adults.
• In older adults, spindle activity was related to increased change in cerebellar and frontal cortical activity more than in younger adults.
CONCLUSIONS
• Motor sequence learning involves the dynamic coordination of core sensorimotor brain networks that differ with age and sleep.
• Age related changes in medial temporal, hippocampal, and striatal activity during encoding drive consolidation related changes in performance, and are related to spindle activity.
• Functional coupling of the hippocampus and precuneus increases following a nap more in older adults than younger adults.
• Spindles mediate consolidation related changes differently with age.
REFERENCES
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The marmoset (*Callithrix jacchus*) as a model for human cognitive aging.

Mélise Edwards[1,2], Emily Rothwell[1], Katy Workman[2] and Agnès Lacreuse[1,2]
[1]Psychological & Brain Sciences, [2]Neuroscience & Behavior Graduate Program, University of Massachusetts, Amherst MA

Background & Significance

With an increasingly aged human population, it is imperative to better understand trajectories of normative cognitive aging as well as pathological decline observed in dementias. Some studies point to of sex differences in trajectories of age-related cognitive decline, which may be due to sex differences in changes in steroid hormones during aging.

Common marmosets are small-bodied New World primates with a rich behavioral repertoire[1], the ability to perform complex cognitive tasks[2] and brain features that resemble those of humans[3,4]. Unlike rodents, marmosets also have human-like consolidated sleep[5]. Marmosets are a great model for human aging[6] because their short lifespan (~10 years) facilitates longitudinal investigations. The two studies in our lab look at aging, cognition with focus on sex differences in aging processes.

Cognitive Testing

Our projects focus on cognition and we utilize a touch-screen apparatus [CANTAB-Cambridge Neuropsychological Test Automated Battery] to test simple discrimination and reversal learning. Marmosets are shown a pair of stimuli and need to perform a simple discrimination followed by a simple reversal. When a marmoset touches the correct stimulus it receives a food reward. The marmosets are tested 5 days/week with each session containing 40 trials.

Fig 1. Marmoset playing cognitive game.

Fig 2. Example of stimuli sets for discrimination & reversal testing.

Aging & Sex Differences

This study investigates sex differences in trajectories of cognitive aging. With a longitudinal approach we aim to characterize healthy cognitive aging vs. pathological decline relevant to Alzheimer's Disease and other dementias.

Middle Age (5-6 yr old) → Old Age (9-10 yr old) Fig. 3. Study Timeline.

Year 1	Year 2	Year 3	Year 4	Brain Assays
Cognition Motor Brain imaging Social stress	Cognition Motor Brain imaging Social stress	Cognition Motor Social stress Sleep	Cognition Motor Sleep Affect Odor testing	

Awake Brain Imaging

fMRI scans revealed greater resting state functional connectivity for male, compared to female, middle-aged marmosets.[7]

Fig. 4. 3D functional network maps from marmosets.[7]

Affective Reactivity

Marmosets will be shown images to induce positive (e.g. food reward), negative (e.g. predator) or neutral (e.g. nature scenes) affect responses. We will measure their emotional response using heart rate variability from heart rate monitors as well as thermal imaging of facial responses.

Fig. 5. Extemal HR monitor worn in small monkey jacket.

Social Isolation Stress

Marmosets were removed from their home cage and isolated in a room outside of the colony for 7 hours. Behavioral stress was measured via agitated locomotion during isolation. Physiological stress was measured via cortisol levels from urine samples that were collected before, during the separation and 24 hours post-separation.

Motor Function

Marmosets complete a Hill & Valley Task to assesses motor function and perceptual spatial impairment. Marmosets reach through an opening using either hand, to retrieve a food reward placed in the middle of each of 5 steps.

Fig. 6. Top- Hill (stairs rise from lateral openings) Bottom- Valley (Stairs rise from central opening)

Sleep

Fig.7. Actograms of variability in sleep.

Fig. 8. Activity monitor collars.

Marmosets wear activity monitors on collars for two-night cycles. The activity monitors show several parameters related to sleep, such as latency to fall asleep, sleep efficiency, and sleep fragmentation.

Odor Testing

Fig. 9. Marmoset sniffing and selecting container.

Marmosets are being tested on an odor discrimination task in which animals are trained to identify a correct scent. They are then presented with two scents and must correctly choose and push back container to retrieve a food reward.

Future Directions

Results from cognitive testing show both sex differences and individual differences in age related cognitive trajectories. From this data we can predict the location and degree of neuropathology in the brain. Aging marmosets naturally develop AD-like neuropathology including the accumulation of β-amyloid plaques[8] and hyperphosphorlyated tau[9]. We will quantify the location and amount of these pathologies in the cortex and hippocampus.

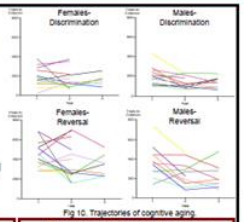
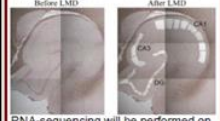


Fig 10. Trajectories of cognitive aging.

Hippocampal Gene Expression

Fig. 11. Laser capture microdissection of marmoset hippocampal subregions from [10]Datson et al. (2009).



RNA-sequencing will be performed on prefrontal cortex the subregions of the hippocampus (DG, CA1, CA2, CA3) that have been dissected with laser capture microdissection. Estrogen receptor subtype expression will be analyzed in these regions as well as other genes of interest.

Brainstem Tau Pathology

AD pathology progresses in a predictable pattern starting with abnormal tau in the brainstem and projects up to higher cortical regions[11]. Early tau pathology can be detected in the locus coeruleus (LC) and other brainstem nuclei decades before cognitive impairment and may underlie neuropsychiatric symptom that characterize pre-clinical AD. We will use stereology to quantify LC tau pathology and associate it with sleep and affect assessments.

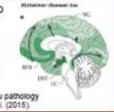


Fig. 12. Progression of tau pathology from [11]Brettschneider et al. (2015).

Conclusions

These studies will help to understand human aging processes, particularly focusing on cognition and sex differences. Two unique advantages to these studies with marmosets include the ability to track age-related cognitive changes longitudinally as well as measure a suite of behaviors in the same marmosets that relate to aging. We plan to associate all *in vivo* behavioral measures with post-mortem brain assays to try to develop profiles of marmosets with healthy vs. pathological cognitive aging. We intend for our research to will contribute to improving the health and well-being of aging humans.

References. [1]Miller, CT, et al. (2016). *Neuron*, 90(2), 219-233; [2]Spinelli, S, et al. (2004) *Cogn Brain Res* 19:123-137; [3]Chaplin, TA, et al. (2013). *J Neurosci 33, 15120-15125*; [4]Belcher, AM et al. (2016). *Front Integr Neurosci, 10*; [5]Gervais, N. et al., (2016). *Neurosci, 337*, 1-8. [6]Tardif, SD, et al (2011). *ILAR J, 52(1), 54-65*; [7]Marshall JW & Ridley RM (2003) *ILAR J, 44(2), 153-160*. [8]Laclair, M., et al. (2019) *eNeuro, 1-19*. [9]Maclean et al., (2000). *J. of Neural Transm, 799-814*; [10]Rodriguez-Callejas et al., (2016), *F in Aging Neurosci*, 1-15; [11]Datson et al., (2009), *Hippocamp*, 739-752; [11]Brettschneider et al., (2015), *Nat Rev Neurosci, 109*.

Acknowledgements. We would like to thank the many students that have contributed to this research over the years as well as the excellent Animal Care and Veterinary support staff at UMass-Amherst. **Funding** for these studies are provided by NIH: AG046266, AG046266-S1, AG054925-01A1.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DISTRIBUTION AND PHYSIOLOGY OF DOPAMINE D1 RECEPTORS IN THE SONGBIRD SECONDARY AUDITORY CORTEX

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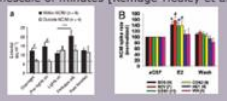
BACKGROUND

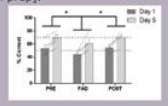
In songbirds, **the caudomedial nidopallium (NCM) is the auditory association cortex**, believed to be analogous to the secondary auditory cortex of humans [Bolhuis et al., 2010].

NCM is also involved in the **association between songs and behaviorally relevant consequences.** Neural activity in NCM reflects the association between song and reward/punishment [Bell et al., 2014].

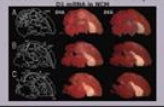
Estradiol (E2) acts as a neuromodulator in the zebra finch NCM, it is rapidly elevated locally during social interactions [Remage-Healey et al., 2008] and enhances neural responses to songs in a timescale of minutes [Remage-Healey et al., 2010].



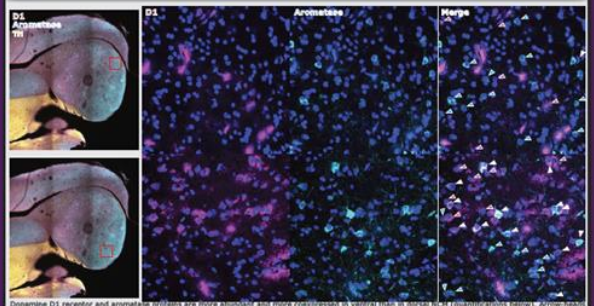
We have shown that **blocking the production of endogenous E2 in NCM impairs auditory learning in a novel operant task with social reinforcement** [Macedo-Lima and Remage-Healey in prep].



NCM shows extensive presence of **mRNA for dopamine D1-like, but not D2-like receptors** [Kubikova et al., 2010], **and of NMDAR subunit NR1** [Saldanha et al., 2004], but their functions have not been explored.

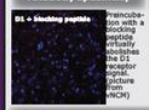


D1-DOPAMINE RECEPTORS COLOCALIZE WITH AROMATASE IN NCM



Dopamine D1 receptor and aromatase proteins are more abundant and more coexpressed in ventral than in dorsal NCM (quantifications below). Arrow-heads indicate single aromatase (cyan), D1 (magenta) positive neurons, and double stained neurons (white)

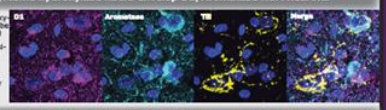
Antibody specificity



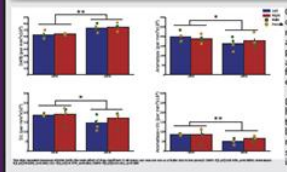
Preincubation with a blocking peptide virtually abolishes the D1 receptor signal. (picture from vNCM)

Tyrosine hydroxylase fibers envelop D1/Aromatase NCM neurons

Tyrosine hydroxylase fibers can be found wrapping aromatase-D1-positive neurons in NCM (picture from vNCM above). Blue is DAPI, a nuclear stain

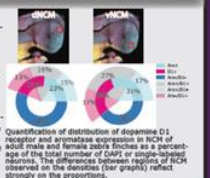


D1 RECEPTOR AND AROMATASE EXPRESSION ARE HIGHER IN THE VENTRAL PORTION OF NCM



Quantification of distribution of dopamine D1 receptor and aromatase expression in NCM of adult male and female zebra finches.

Despite the dNCM having higher density of cell nuclei (top left), D1 and aromatase proteins are still more abundant in the vNCM.

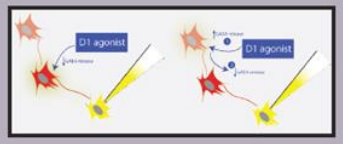


Quantification of distribution of dopamine D1 receptor and aromatase expression in NCM of adult male and female zebra finches as a percentage of the total number of DAPI or single-labeled neurons. The differences between regions of NCM observed on the densities (bar graphs) reflect strongly on the proportions.

THE MAJORITY OF D1 RECEPTOR-POSITIVE NEURONS PRODUCE GABA

CONCLUSIONS

- NCM shows high expression of dopamine receptor D1 protein (~25%), **especially in its ventral portion, where aromatase is also more abundant.**
- Tyrosine hydroxylase fibers can be found wrapping NCM neurons expressing aromatase and D1 receptors
- Most of the D1 receptor-expressing neurons are GABAergic (~60%)
- Activating D1 receptors in vitro reduces GABAergic neurotransmission in NCM neurons. Because no effects were observed on the miniature currents, effect is likely presynaptic. Two possible scenarios:



- These receptors also increase the frequency but reduce the amplitude of NMDA-dependent currents. The lack of effect on miniature currents suggests a presynaptic effect.

Mutation of $GABA_A$ receptor α subunits reveals selectivity in regulating locomotor behavior

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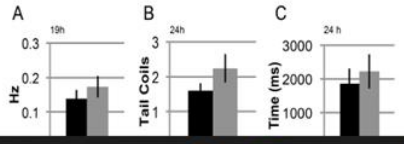
Biology Dept. Amherst College[3], Amherst MA 01003

Introduction

- $GABA_A$ receptors ($GABA_A$Rs) are pentameric ion channels essential for rapid responses to GABA.
- $GABA_A$ signaling is a robust regulator of hindbrain and spinal cord locomotor networks but its precise roles and mechanisms remain unclear.
- There are 19 different subunit types in mammals. Only the widely expressed γ2 and β3 knock-out mice show a motor phenotype, which has not been well characterized. Other subtypes are present but their contribution to motor networks is unknown.
- **Our goal is to investigate how $GABA_A$Rs first establish then maintain control of hindbrain and spinal cord locomotor circuits**



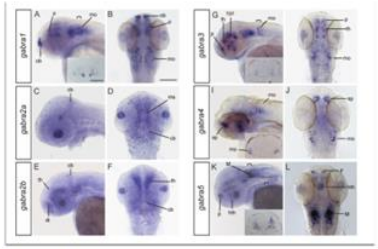


Figure 3. Most $GABA_A$R a subunits are expressed in distinct patterns in the brain at 48h. *In situ* hybridization results are shown in lateral (A, C, E, G, I, K) and dorsal (B, D, F, H, J, L) views. *gabra1*, *gabra2a*, *gabra2b*, *gabra3*, *gabra4*, and *gabra5* were detected at this time point. The scale bar=0.1 mm. Brackets in A, G, I, and K indicate cross sections within the insets. Abbreviations: cb, cerebellum; di, diencephalon; hth, hypothalamus; M, Mauthner cell; mo, medulla oblongata; ms, mesencephalon; ob, olfactory bulb; p, pallium; sp, subpallium; t, tegmentum; th, thalamus.

- **What subunits are essential?**
- **Which cells require $GABA_A$R activity?**
- **Can the diversity of $GABA_A$Rs be used to identify different roles of GABA in governing locomotion?**

Results

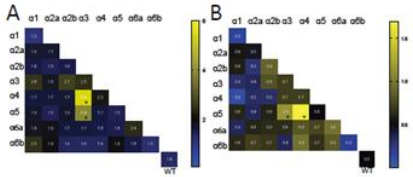


Figure 6. Increased hyperactivity in a4-a3 F_0 injection combination at 48hpf compared to single targets suggest subunit selectivity is present in locomotion. Each box representing a different combined injection for the $GABA_A$R subunit screen at 48 hpf (n=7-18). The number centered in each box indicates (A) the average number of C-bends performed or (B) the average duration of the escape response in seconds. Significant comparisons were identified using an ordinary one-way ANOVA. *=p<0.01

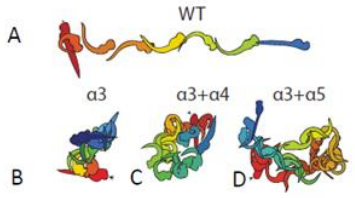
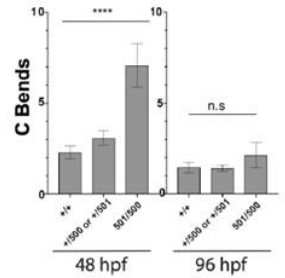


Figure 8. Select CRISPR injected combinations containing *gabra3* show significantly increased C-



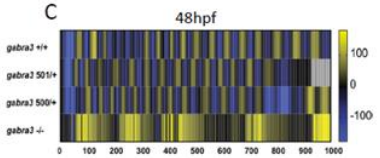


Figure 10. *Gabra3* mutant embryos show select significant differences compared to sibling controls at 48 but not 96 hpf. Behavioral results from *gabra3* null transheterozygote. (A) Color codes showing body angles/time. 0º is a straight body (*black*), while 180º represents head-to-tail touches in one direction (*blue*) or the opposite direction (*yellow*). (B) Showing the average number of C-Bends performed by sibling wildtype,

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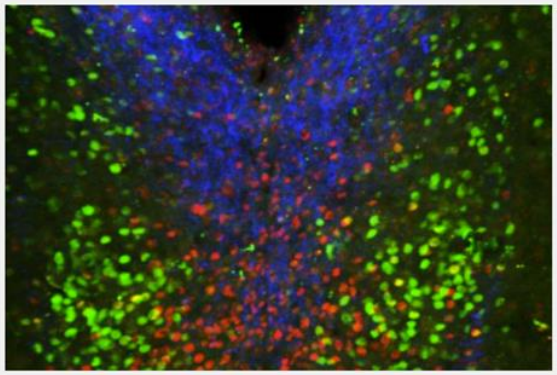

Welcome to the Neuroscience & Behavior Program

The **Neuroscience and Behavior (NSB) Graduate Program** at UMass Amherst is one of eight Graduate Programs in the Life Sciences and part of a larger Neurosciences community at the University. NSB brings together faculty members from various departments to provide exciting, cutting-edge research training. The program spans several areas of research including: Neuroendocrinology, Cellular and Molecular Neuroscience, Animal Behavior and Learning, Neural and Behavioral Development, and Sensorimotor, Cognitive, and Computational Neuroscience. Find out more about the Initiative on Neurosciences (IONs). Follow Neurosciences at UMass on Facebook and Twitter.

Program Overview | Apply to NSB

News & Announcements

Student spotlight – Sarah Winokur

Neuroscience and Behavior PhD student, Sarah Winokur, received three awards to support her dissertation research: The Dissertation Fellowship from the Center for Research on Families, The Psychological and Brain Sciences Department's Rayner Memorial Fund Award, and The UMass Amherst Graduate School's Dissertation Research Grant. Read more

Upcoming Events

Wednesday, Feb 12
Wayne Barnaby (Downes lab)
NSB Graduate Student Talk
Mutagenesis of GABA(A) Receptor alpha Subunits Reveals Selectivity in Regulating Locomotor Behavior

Wednesday, Feb 19
Eve Marder
Differential resilience to perturbation

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Effect of voluntary binge drinking on microglial cells in the medial prefrontal cortex (mPFC) and hippocampus of male and female rats

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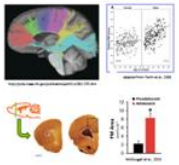
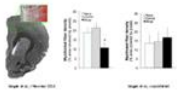
*A. SILVA-GOTAY[1], E. TAVARES[2], A. LIN[2], W. VARGAS RIAD[3], M.K. HOLDER[4], H. N. RICHARDSON[2];
[2]Psychological and Brain Sci., [1]Univ. of Massachusetts Amherst, Amherst, MA; [3]BGB Group, New York, NY;
[4]Neuroscience Institute, Georgia State Univ., Atlanta, GA

Introduction

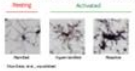
Myelination of axons during adolescent development



Adolescent binge drinking reduces myelin the mPFC



Microglia are the resident immune cells of the brain



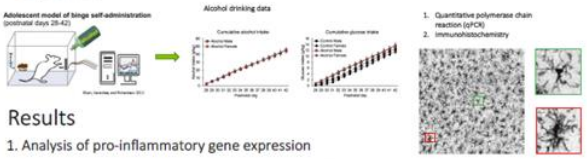
Hypotheses:

Alcohol binge drinking has a pro-inflammatory effect on the developing brain, with a greater effect on males.

Experimental Design

Animals

- Wistar Rats
- Male and Female
- Early Adolescence

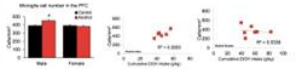


Results

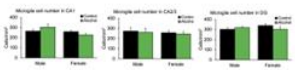
1. Analysis of pro-inflammatory gene expression

2. Immunohistochemical analysis of microglia

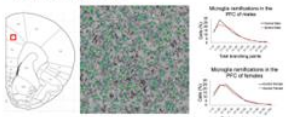
Medial prefrontal cortex
Cell counts



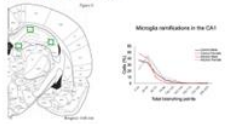
Hippocampus subregions
Cell counts



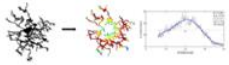
Microglia morphology



Microglia morphology



Future Directions: Sholl Analysis



Conclusions

- Adolescent male and female rats consumed similar levels of alcohol during the 2-week exposure period (~4Sg/kg).
- Adolescent binge drinking significantly increased TLR4 gene expression in the mPFC and hippocampus. IL1β is only increased in the mPFC.
- Microglia appear to be recruited to the mPFC 24 hours after last alcohol binge in males, but not in females.
- Microglia are not affected in the hippocampus 24 hours after last binge. This is consistent with previous literature showing microglia are recruited in hippocampus after 48 hours (Nixon et al., 2008)
- These preliminary findings highlight the negative impact alcohol has on the developing brain. Future analyses with larger sample sizes will be useful for confirming these results.

Acknowledgements

I would like to thank Lynn Bengston, Kyle Lucier, and Jillian Davis for expert technical assistance and the Hazen lab for access to equipment used in the gene expression studies.

Funding Sources:
R01AA024774 (HNR); NSF HRD 0450339 (WV); NIH-NIGMS 5R25GM099649-03 (AS)

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The role of reward signaling in prairie vole peer relationships

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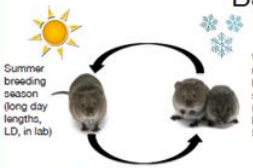
Presentation Number: 069.22

Background



- **Meadow vole** (*Microtus pennsylvanicus*)
  - Seasonally group living
  - Socially non-monogamous
  - No bi-parental care
- Females housed in SD display same-sex partner preferences.
- **These peer relationships are not dependent on dopamine signaling** (Beery & Zucker, 2010).

- **Is reward essential for prairie vole peer relationships?** Or does reward only play an essential role in highly motivated reproductive relationships?
- **The goal of this project** is to elucidate the role of reward and dopamine neurotransmission in same-sex prairie vole peers, and to compare its role in prairie vole peers to:
  1) meadow vole peer relationships
  2) prairie vole pair bonds.

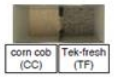
- **Prairie vole** (*Microtus ochrogaster*)
  - Socially monogamous
  - Bi-parental care
- Females also display selective, stable same-sex partner preferences.
- These peer relationships are not day length-dependent.
- **Dopamine neurotransmission is essential to prairie vole pair bond formation and maintenance** (Wang et al., 1999; Aragona et al., 2003).

Methods

- The **partner preference test** (PPT) was used to measure partner preference formation and strength. A familiar partner and a stranger were tethered to the apparatus (one on each end). The focal vole moved freely through the apparatus for 3 hr.

- **Haloperidol** (DA antagonist) and **apomorphine** (DA agonist) or vehicle controls were administered via IP injection at doses previously found effective in prairie voles (0.5-120 μg).
- Haloperidol was injected immediately prior to pairing with a new same-sex partner, followed by a **24 hr cohabitation** (usually sufficient for partner preference formation). Apomorphine was injected immediately prior to pairing, followed by a **6 hr cohabitation** (insufficient).

- **Socially conditioned place preference** (SCPP) was used to measure reward value of and motivation for familiar partners.



- Voles were expected to show initial preference for TF bedding, and those that did not were excluded. TF bedding was then associated with isolation and non-preferred CC bedding with social housing (**counter conditioning**).
- Pre- and post-tests were each 30 min long. Haloperidol was injected prior to post-tests. Voles remained with their same-sex partners from weaning or were re-paired in adulthood.

Results

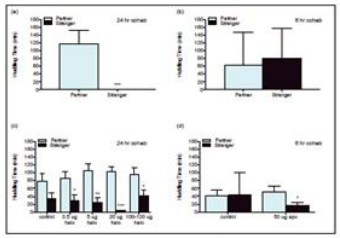


Fig 1. **Partner preference tests: Haloperidol does not block partner preference formation, but apomorphine induces it.** (a) 24 hr cohabitation is sufficient for partner preference formation in female prairie vole peers (Lee et al., 2019). (b) 6 hr cohabitation is not sufficient for partner preference formation in female prairie vole peers. (c) Haloperidol does not block partner preference formation at any dose after 24 hr cohabitation. (d) Apomorphine induces partner preference formation after 6 hr cohabitation. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$.

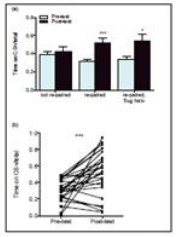


Fig 2. **Socially conditioned place preference tests: Female prairie voles exhibit socially conditioned place preference for peers.** (a) Only prairie voles re-paired with new same-sex partners in adulthood exhibit significant socially conditioned place preference. Haloperidol does not block this behavior. (b) Individuals from the re-paired group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$.

Conclusions

- **Dopamine is not necessary for partner preference formation in prairie vole peers**, unlike prairie vole pair bonds and like meadow vole peer relationships.
- **However, dopamine is sufficient for partner preference formation in prairie vole peers**, like prairie vole pair bonds.
- Female prairie voles can be socially conditioned for new same-sex partners in adulthood, suggesting that there *is* a degree of social motivation and reward attached to the formation of peer relationships.
- Still, **dopamine signaling appears to mediate prairie vole mate relationships differently from prairie vole peer relationships**.
- It is likely that prairie vole peer relationships are mediated similarly to meadow vole peer relationships rather than prairie vole pair bonds because non-reproductive affiliation (in contrast to affiliation between mates or between parent and offspring) is less highly motivated.
- This research **supports further study of the mechanisms underlying peer affiliation**, which is important for many social animals but is less well understood than parental and pair bonding behaviors.

Acknowledgements

The authors would like to thank the Smith College Animal Care Facility Staff for their assistance and dedication, as well as Kate Shambaugh, Sarah Lopez, Karina Lieb, Paige Salters, Jessie Marsh, Asia Derosby, and Maddie Lerner for their assistance in animal handling and behavioral scoring. This project was supported by NIH grant 638089 to AKB.

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Prefrontal and orbitofrontal cortex neurons are differentially activated during passive and active alcohol acquisition: Influences of individual preference and chronic exposure

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Department of Psychological and Brain Sciences and Neuroscience and Behavior Program, University of Massachusetts, Amherst

414.17 X7

Introduction

PROBLEM:
Analysis of neuronal firing across individual differences in EtOH preference is confounded by behavior differences

High drinkers = complete trials to receive EtOH at reward port (ex. well entry)

Low drinkers = no action

Does EtOH preference and exposure correlate with neuronal firing? Can we disentangle value of a predicted outcome and motivation needed to obtain the reward?

Methods

Intermittent home cage drinking: 20% alcohol in home cages using a two-bottle choice test three days a week (Carnicella et al., 2014). One group had 4 weeks of access (**'acute'**) and the other 12 weeks of access (**'chronic'**) (Hopf, 2010).

Intraoral Catheters (IOC): Unilateral implantation of a catheter from the top of the head into the mouth for sucrose, EtOH, or quinine delivery (Samuelson et. al., 2012).

Electromyography (EMG): Two wires into the anterior digastric muscle to quantify licks and gapes (Li et. al., 2016).

Drivable tetrode array: 4 tetrodes in prelimbic cortex (±0.6 mm ML; 3.0mm AP; -3.2mm DV). 4 tetrodes in infralimbic cortex (±0.6 mm ML; 3.0mm AP; -4.5m DV). 7 tetrodes in orbital frontal cortex. Custom drive (1.6g, total with shield 3.1g). Recorded with Neuralynx or OpenEphys, sorted with KiloSort2, analyzed with Matlab.

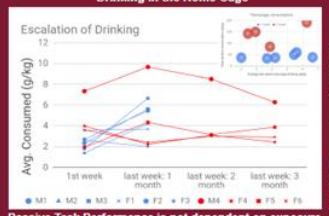
Discussion

- Sheer volume of alcohol consumption does not segregate behavior or neural states.
- Next step: take a multidimensional profile of each rat to categorize neural states.

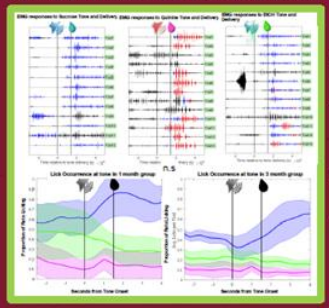
Acknowledgements

Supported by NIH grants AA024571 and DA041674. A special thanks to Jennifer Li, Ph.D., Chad Samuelson, Ph.D., Maddy Berkowitz-Cerasano, Arie Burman, Jessica Caballero and Christopher G. Park, Ph.D. Moorman Lab rules!

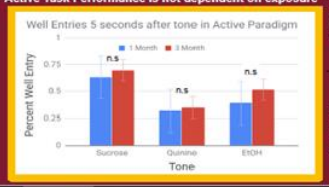
Drinking in the Home Cage



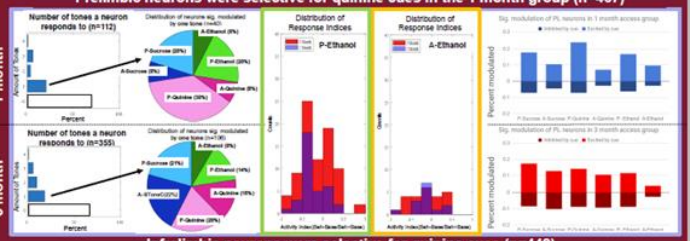
Passive Task Performance is not dependent on exposure



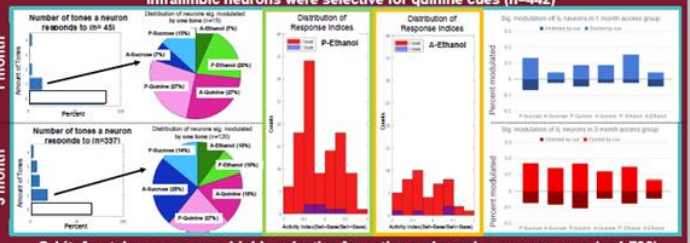
Active Task Performance is not dependent on exposure



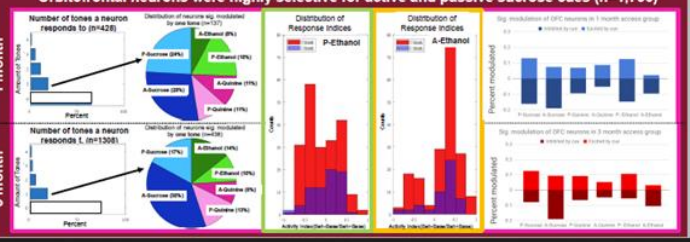
Prelimbic neurons were selective for quinine cues in the 1 month group (n=467)



Infralimbic neurons were selective for quinine cues (n=442)



Orbitofrontal neurons were highly selective for active and passive sucrose cues (n=1,736)



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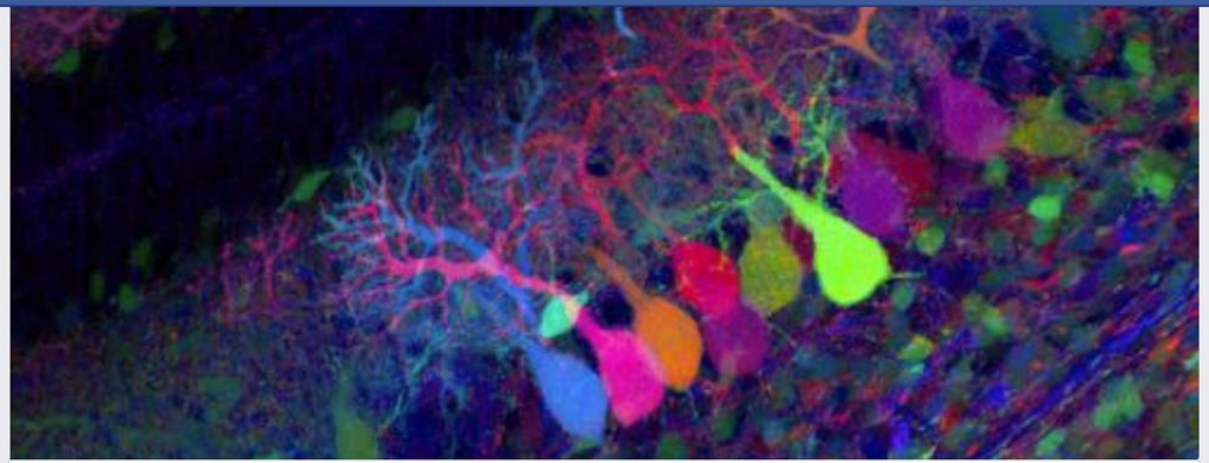

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Goal-directed behaviors in response to olfactory and visual stimuli in the nudibranch *Berghia stephanieae*

Phoenix D. Quinlan[1,2], Niah G. Holtz[2], Paul S. Katz[1,2]
Neuroscience and Behavior Graduate Program[1], Department of Biology[2], University of Massachusetts Amherst

UMassAmherst Neuroscience and Behavior Graduate Program
BRAIN INITIATIVE U01-NS108637

The ***Berghia* Brain Project** is developing new tools for high-throughput analysis of connectivity and neural activity of a 4,000 neuron brain to determine the neural mechanisms of behavior in the nudibranch *Berghia stephanieae*.

- Nudibranchs have meso-scale nervous systems and individually identifiable neurons, allowing cellular resolution of neural circuits.
- *Berghia* has a short generation time and can be raised in the lab in large numbers.

Build a cellular resolution brain atlas and connectome → Characterize goal-directed behaviors → Record brain activity during behavior at single-cell resolution

Olfactory-guided navigation

Berghia preys on the anemone *Exaiptasia pallida*

Hungry *Berghia* locate prey in a Y-maze with water flow

Unlike *Tritonia diomedea* and *Aplysia californica*, *Berghia* can locate prey in still water

Berghia needs both rhinophores to find prey in still water

Visually-guided navigation

Berghia has simple eyes

Berghia's eyes sit on the brain

The eye contains 5 photoreceptor cells

Berghia navigates to a black stripe on a white background

Berghia may be using visual cues to navigate toward shelter

Berghia turns in response to a moving environment

Conclusion

Berghia has robust, quantifiable goal-directed behaviors

Satiety Hunger

Voltage-sensitive dyes allow the activity of many neurons to be recorded simultaneously

- Voltage-sensitive dyes allow action potentials in dozens of neurons to be recorded simultaneously
- Semi-intact preparation will allow neuronal activity to be recorded during presentation of sensory stimuli
- We predict the application of food odors to one rhinophore will evoke asymmetric activity and fictive turning in an isolated brain preparation

Acknowledgements

The *Berghia* Brain Project Collaborators:
Dr. William N. Frost, Rosalind Franklin University
Dr. Jeff W. Lichtman, Harvard University
Dr. Diendre G. Lyons, Scripps Oceanographic Institute
Dr. Vincent P. Lyzinski, University of Massachusetts Amherst

Katz Lab members who contributed:
Dr. Desmond Ramirez, Dr. Brandon Drescher, Amanda Cho, Jackson Southard

https://tinyurl.com/BerghiaBrain

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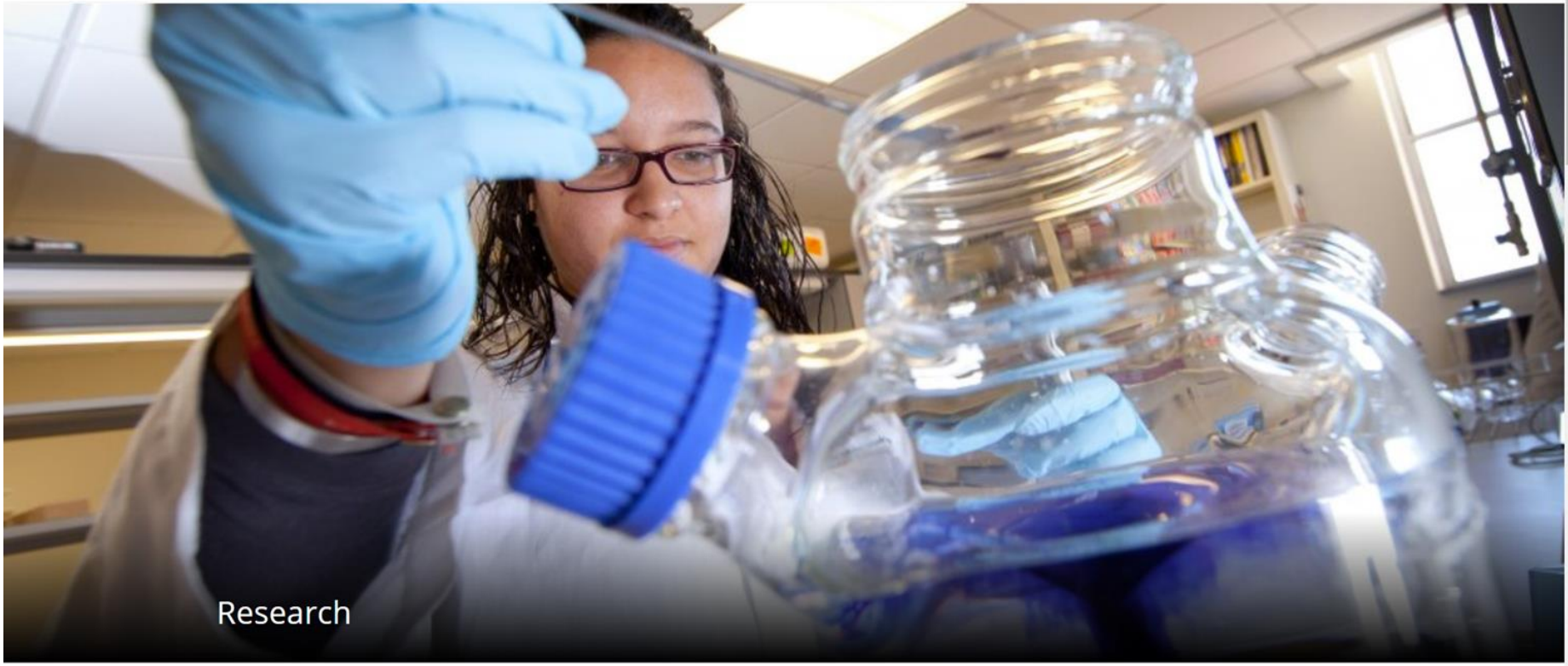

Neural Correlates of Recognition Memory in the Human Visual Ventral Stream

Natasha de la Rosa[1], Krystal Leger[3], Nick Blauch[4], Rosemary Cowell[1,2]
1. Neuroscience and Behavior Program, University of Massachusetts Amherst, MA
2. Department of Psychological and Brain Sciences, University of Massachusetts Amherst, MA
3. Department of Psychology, Brandeis University, Waltham, MA
4. Ctr. for the Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh, PA

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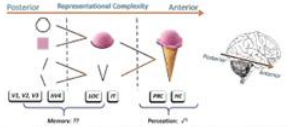
Introduction

Representational-Hierarchical Theory:

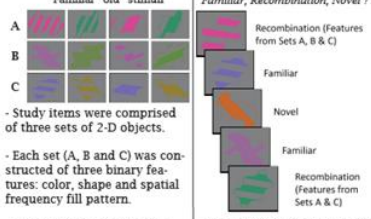
The brain contains a hierarchy of stimulus representations: simple features in visual cortex, conjunctions of features in temporal cortex, high-dimensional associative representations of scenes or events in hippocampus. Function of each region is determined by content of its representations



Do we find regions traditionally thought to be dedicated to vision (outside of MTL in the visual cortex) involved in memory?

	Perception	Memory
Visual Ventral Stream	✓	?
Medial Temporal Lobe	✓	✓

Experimental Paradigm

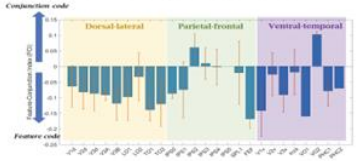


- Study items were comprised of three sets of 2-D objects.
- Each set (A, B and C) was constructed of three binary features: color, shape and spatial frequency fill pattern.
- Each set has 8 objects (but only 4 are shown above), totaling 24 studied items.
- 72 recombination objects were constructed between the three sets.
- Participants were instructed to respond what type of item is being presented:
  - *Familiar (old)*
  - *Recombination*
  - *Novel*

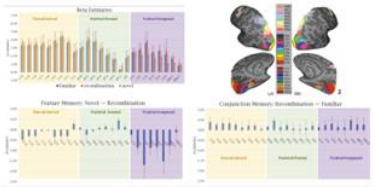
Study phase:
- Total runs = 10
- 1.5 s/stimulus; ISI = 2-12 s

Results

Feature-Conjunction Indices



Beta Estimates: Test Phase



Methods

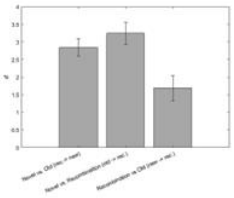
Analysis:
- 4 subjects (23- 28 ages)
- Preprocessing with FMRIPREP 1.4.1
- SPM12 used for univariate analysis (GLMs)
- CosmoMVPA toolbox used for classifier.

Feature-Conjuction Index (FCI)[3]:
- Predicted object accuracy = product of three, separate 2-way classification of each feature.
- Empirical object accuracy = 8-way classification of objects.

$$FCI = \ln\left(\frac{empirical\ object\ accuracy}{predicted\ object\ accuracy}\right)$$

- Positive FCI = conjunction coding
- Negative FCI = feature coding

Behavioral Responses (test phase)

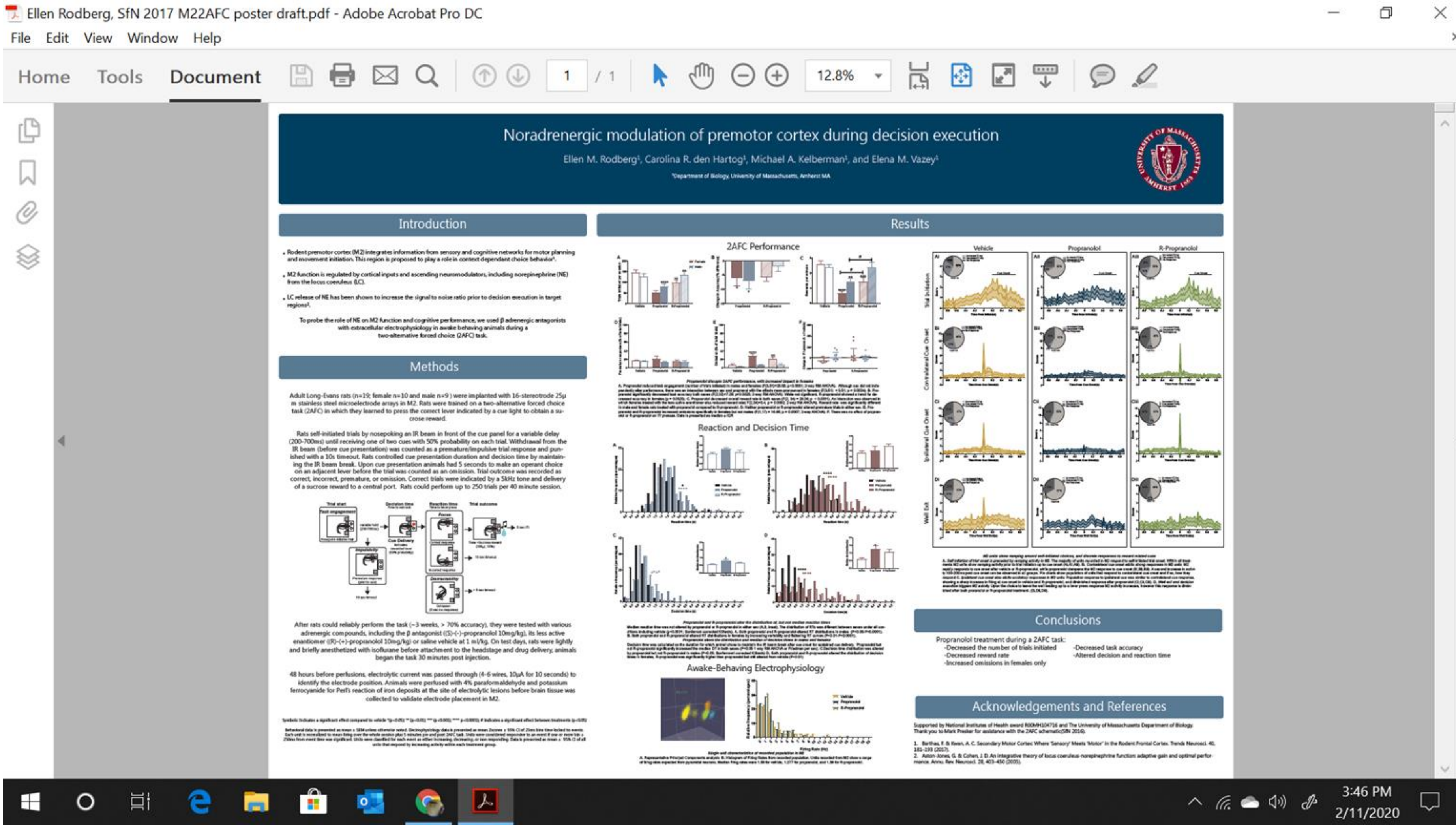


- Total runs = 8
- Familiar items presented 4x.
- Recombination and novel items were only shown 1x.
- 4 s/stimulus; ISI = 2-6 s

Conclusions

- A positive FCI suggests conjunction code for these stimuli in IPS2 and ventral-occipital (VO) 2.
- We tested for Feature Memory and Conjunction Memory.
- Small number of subjects, but hints of:
  - (1) Feature Memory in ventral visual and early dorsal ROIs
  - (2) Conjunction Memory in dorsal ROIs and possibly VO2
- Preliminary suggestions of a role of VO2 in both conjunction coding and conjuntion memory?
- Future plan: redesign learning phase using visual search to overtrain the studied items. Stronger memory responses?

References: 1. Ross, et al. (2018) Cerebral Cortex. 2. Wang et al. (2015) Cerebral cortex. 3. Cowell et al. (2017) Journal of Neurophysiology. 4. Destrieux, et al. (2010) Neuroimage.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Noradrenergic modulation of premotor cortex during decision execution
Ellen M. Rodberg[1], Carolina R. den Hartog[1], Michael A. Kelberman[1], and Elena M. Vazey[1]
Introduction
Methods
Results
2AFC Performance
Reaction and Decision Time
Awake-Behaving Electrophysiology
Vehicle
Propranolol
R-Propranolol
Conclusions
Propranolol treatment during a 2AFC task:
-Decreased the number of trials initiated
-Decreased reward rate
-Increased omissions in females only
-Decreased task accuracy
-Altered decision and reaction time
Acknowledgements and References
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Environmental circadian desynchronization prolongs sickness behavior and alters immune responses in mice

Gregory L. Pearson, Marina Savenkova, & Ilia N. Karatsoreos
Department of Integrative Physiology & Neuroscience, Washington State University, Pullman, WA, USA

BACKGROUND

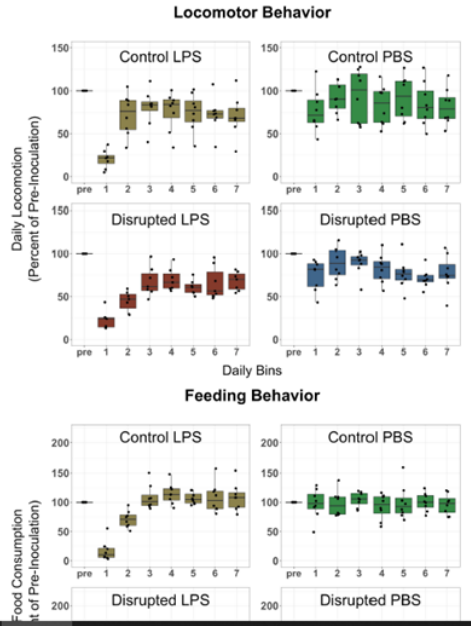
- Sickness behaviors are elicited by the immune system's response to an antigenic stimulus.
- Many aspects of the immune system are regulated by the circadian (daily) clock.
- We previously demonstrated that circadian desynchronization (CD) in mice alters both peripheral and central immune responses following a low-dose lipopolysaccharide (LPS) challenge [Phillips 2015].
- We posit that if CD alters inflammatory responses of mice to a peripheral LPS challenge and if inflammatory responses induce sickness behavior, then CD will alter sickness behavior in mice.

APPROACH

- Male mice (8/group) were housed in

RESULTS

Sickness behaviors are increased in CD mice following LPS inoculation



RESULTS

CD results in changes to LPS induced transcriptional events in liver, spleen and hypothalamus