New Mexico EEG and Behavior
From the Clinic to the Laboratory and Back

October 3rd & 4th 2018
University of New Mexico Health Sciences Center
Albuquerque, NM

Supported by:
The Center for Brain Recovery and Repair
1P20GM109089
Dear Colleagues,

We are delighted to welcome you to Albuquerque and the New Mexico EEG & Behavior Meeting 2018 at the University of New Mexico Health Sciences Center! An increased appreciation of the translational utility of electrophysiology has created new opportunities for comparing neural activity during behavior across species. Novel recording and analytic techniques afford the opportunity to develop methods for quantitative translation between species. However, these exciting opportunities bring challenges as well, and we are excited to have scientists of all levels here in Albuquerque to discuss how to move the field forwards.

All morning and afternoon sessions will be held at the Pete & Nancy Domenici Hall located on UNM’s North Campus. Please find a map and driving directions on the next page of the meeting program. Both morning and afternoon sessions will include talks by leading researchers in human, rodent and translational EEG approaches. In addition, there will be opportunities for discussion and debate of what we think are critical issues in the field, as well as interactive workshops on data analysis and rodent recording approaches.

Finally, please join us for the Poster Session and reception on October 3rd from 6 pm to 9 pm at the Hotel Parq Central (806 Central Ave. SE, Albuquerque, NM) in the parlor and courtyard. This should be a fantastic opportunity to discuss results and everything else in a more relaxed atmosphere.

Once again, we want to welcome you to the meeting, and to New Mexico!

Jonathan, Jim and Bill

Jonathan L. Brigman, PhD
Meeting Organizer
Associate Professor, Department of Neurosciences
University of New Mexico Health Sciences Center

James F. Cavanagh, PhD
Program Chair
Assistant Professor, Department of Psychology
University of New Mexico

C. William Shuttleworth, PhD
Director, Center for Brain Recovery and Repair
Regents’ Professor, Department of Neurosciences
University of New Mexico Health Sciences Center
New Mexico EEG and Behavior 2018
General Information

Morning and Afternoon Session:
The Center for Brain Recovery and Repair
UNM HSC North Campus, Domenici Hall
1101 Yale Blvd NE, Albuquerque, NM 87131

Map:

Parking:
Free daily parking is available; please see the registration desk in the lobby.

Evening Poster Session:
The Hotel Parq Central
West End Patio
806 Central Ave Se, Albuquerque, NM 87102
(505) 242-0040
New Mexico EEG and Behavior 2018
Program Schedule

Wednesday, October 3rd, 2018

Morning Session

8:00 AM – 8:45 AM  Registration and Breakfast

8:45 AM – 9:00 AM  Bill Shuttleworth, Director, Center for Brain Recovery and Repair
                   Welcome and Opening Remarks

9:00 am – 9:30 am  Steve Siegel, University of Southern California.
                   Critical assessment of the translational potential of EEG assessment in mice

9:30 am – 10:00 am Christopher Lapish, Indiana University - Purdue University Indianapolis
                   Targeting corticostriatal oscillations in a rodent model of excessive alcohol drinking

10:00 am – 10:30 am Break

10:30 am – 11:00 am Kaori Takehara, University of Toronto
                   Aberrant oscillatory coupling in a rat model for presymptomatic stages of Alzheimer’s disease

11:00 am – 11:30 am Julia Stephen, The Mind Research Network
                   Using preclinical studies to inform MEG/EEG studies for clinical translation

11:30 am – 12:00 pm Jill Silverman, University of California Davis
                   Translation in fast forward: Patient driven research in Angelman syndrome

12:00 pm – 1:00 pm  Catered Lunch for Registered Attendees
                    Domenici Hall Atrium
**New Mexico EEG and Behavior 2018**

**Program Schedule**

**Wednesday, October 3rd, 2018**

### Afternoon Session

1:00 pm – 1:30 pm

Jared Young, University of California, San Diego  
*Toward cross-species neural biomarkers of reward learning and motivation*

1:30 pm – 2:00 pm

Mykel Robble, Harvard University  
*Development of a touchscreen-based Flanker task in rats for cross-species neurophysiological studies of cognitive control*

2:00 pm – 2:30 pm

Discussion: *Can we make inferences from within specific regions in rodents about whole head signals in humans? Insights from the UH2 Consortium*

2:30 – 4:30

James Cavanagh, University of New Mexico  
*Analysis workshop on applying cutting-edge analytic techniques using open-source tools.*

### Evening Session

6:00 pm – 9:00 pm

Poster Session and Reception  
*hors d'oeuvres, tea/coffee/water provided; cash bar*

Hotel Parq Central, 806 Central Ave. SE, Albuquerque, NM

*Poster Presentation Guidelines. The poster boards are 40 inches X 60 inches long (landscape orientation). The maximum recommended size for the poster boards is 36 inches X 48 inches. Push pins will be provided.*
# New Mexico EEG and Behavior 2018

## Program Schedule

*Thursday, October 4th, 2018*

### Morning Session

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>8:00 am – 9:00 am</td>
<td>Breakfast for Registered Attendees</td>
</tr>
<tr>
<td>9:00 am – 9:30 am</td>
<td>Bita Mogahaddam, Oregon Health Sciences University <em>Prefrontal cortex computation of anxiety</em></td>
</tr>
<tr>
<td>9:30 am – 10:00 am</td>
<td>Stephen Cowen, University of Arizona <em>Neural synchrony, memory, aging, and Parkinson’s disease</em></td>
</tr>
<tr>
<td>10:00 am – 10:30 am</td>
<td>Break</td>
</tr>
</tbody>
</table>
| 10:30 am – 11:00 am| Lois Winsky, Chief, Molecular, Cellular, and Genomic Neuroscience Research Branch, NIMH  
Margaret Grabb, SBIR/STTR Coordinator, NIMH *NIMH support for translational research* |
| 11:00 am – 12:00 am| Roundtable Discussion: *Theory, Practice, Dissemination and Funding: Opportunities and roadblocks in translational EEG research.* |
| 12:00 pm – 1:00 pm | Catered Lunch for Registered Attendees  
*Domenici Hall Atrium*  
Lee Anna Cunningham, Director, CBRR Preclinical Core *Pushing your research forward: Training and testing opportunities at the CBRR*  
*Lunchtime overview of resources available to IDeA states investigators through the Center for Brain Recovery and Repair Preclinical Core.* |
## New Mexico EEG and Behavior 2018
### Program Schedule

**Thursday, October 4th, 2018**

### Afternoon Session

<table>
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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Topic</th>
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<tr>
<td>1:00 pm – 1:30 pm</td>
<td>Andre Der-Avakian, University of California, San Diego</td>
<td><em>Electrophysiological correlates of probabilistic reversal learning in rats using a translational task</em></td>
</tr>
<tr>
<td>1:30 pm – 2:00 pm</td>
<td>Greg Light, University of California, San Diego</td>
<td><em>EEG measures of neural system engagement following initial exposure to procognitive interventions in Schizophrenia</em></td>
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<tr>
<td>2:00 pm – 4:00 pm</td>
<td>Jonathan L. Brigman, University of New Mexico, SOM</td>
<td><em>Approaches to recording EEG in rodents: Dura to depth</em> This workshop will cover the basics of utilizing EEG recording in rodent species. Topics will include options for building/purchasing electrodes, implantation approaches, capturing signals, and integration with behavioral paradigms.</td>
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<tr>
<td>4:00 pm</td>
<td>James F. Cavanagh, UNM</td>
<td><em>Closing remarks</em></td>
</tr>
</tbody>
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- Adjourn -
The Pre-Clinical Core is a component of the Center from Brain Recovery and Repair. Its mission is to establish a centralized resource and expertise on automated behavior, in-vivo detection of neuronal activity, and structural analyses applicable to a range of pre-clinical models of brain and behavioral illnesses.

Consultation
We will work with you to design and implement your experiments to integrate behavioral assays, in-vivo multichannel electrophysiology, optogenetics, multi-photon imaging, cerebral blood flow imaging (laser speckle contrast imaging), immunohistochemistry, and morphological analysis. In addition, we can consult on animal protocol amendments regarding the work to be done within the Preclinical Core, and provide letters of support for grant submissions.

Training
We will provide training to PIs and/or lab personnel on behavioral tasks, in-vivo electrophysiology, imaging, tissue processing, and morphological analysis. Training for the equipment usually takes 1 – 2 hours and we help when needed until the users are comfortable with the assay.

Service
We offer services for behavioral assessment (automated tracking and motor assessment), automated fear conditioning and touch-screen behavioral tasks. Tissue processing and mounting, tissue sectioning (sliding knife, vibratome, and cryostat), basic immunohistochemistry and Imaris 3D and 4D image analysis.

Learn More
Join us for a brief overview during the lunch break on October 4th or contact us for more information or to schedule a consultation:

Lee Anna Cunningham
Director
leeanna@salud.unm.edu

Jonathan L. Brigman
Associate Director
jbrigman@salud.unm.edu

Russell Morton
Operations Manager
ramorton@salud.unm.edu
1. Semantic memory processing buffers women against negative behavioral consequences in social identity threatening contexts

Rachel Amey*, Adam B. Magerman, and Chad E. Forbes
Department of Psychological and Brain Sciences, University of Delaware, Newark, DE

Social identity threats (SIT) elicit the automatic episodic encoding of SIT information leading to disengagement. This is especially prominent for women in STEM domains who experience SIT regularly. Yet even with this constant stressor there are women who thrive in STEM; how some individuals maintain positive STEM identities in the face of SIT remains unknown. Observing women in a SIT STEM context with EEG methodology to capture in the moment neural network activity over time, results show women who were resistant to SIT processed SIT information using semantic memory vs. automatic episodic memory processes. These processes were operationalized by increased connectivity within the semantic and episodic memory networks using graph theory. Results suggest that when women use more episodic memory processes to encode SIT information, they demonstrate typical SIT behavior patterns over time. In contrast, women who utilize more semantic processing demonstrated increased domain value, self-enhancement, and positive autobiographical STEM memories one week later, reversing the effects of SIT. Results provide insight into how episodic and semantic processes in SIT contexts have important effects on the downstream consequences of SIT, those susceptible to SIT may thrive in these domains by biasing memories using more semantic processes.

2. Processing self-relevant stimuli and consequences for performance

Robert Backer* and Chad E. Forbes
Department of Psychological and Brain Sciences, University of Delaware, Newark, DE

Recent work has demonstrated that self-relevant stimuli are prioritized in our perceptual and cognitive processes, contributing to important downstream behaviors. In social encounters, impressions of similarity are formed on the order of milliseconds, which bias depth of processing, empathy, and consequent decision-making. Research on public service campaigns demonstrates that greater responsiveness from neural areas related to the self predicts motivation to act based on viewing an ad. Too much self-related processing can be counterproductive, as observed in the case of addictive self-disclosure on social media. However, the nature of the relationship between self-relevant stimuli and practical performance remains less clearly understood. This study will examine the relationship of self-relevancy in stimuli with performance outcomes, exploring markers of successful performance derived from EEG measurement of whole-brain activity during problem-solving. We will make use of a modified version of an “n-back” task, wherein subjects must remember as much as possible from scenes of various compositions of objects “n” scenes prior to a current scene. Prior to the task, subjects rate objects on personal relevancy. In a within-subjects, counterbalanced design, subjects will participate in two versions of the n-back task—one without explicit instruction to focus on any particular stimuli, and the other with instruction to pay special attention to objects of less rated relevance. Eye-tracking data will also be collected, for examination of where subjects allocate attention for each scene. Taking a data-driven approach, we will explore neural network states (i.e. statistically significant whole-brain connectivity between regions) that predict performance when self-relevance is high versus low, across tasks without explicit instruction versus those that instruct participants to attend to less self-relevant stimuli. This study will advance our understanding in two ways: First, by collecting EEG data during the n-back tasks, we will be able to assay neural markers that inform how self-relevance influences cognitive processing in a more realistic, temporally-sensitive manner. Second, by examining the effects of self-relevancy in facilitative or detracting, goal-specific scenarios, we will be able to better distinguish how this variable may help or hinder based on contextual demands.
3. Characterization of cellular correlates of spatial navigation in the TgF344-AD rat model of Alzheimer’s disease
Laura E. Berkowitz, Ryan H. Harvey, and Benjamin J. Clark
Department of Psychology, University of New Mexico, Albuquerque, NM
Spatial navigation and memory are impaired in early stages of Alzheimer’s disease (AD), and may be a defining behavioral marker of preclinical AD. The TgF344-AD rat model of AD expresses the full spectrum of AD pathology found in humans and may serve as a better rodent model for elucidating the underlying mechanisms of AD-related spatial memory impairment. Pathological markers of AD emerge in the hippocampus as early as 6 months of age and progressively increase during aging. Behavioral studies have identified that these rats exhibit less precise swim paths to an escape platform in the Morris Water task at 10 months and have selective deficits with object-place paired associations from 12 months. Similar behavioral profiles have been identified in lesion studies of the hippocampus or anterior thalamus indicating that pathology in TgF344-AD rats may be disrupting cells involved in spatial navigation and memory. This study aimed to characterize spatial cells types in the hippocampus, anterior thalamus, and presubiculum of 11-12 months female TgF344-AD (n=6) and Fischer 344 (n=6) controls while animals foraged for cereal in a cylindrical environment. A maze cue was rotated in one session to assess whether spatial cells were aligned with the allocentric reference frame. Cells modulated by location, direction, and theta rhythm were identified in both groups. Preliminary assessment indicates that directionally modulated cells recorded from TgF344-AD rats are less stable within a session, although cue rotation was found to modulate these cells types in both groups. Overall, these results suggest subtle circuit level differences between TgF344-AD rats and controls which may underlie spatial navigation deficits.

4. Acetylcholinergic mechanisms of depressive-like behaviors induced by seasonally relevant reductions in active photoperiod
Zackary A. Cope1, Maria L. Lavadia2, Aniek J.M. Joosen3, Davide Dulcis1, Jared W. Young1,4
1Department of Psychiatry, School of Medicine, University of California San Diego 2University of California San Diego, La Jolla, CA 3Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands 4Research Service, VA San Diego Healthcare System, San Diego, CA
Seasonal variations in day length influence switching between moods in bipolar disorder (BD). Treatments maintaining stability of photoperiod support euthymia (Young and Dulcis, 2015). Pharmacological induced increase of acetylcholine (ACh) using physostigmine increases depressive-relevant behavior in mice, such immobility in the Forced Swim Test (FST, Mineur et al., 2013) and patients with BD (Janowsky et al. 1972). These studies were designed to test the hypothesis that ACh signaling, particularly in the hippocampus, is necessary for expression of depressive-like behaviors following exposure to a winter-like short-active photoperiod (SAP). Pretreatment of C57BL/6 mice with the AChesterase inhibitor physostigmine 30 min before FST increased immobility, which was blocked by muscarinic (scopolamine, SCOP, F(2,47)=5.3, p<0.01) and nicotinic (mecamylamine, MEC, F(2,53)=4.6, p<0.05) antagonists. In experiment 2, mice were housed in SAP (19H light : 5H dark) for 2 weeks before FST, when they received SCOP or MEC. SAP increased immobility in two cohorts (F(1,70)=6.5, p<0.05, F(1,143)=4.3, p<0.05). In cohort 1, 0.03 mg/kg SCOP reduced immobility irrespective of photoperiod (F(1,70)=6.9, p<0.05). As per our a priori hypotheses, this effect was driven by reduced immobility in the SAP (p<0.05), not in normal active photoperiod (NAP; 12:12) mice. In cohort 2, 0.56 mg/kg MEC slightly reduced immobility irrespective of photoperiod, but not significantly (F(1,143)=2.0, p=0.15). In combination, two ineffective doses of antagonist (0.3 mg/kg MEC, 0.01 mg/kg SCOP) additively decreased FST immobility (F(3,142)=3.0, p<0.05). Regionally specific viral expression of human AChesterase in the hippocampus reduced FST immobility selectively in
SAP exposed mice ($F_{1,78} = 11.13$, $p < 0.001$) indicating regional necessity of hippocampal ACh in the expression of SAP induced immobility. Patients with MD frequently present with anhedonia (insensitivity to reward) and hypersensitivity to punishment, which is reflected in poor correction of behavior following punishment. Mice receiving physostigmine before a probabilistic reversal learning task exhibited greater lose-shift behavior ($F_{2,38} = 6.2$, $p < 0.005$). It is clear then, that SA photoperiod induces depression-relevant behaviors via circuitry already implicated in MD (Mineur et al., 2013). Future efforts will focus on characterizing EEG biosignatures of reward and punishment encoding relevant to clinical presentation of depression.

5. Preclinical global electroencephalography and seizure characterization in a neuron-specific Ube3a overexpression model

Nycole A. Copping* and Jill L. Silverman
MIND Institute Brain Endowment for Autism Research Sciences, University of California, Davis

Maternally derived duplications or triplications of 15q11.2-q13 are one of the most common genetic variations associated with neurodevelopmental disorders and are detected in ~1-3% of cases. The ubiquitin-protein E3A ligase gene (UBE3A) located within the 15q11.2-q13 region codes for ubiquitin protein ligase (UBE3A). UBE3A is only maternally expressed in neurons but is biallelically expressed in all other cell types and has a variety of cellular and transcriptional functions. Overexpression of UBE3A has been theorized to cause symptoms observed in Dup15q Syndrome (Dup15q) including intellectual disability and epilepsy. Due to the high prevalence of seizures (~60%) in the Dup15q population EEG has been employed as a tool for biomarker detection, and clinical studies suggest increased beta power as an electrophysiological signature (Frohlich et al., 2016). Our objectives were to evaluate if adverse behavioral impairments or altered brain activity were detectable and/or attributable to the overexpression of Ube3a using a tailored battery to address cognitive impairment, seizure susceptibility, and EEG characterization. We also wanted to visualize if the relative beta power recapitulated that seen in the clinical population. To test the role of overexpression of Ube3a, we used our unique, conditional tTA/Ube3a−2 transgenic mouse that overexpresses Ube3a in excitatory neurons within the forebrain (Copping et al., 2017). At 8 weeks, mice were anesthetized and implanted with a wireless telemetry device designed to measure EEG and EMG in freely moving animals (DSI®). To capture global EEG, two biopotential leads were attached to surgical screws (1.0, 0.5, above dura and -1.0, -0.7, above dura). EMG activity was measured via two leads rooted in the trapezius muscles. One-week post-surgery subject EEG, EMG, and temperature were recorded for a 24-hour baseline, then seizures were induced using pentylenetetrazole, a chemoconvulsant that acts as a GABA antagonist. EEG analysis and seizure characterization were evaluated using Neuroscore software. In two separate, surgically naïve cohorts, cognitive deficits were assayed using a contextual and cued fear conditioning paradigm. Transgenic mice overexpressing Ube3a exhibited clear, robust contextual memory deficits and atypical EEG activity as well as recapitulated the clinical finding of increased beta power when compared to wildtype controls. Altogether, these findings provide critical data necessary to further investigate the possibility of a cross-species EEG biomarker and will be essential in subsequent studies investigating cognitive dysfunction and corollary EEG in rodent models of Dup15q. Supported by the UC Davis MIND Institute and NIH R01NS097808.
6. Evaluating translational neurophysiological measures to improve efficacy of preclinical therapeutic target discovery

David J. Gregg¹*, James F. Cavanagh²,³, Gregory Light⁴,⁵, Jared W. Young⁴,⁵ and Jonathan L. Brigman¹,³

¹Department of Neurosciences, University of New Mexico School of Medicine, Albuquerque, NM; ²Department of Psychology, University of New Mexico, Albuquerque, NM; ³Center for Brain Recovery and Repair, University of New Mexico Health Sciences Center, Albuquerque, NM; ⁴Department of Psychiatry, University of California, San Diego; ⁵Research Service, VA San Diego Healthcare System

Preclinical studies can provide many potential therapeutic targets for neuropsychiatric disorders. However, many such targets prove ineffective during clinical trials. The failure to convert preclinical findings into clinical treatments suggests that behavioral similarity without biomarkers demonstrating similar brain function is not sufficient. Using pharmacology and EEG-like behavioral recordings we assessed the translational validity of several cognitive tests measuring specific Research Domain Criteria (RDoC) which can be performed by both humans and mice. Amphetamine was given to both species during preliminary testing as a pharmacological validation of translatability between species. Male and female C57BL/6J mice were trained and assessed in a touch-screen based operant system. Once training criteria was reached, mice were fitted with dura-resting leads targeting mPFC, PPC and M1 with a ground centered over the cerebellum. During each recording session oscillatory activity was captured via a multichannel acquisition processor and assessed. Comparable data were obtained from healthy human participants using invasive EEG procedures. Increased accuracy as measured by hit rate for target stimuli was observed in both species following amphetamine administration. Analysis of activity during each rodent task found that oscillatory activity correlated strongly with that seen in EEG of healthy human volunteers tested on a reverse-translated variant of the rodent touch-screen task. Taken together, these data support the use of EEG-like recording to examine neurophysiological biomarkers in rodents and humans.

7. Spatial and temporal stability deficits in hippocampal place cells following moderate prenatal alcohol exposure

Ryan E. Harvey¹, Laura E. Berkowitz¹, Daniel D. Savage²,³, Derek A. Hamilton¹,³, Benjamin J. Clark¹,³

¹Department of Psychology, University of New Mexico, Albuquerque, NM; ²Department of Neurosciences, University of New Mexico School of Medicine, Albuquerque, NM; ³New Mexico Alcohol Research Center, Albuquerque NM

Spatial memory and navigation impairments are common following prenatal alcohol exposure (PAE) in humans and in animal models. Hippocampal neurons, some of which are highly modulated by environmental locations i.e. place cells, display significant synaptic and structural alterations after PAE. Each hippocampal place cell fires in a unique environmental location indicating that a large population of these cells covers the spatial layout of each environment encountered by the animal. It is currently unknown whether the spatial and temporal coding characteristics of hippocampal place cells are altered in PAE. Thus, we performed electrophysiological recordings from the hippocampus (CA1 and CA3) of adult male rats exposed to either moderate amounts of ethanol or saccharin prenatally. Hippocampal neural activity was monitored in two behavioral paradigms in which rats performed laps to each end of a narrow linear track (120 x 9cm) or while randomly foraging in a circular open field (76cm in dia). Each recording session on the track or in the cylinder was ~20 min in duration. Similar numbers of hippocampal place cells were identified in both PAE and saccharin exposed animals. However, place cells recorded in PAE animals exhibited larger field sizes in both the linear and circular environments. Further, place cells...
recorded in PAE animals on the linear track displayed inconsistent firing as they progressively ran laps and often took several laps on the linear track to initiate firing. In contrast, place cells from control animals displayed stable firing throughout all laps. Finally, place cells are known to change their spike timing in such a way that cells fire at progressively earlier phases of the extracellular theta rhythm as the animal passes through their respective place fields. This phenomenon is known as theta-phase precession, and is thought to be supported by medial entorhinal cortex input. Importantly, while place cells from PAE animals had deficits in stable firing, they did not show deficits in theta-phase precession relative to control place cells. Collectively, the broader tuning and instability of hippocampal place cells provides a potential mechanism to explain spatial memory impairment after PAE.

8. Temporal information guides prefrontal preparatory activity in cognitive control
Jacqueline R. Janowich* and James F. Cavanagh
Department of Psychology, University of New Mexico, Albuquerque, NM
Proactive preparation for an upcoming goal differs from last-minute reactive adaptation, but it is unclear how preparatory mechanisms change based on when in the future a goal needs to be executed. To assess how timing information is integrated into preparatory control, we designed a novel variant of the Dot Pattern Expectancy (DPX) task, where each cue signaled both task rule and delay duration (known short, known long, or unknown) between cue and probe. We recorded EEG while healthy young adult participants (n=36) performed this task, and found that delay demands elicited distinct prefrontal preparatory activities. Medial prefrontal amplitude was sensitive to delay knowledge and delay length. In addition, inter-site theta phase consistency between mid-frontal and right pre-frontal sites was strengthened for known short delays. These results show that different prefrontal preparatory control processes are elicited depending on goal timing demands, and highlight the need to consider timing dynamics in control preparation. Importantly, given that DPX has been performed successfully in non-human primates (Blackman et al., 2016), and that non-human species including rodents are capable of interval timing (Emmons et al., 2017; Kim et al., 2013), this paradigm has direct and immediate relevance for cross-species translational work.

9. Restoring timing of orbitofrontal neurons to decrease perseverative responding by prenatal alcohol exposed mice in a touchscreen-based visual reversal learning task.
Johnny A. Kenton1*, Kristin Marquardt1 and Jonathan L. Brigman1,2
1Department of Neurosciences, University of New Mexico School of Medicine, Albuquerque, NM, USA.
2New Mexico Alcohol Research Center, Albuquerque NM
Prenatal alcohol exposure (PAE) leads to deficits in executive function that persist into adulthood. Previously, we showed that moderate PAE (BAC: ~90mg/dL) in mice impairs behavioral flexibility by increasing perseverative responding on a touchscreen-based visual reversal learning task. In vivo electrophysiology recordings during behavior showed decreased inter-trial phase consistency during early reversal in the orbitofrontal cortex (OFC) after unexpected rewards in PAE mice. Additional ex vivo analysis indicated an increase in GABAergic output in the OFC of PAE mice. Here, we 1) used optogenetics to stimulate pyramidal neurons in the OFC following unexpected rewards to restore phase alignment and reduce perseveration in PAE mice and 2) examined the effect of PAE on populations of inhibitory interneurons. PAE and saccharine control (SAC) mice were trained, microinfused with channelrhodopsin- or EYFP-expressing adenovirus directly into the OFC, and implanted with recording optrodes targeting the OFC and dorsal striatum. PAE and SAC mice were given a reminder session followed by reversal. During a
highly perseverative period, PAE and SAC mice received 465nm, 5mW, 10Hz, 5ms pulses for 1 sec following a correct choice. Targeted stimulation during early reversal reduced perseveration in ChR2+ PAE mice compared to ChR2+ SAC and EYFP controls. Additionally, the number of somatostatin-positive inhibitory interneurons in the OFC of PAE mice was significantly increased compared to controls.

10. Auditory sensory gating and processing deficits following mild traumatic brain injury

*Jeffrey David Lewine, John Davis, Kim Paulson and Robert J. Thoma*
*The Mind Research Network, Albuquerque NM*

Following mild traumatic brain injury, some subjects complain of persistent auditory processing problems, such as difficulties tracking conversations in noisy environments (e.g., restaurants). To better understand the relevant neurobiology, a paired-tone auditory evoked response paradigm was used to examine basic auditory processing, rapid auditory processing, and sensory-gating in 70 normal control subjects and 60 patients with persistent (>6 months) post-concussive symptoms following a mild traumatic brain injury. No significant differences were seen between the control and mTBI groups on measures of basic auditory processing or rapid auditory processing. For sensory gating, the average gating ratio for control subjects was 0.38. In contrast, the average gating ratio for TBI subjects was 0.64. A high gating ratio indicates a failure in the normal suppression/gating of brain activity evoked by the second redundant stimulus in a pair of rapidly presented identical stimuli. This difference was highly significant, F(1,129)=84.32, p<0.001. Using a cutoff gating ratio of 0.05, 84% of all subjects were correctly classified as coming from control versus TBI groups. Thirty-four of the TBI patients also completed the SCAN-III, a behavioral evaluation of central auditory processing abilities. The correlation between the sensory gating ratio and SCAN-III score was -0.76, an indication that gating impairments (high S2/S1 ratios) were associated with poor auditory processing abilities. The data demonstrate that mild traumatic brain injury is associated with correlated deficits in central auditory processing as measured by both behavioral and electrophysiological methods.

11. Role of perineuronal nets in the medial prefrontal cortex during fear extinction and reinstatement after adolescent intermittent ethanol exposure

*Kristin Marquardt*, Justin T. Gass and L. Judson Chandler
*Medical University of South Carolina, Alcohol Research Center, Charleston, SC*

Adolescent alcohol use is thought to uniquely prime reward learning and alcohol-cue conditioning systems, contributing to an elevated risk for development an alcohol use disorder in adulthood. Conditioned cue-associations can be modeled in rodents utilizing a fear conditioning paradigm in which a mild foot shock is paired with a tone, the conditioned cue. During extinction, new learning occurs that the tone no longer predicts a shock. This learning is mediated by an infralimbic (IfL) prefrontal cortex and basolateral amygdala circuit. We have shown that adult rats exposed to intermittent ethanol during adolescence (AIE) have slowed extinction learning and impaired recall of the extinction memory. Intriguingly, extinction learning is enhanced when the specialized extracellular matrix, perineuronal nets (PNN) are disrupted in the amygdala. PNNs form preferentially around parvalbumin positive fast-spiking interneurons (PV+) during adolescence in the prefrontal cortex (PFC), including the IfL, making developing PNNs a vulnerable target during AIE. Additionally, studies show PNN density is increased after chronic exposure to alcohol in adulthood. We hypothesize that impairment of fear extinction learning and recall in male rats after adolescent alcohol exposure is mediated by increases in PNN density in the IfL cortex. Beginning on postnatal day 28, adolescent rats underwent five cycles of intermittent ethanol vapor
chamber exposure. Each cycle consisted of two consecutive 24-hour sessions: 14-hour vapor chamber exposure, followed by 10-hours out of the chamber, resulting in an average blood ethanol concentration of 250 mg/dl at the end of each cycle. Data suggest that AIE increases PNN density in the medial prefrontal cortex 7 days following the last cycle, and that this increase persists into adulthood at postnatal day 70. Furthermore, our data show that fear extinction learning increases PNN density in the IFL, and that disruption of PNN in the IFL by chondroitinase ABC impacts extinction learning and later extinction retention. Current experiments are using fiber photometry and bipolar single electrode intracranial electrophysiology to determine how PNN density increases after AIE impact PV+ and pyramidal signaling during fear extinction and recall. We believe these experiments will provide meaningful insight into the mechanisms of adolescent ethanol exposure that may lead to later alcohol misuse, and inform the development of efficacious treatments. Work was funded through NIAAA T32 AA007474.

12. Prenatal alcohol exposure increases responding to non-target stimuli in a sex dependent manner using a touch screen continuous performance task

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Attention is the ability to concentrate on a specific task and ignore distractions. This is impaired in a number of neuropsychiatric disorders including schizophrenia, attention deficit hyperactive disorder, fetal alcohol spectrum disorders and some addiction models. A clinical measure of attention, vigilance, and inhibition in humans is called the Continuous Performance Task (CPT) in which a person must respond to a single visual stimulus and ignore multiple stimuli. CPT has been previously adapted to an operant chamber for mice, while we have adapted this task to a touchscreen system that is more akin to an iPad which allows for better clinical modeling. Here, we obtained mice from the New Mexico Alcohol Research Center that were prenatally exposed to ethanol (PAE) via a drinking-in-the-dark model (10% sweetened EtOH available 4 hours/day, throughout gestation; BAC: ~90mg/dL; controls=0.066% sweetened water, “SAC”). In our task mice first train to touch a single stimuli that appears pseudorandomly in one of 5 available windows (“go” trial). Once they were able to respond quickly and accurately we introduce hold trials in which all 5 squares were illuminated and the mice must withhold responding in order to be rewarded. Two ratios of “go” to “hold” trials were used to assess attention, vigilance, and inhibition: 2:1 and 5:1. All mice were able to perform the single stimuli stage equally regardless of sex or treatment. With the addition of hold trials, male and female PAE mice made significantly increased false alarms (responses to non-target stimuli) on hold trials versus controls. Compared to SAC, female PAE had a significantly lower sensitivity index, indicating they responded more often to non-target stimuli than target stimuli while the male PAE and SAC mice both demonstrated a negative sensitivity index, indicating they were more likely to respond to non-target, versus target, stimuli. A preliminary cohort of animals were implanted with dura-resting screws for EEG-like recording during the 5:1 ratio of the CPT. Since we see a decrease in attention and response inhibition in the PAE exposed animals we expect to see a decrease in theta (4-10Hz) oscillatory signaling in the medial prefrontal cortex during target trials as well as loss of parietal beta (13-25Hz) power during non-target trials. Our findings suggest that moderate exposure to alcohol during development can have long lasting effects on attention, vigilance, and inhibition.
13. Effect of peripheral vibrotactile stimulation on cortical sensory activity in stroke survivors

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Peripheral sensory stimulation has been used as a method to facilitate sensorimotor recovery in neurologic patients such as those who had a stroke. To improve delivery modality and usability, a new stimulation method has been developed in which imperceptible random-frequency vibration is applied to the wrist concurrently during hand activity. The objective of this study was to investigate the effect of this new sensory stimulation on sensory processing of fingertip touch in stroke survivors. Chronic stroke survivors were tested. Somatosensory evoked potentials resulting from a fingertip touch were recorded using electroencephalogram (EEG), while the wrist stimulation was on or off in a random order. The EEG data were analyzed using CURRY 8 (Compumedics). For source localization, brain MRI was obtained for individual stroke subjects without contraindications to MRI. Preliminary results of this work are presented. This project was supported by funding from NIH/NIGMS P20GM109040 COBRE for Stroke Recovery (PI: Kautz) and NIH/NIGMS U54-GM104941 (PI: Binder-Macleod).

14. What is the neural basis of memory impairment after prenatal alcohol exposure? Insight from tests of object-place and discrimination of perceptually similar objects

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Memory impairments, including spatial and object processing, are often observed in individuals with Fetal Alcohol Spectrum Disorders. The neurobiological basis of memory deficits after prenatal alcohol exposure (PAE) is often linked to structural and functional alterations in the medial temporal lobe, including the hippocampus. Recent evidence suggests that the medial temporal lobe plays a critical role in processing high-order sensory stimuli such as complex objects and their associated locations in space. In the present study, we tested rat offspring with moderate PAE in a medial temporal-dependent object-place paired-associate (OPPA) task. The OPPA task requires a conditional discrimination between an identical pair of objects presented at two spatial locations 180° opposite arms of a radial arm maze. Food reinforcement is contingent upon selecting the correct object of the pair for a given spatial location. Adult rats were given a total of 10 trials per day over 14 consecutive days of training. PAE rats made significantly more errors than saccharin (SACC) control rats during acquisition of the OPPA task. In Experiment 2, rats performed an object-discrimination task in which a pair of objects were presented in a single arm of the maze. Moderate PAE and SACC control rats again exhibited comparable performance. In Experiment 3, we tested animals in a more challenging object discrimination task in which the degree of feature overlap between the object pairs was systematically increased. Moderate PAE and SACC control rats again exhibited comparable performance. In Experiment 4, rats were tested over 10 days in a spatial reference memory variant radial arm maze task and determined that PAE animals made greater errors across training. Collectively these results point to PAE induced impairments in spatial processing but also when associating specific items within a spatial framework. The results of this study will be discussed in relation to the hippocampal-parahippocampal basis of object and place discrimination learning and the effects of moderate prenatal ethanol on this neural representations and oscillatory signals within this circuitry.
15. Midfrontal theta activity is reduced during cognitive control in Parkinson’s disease
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Mid-frontal theta activity (4-8 Hz) underlies cognitive control. These 4-8 Hz rhythms are modulated by cortical dopamine and can be abnormal in patients with Parkinson’s disease (PD). However, the role of mid-frontal theta deficits in PD during a task explicitly involving cognitive control has not been investigated. Here, we collected scalp EEG from high-performing PD patients (n=28) and demographically matched controls (n=28) during performance of a modified Simon reaction-time task. This task involves cognitive control to adjudicate response conflict and error-related adjustments. Task performance of PD patients was indistinguishable from controls, but PD patients had less mid-frontal theta modulations around cues and responses. Critically, PD patients had attenuated mid-frontal theta activity specifically associated with response conflict and post-error processing. These signals were unaffected by medication or motor scores. Post-error mid-frontal theta activity was correlated with disease duration. Classification of control vs. PD from these data resulted in a specificity of 69% and a sensitivity of 72%. These findings help define the scope of mid-frontal theta aberrations during cognitive control in PD, and may provide insight into the nature of PD-related cognitive dysfunction. Supported by NIGMS 1P20GM109089-01A1.

16. Reporting perceived direction: Motion estimation in human and non-human primates
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In what ways does active behavior shape visual perception? How do perceptual systems extract task-related information from sensory data to ultimately achieve a goal or action? What are the physiological properties of the perceptually relevant neurons that compute the percepts guiding such decision-making? Motion is a unique perceptual attribute that offers the opportunity to study information processing from sensation to action. More than 90% of neurons in the middle temporal visual area (MT) are direction-selective neurons, but the relationship between the neural response and the visual perception of motion is unclear. This study compares marmoset—New World monkey—performance to human behavior in the identical estimation task. This task required subjects to estimate the direction of motion of a dot field by making a saccade to an outer ring in the perceived direction of the stimulus. Both marmoset and human choices reflect a pooling of direction signals. This study concludes that marmoset direction-estimation sensitivity is similar to human performance on estimation tasks and that both human and non-human primate exhibit a systematic bias; the subjects’ implicit bias increases as the signal strength is reduced. Further directions of this research include electrophysiology paradigms and modeling the contextual biases involved in motion processing.

17. Sucrose rewards elicit distinct cue encoding patterns compared to brain stimulation reward
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Reward processing provides information regarding the outcomes of behavior by integrating the expected utility of an action with its outcome. Dysfunctional reward processing can lead to obesity or psychiatric diseases such as anorexia and addiction. Thus, it is critical that we understand the neurobiological systems
that are responsible for this essential cognitive domain. Much of our understanding of reward processing has been derived from studies relying on food as a reinforcer. However, food rewards recruit complex neural systems responsible for taste reactivity, energy homeostasis, and satiety, in addition to reward processing. Thus, determining what neural circuits are critical for the processing of food rewards is challenging. Unlike food rewards, brain stimulation reward (BSR) provides direct electrical stimulation to discrete areas of the mesocorticolimbic reward circuit in a controllable manner. To aid in our understanding of the neural systems responsible for the complex encoding of food rewards, we examined how food rewards activate neural circuitry differently than (BSR), which is free of sensory processes, is more temporally precise, and activates only selected neural circuits. We compared encoding of BSR and food-reward on one critical aspect of reward processing: reward-predictive cue encoding. Combining a classical conditioning paradigm with in vivo electrophysiological recordings, we determined how the encoding of food-predictive cues in the nucleus accumbens (NAc) is biased by non-reward processes (which BSR is free of). Following recording, all animals performed behavioral tests to determine reward sensitivity and match subjective reward magnitudes across reward types. We compared the timescale and intensity of food-evoked cue encoding to BSR, and found that food rewards produce less intense, yet longer-acting neural activity in the NAc than BSR. Such results suggests that food rewards activate neural circuitry for a briefer and less powerful manner than BSR, highlighting how the complex neural encoding of foods may bias reward encoding. These findings shed light on the basic neurobiology controlling both food reward and BSR, which are widely used in reinforcement research.

18. The time course of race and status-based person perception

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Humans are often social experts. Within fractions of a second of encountering another, we can identify, make inferences, and decide how to act towards others. These decisions are deeply rooted in a very early, automatic process: categorization. Previous work has explored attentional and evaluative differences in event related potentials (ERP’s) related to race and status perception; however, none have examined ERP’s related to both variables simultaneously. This pre-registered investigation (n=60) will examine P200s, N200s, and P300s during a categorization task. Participants will view face primes that vary in race and social status. Participants will be initially trained to associate social status with a colored background superimposed on the face image. Following the presentation of the face stimuli, participants will be asked to categorize the face by either race (black or white) or by status (high or low). We hypothesize larger P200’s for high-status Black faces and larger N200’s for high-status White faces. We also anticipate finding greater P300’s for low-status Black faces. Additionally, we expect to observe the fastest response times to high-status Black faces. The implications of this examination will be discussed.

19. It’s about time: Electrophysiological evidence for temporally mediated consolidation of spatial memories

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Formation and retrieval of new spatial information is highly dependent on the hippocampus (HC), but over time these memories become increasingly reliant on other areas, including the anterior cingulate cortex.
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(ACC). We hypothesized that if this were the case then the retrieval of older spatial memories would engender different interactions between the HC and ACC than more recent memories would. Specifically, there should be changes in synchrony between these two areas and the direction of the interactions should shift from the HC leading for recent memories to the ACC leading for more remote retrieval. To assess this, we recorded both single units and local field potentials from the ACC and HC as animals were exposed to unique spatial environments and then re-exposed to those same environments at differing time delays (1-14 days). Behavioral data revealed a significant decrease in exploration-related movement as early as the second exposure regardless of the delay period, indicating that the animals quickly became familiar with the environments. We found that neural synchrony between the ACC and HC was significantly stronger on the remote retrieval days, despite no discernible behavioral differences from recent retrieval days. These effects were found in theta and gamma band coherence, phase synchrony, and ACC unit phase locking to HC theta. Time-lag correlation analysis revealed that while on days 1-7 HC theta activity led the ACC, on day 14 this effect reversed and theta in the ACC now led the HC. Additionally, there were no significant changes in ACC-HC synchrony until 14-days after initial exposure regardless of the number of previous experiences, supporting the conclusion that the operative variable affecting these interactions was the passage of time. We also observed increases in bilateral ACC synchrony on day 14, which may be indicative of an ACC mediated retrieval of remote memories. These results reveal a clear electrophysiological signature of spatial memory consolidation to the ACC.

20. Loss of psychiatric disease-related circRNA impairs reward-tracking behavior and reduces executive control.
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Schizophrenia (SCZ) and Bipolar Disorder (BD) are debilitating psychiatric disorders marked by impairments in learning and memory as well as executive control. Among the most disruptive behavioral impairment associated with these disorders is the inability to behave flexibly in response to changing environmental stimuli. Lesion studies in rodents and non-human primates have demonstrated that loss of function in the frontal cortical regions, specifically the orbitofrontal cortex (OFC), underlies the loss of executive control on specific tasks that require an individual to behave flexibly in response to changing contingencies. NMDA receptor function and postsynaptic density organization have been posited to be critical to the mechanism underlying alterations in synaptic plasticity related to learning and memory impairments and loss of executive function. In a clinically relevant rodent touch screen task, we demonstrate the loss of a plasticity-related circular RNA, circhomer1, impairs mice on a discrimination-reversal task, which is a measure of behavioral flexibility. Through neuronal recordings, we have found the loss of circhomer1 leads to increased neuronal excitability and impaired ability to update behavior when reward contingencies change in chance-to-late-stage reversal learning. The switch from the early (perseverative) reversal stage to the above-chance (learning) reversal stage requires changes in neuronal spike firing and spike-field coupling. Neurons in the OFC must switch tracking of error trials in early reversal to track rewarded trials during late reversal in order to properly update reward valuation and behavioral response. We hypothesize that reduced spike-field coupling to local field potentials during the chance stage of reversal could contribute to the impairment in the ability to properly switch from error-tracking to reward-tracking, which results in slowed learning during late-stage reversal.