Pavlovian Society

Pavlovian Society Annual Meeting

Hyatt Regency Jersey City

September 20 – 23, 2012

September 20, 2012

Welcome to the 2012 meeting of the Pavlovian Society. In addition to a great meeting we hope you enjoy both Jersey City and nearby New York City. You will find information about transportation and local restaurants right after the program.

A big thank-you goes to Barnard College for supporting the meeting and to Beatrice Ward for handling the local arrangements. Nicholas Balderston was the superb webmaster that allowed us to have the electronic submission system. It was amazing easy to use. We are very grateful to Jersey City resident Meghan Caulfield for assembling the information about local places of interest and to Patricia Kabitzke and Kathleen Taylor for their assistance with the program.

We are also trying to connect employers in our fields with potential applicants. If you or your department is looking to hire a faculty member, post-doc or technician please post the job listing on Poster 100 and be sure to leave contact information.

Enjoy good science, good food and good conversation.

Peter Balsam

President, Pavlovian Society

SCHEDULE

Thursday

Riverside Room

6:00 PM	Welcome Reception - Cash Bar & Music	

Friday

Hudson I, II, III

8:25 AM	WELCOME	Peter Balsam
8:30 AM	Address: Adventures in the Neurobiology of Trace Conditioning	Fred Helmstetter
9:20 AM	Magazine approach during a signal for food depends on Pavlovian, not instrumental, conditioning	Justin Harris
9:40 AM	Different kinds of savings and an analysis of their mechanisms	Michael Mauk
10:00 AM	Break	
Symposium	*Stabilization of Memory*	
10:10 AM	The dynamic of memory storage: Mechanisms and the passage of time	Christina Alberini
10:35 AM	Enhancing, erasing, and tracing long-term memories by targeting PKMζ	Todd Saktor
11:00 AM	Inhibiting PKMζ reveals dorsal lateral and dorsal medial striatum store the different memories needed to support adaptive behavior	Wolfgang Pauli
11:25 AM	Synaptic and morphological consequences of memory erasure and of memory reconsolidation failure in Aplysia	David Glanzman
12:00 PM	Lunch	
Symposium	*Stress, Anxiety and Fear Conditioning*	
1:15 PM	Acute SSRI treatment enhances fear conditioning: a role for the extended amygdala	Elizabeth Bauer
1:40 PM	Learning not to fear: Implications to PTSD and beyond	Mohammed Milad
2:05 PM	Thinking outside the "HPA Box": New targets for preventing stress-related enhancement of fear	Ki Ann Goosens
2:30 PM	US devaluation effects in flavor preference conditioning: Potential neural substrates	Andrew Delamater
2:55 PM	Break	
3:05 PM	Address: What does Pavlovian fear conditioning condition?	Joseph LeDoux
3:55 PM	Nucleus accumbens involvement in Pavlovian approach	Jon Horvitz
4:15 PM	The effect of stimulus duration distribution form on the acquisition and rate of conditioned responding	Charlotte Bonardi
4:35 PM	How associative mechanisms in the hippocampus guide decisions: Evidence from sensory preconditioning in humans	Daphna Shohamy
5:00 PM	Posters and Cash Bar (2 hours - Hudson & Palisades Ballrooms)	

Saturday

Hudson I, II, III

8:40 AM	On the superiority of females: Evidence from appetitive conditioning	Susan Swithers
9:00 AM	Address: Structural plasticity and cognitive function	Elizabeth Gould
9:50 AM	Break	
Symposium	*Development of Eyelid conditioning*	
10:00 AM	Developmental changes in forebrain modulation of cerebellar learning	John Freeman
10:25 AM	Eyelid conditioning during sleep in newborn Infants: Behavioral and EEG measures of learning	William Fifer
10:50 AM	Applications of eyeblink conditioning to developmental neurobehavioral disorders	Mark Stanton
11:15 AM	Analyzing the role of adult-born hippocampal neurons in “pattern separation” using touch screen operant conditioning	Michael Drew
11:35 AM	Fear conditioning selectively and associatively alters the representation of sensory stimuli in primary sensory neurons in vivo	John McGann
11:55 AM	Lunch *Satellite activity:* Women in Learning Lunch	
Symposium	*Extinction and Fear Memory Updating*	
1:30 PM	Effects of extinction trial spacing and retrieval - extinction manipulations on renewal of extinguished alcohol seeking	Gavan McNally
1:55 PM	A computational perspective on erasing fear	Sam Gershman
2:20 PM	Exploration of factors that promote or hinder fear memory updating	Marie Monfils
2:45 PM	Associative Bases of Causal Learning in Rats	Ralph Miller
3:10 PM	Break	
3:20 PM	Address: Mice take calculated risks	Randy Gallistel
4:10 PM	Climbing fibers encode information about the strength of an airpuff UCS at the single-cell and population levels	Javier Medina
4:30 PM	Inhibitory after all: Contexts do become inhibitory during extinction	Gunes Kutlu
4:50 PM	Olfactory discrimination of oxygen based explosives and propellants by rats	Kimberly Kirkpatrick
5:10 PM	Posters and Cash Bar (2 hours - Hudson & Palisades Ballrooms)	

Hudson IV, V, VI

6:30 PM	Banquet & Speaker: Evolution of a new language	Ann Senghas

Sunday

Satellite meeting of Society for Computational Modeling of Associative Learning

Talk Abstracts

Friday, 8:30. Adventures in the Neurobiology of Trace Conditioning.

Helmstetter, F.J.
University of Wisconsin - Milwaukee

I will review a series of recent studies from our lab using trace fear conditioning (TFC) in rodents and human volunteers. Since TFC requires more than the "essential" neural circuit sufficient for standard delay conditioning it provides some excellent opportunities for understanding cortical-subcortical interactions during memory formation and retrieval. One focus has been on understanding the relative roles of the amygdala, hippocampus, and prefrontal cortex in forming the TFC memory. Recent work has suggested that training with a trace interval may fundamentally change the way information in encoded and stored at the circuit level. The presentation will include data from gene expression, pharmacological manipulation, and non-invasive imaging (fMRI, MEG) studies.

Friday, 9:20. Magazine approach during a signal for food depends on Pavlovian, not instrumental, conditioning.

Harris, J.A., Andrew, B.J., Kwok, D.W.S.
University of Sydney, School of Psychology

In the conditioned magazine approach paradigm, rats are exposed to a contingent relationship between a conditioned stimulus (CS) and the delivery of food (the unconditioned stimulus, US). As the rats learn the CS-US association, they make frequent anticipatory head entries into the food magazine (the conditioned response, CR) during the CS. Conventionally, this is considered to be a Pavlovian paradigm because food is contingent on the CS and not on the performance of CRs during the CS. However, because magazine entries during the CS are reliably followed by food, the increase in frequency of those responses may involve adventitious ("superstitious") instrumental conditioning. The existing evidence, from experiments using an omission schedule to eliminate the possibility of instrumental conditioning (Farwell & Ayres, 1979; Holland, 1979), is ambiguous: rats acquire magazine CRs despite the omission schedule, demonstrating that the response does not depend on instrumental conditioning, but the response rate is greatly depressed compared with that of rats trained on a yoked schedule, consistent with a contribution from instrumental conditioning under normal (non-omission) schedules. Here we describe experiments in which rats were trained on feature-positive or feature-negative type discriminations between trials that were reinforced on an omission schedule versus trials reinforced on a yoked schedule. The experiments show that the difference in responding between omission and yoked schedules is due to suppression of responding under the omission schedule rather than an elevation of responding under the yoked schedule. We conclude that magazine responses during the CS are largely or entirely Pavlovian CRs.

Friday, 9:40. Different kinds of savings and an analysis of their mechanisms.

Mauk, M.D.
The University of Texas at Austin, Center for Learning and Memory

Members of the Pavlovian society are familiar with the concept of savings. Eyelid conditioning demonstrates that savings is not a unitary phenomenon. In addition to the essential observation that relearning after extinction is faster than original learning (same-CS savings), eyelid conditioning displays i) different-CS savings where relearning is faster even when a new CS is used, ii) savings of timing where changing the inter-stimulus interval for relearning reveals that early responses during relearning show the original timing, and iii) savings of amplitude where responses during relearning jump immediately to the previous amplitude rather than increasing monotonically over several dozen trials as seen in original learning. We showed previously that same-CS savings is mediated by residual plasticity in the cerebellar deep nuclei that is not reversed by extinction. Since this plasticity is stimulus-specific, different CS savings presents a problem. Two observations demonstrate that different-CS savings involves the same-CS savings mechanism and a contribution from an input arising from prefrontal cortex. 1) Learning supported by mossy fiber stimulation as the CS shows same-CS but not different-CS savings, and 2) animals with lesions in medial prefrontal cortex also show normal same-CS, but impaired different-CS, savings. Preliminary experiments and computer simulations suggest that the same interactions underlie savings of timing. Ongoing studies are focused on whether savings of amplitude can be explained by the same interactions between prefrontal cortex and cerebellum. Early indications suggest that savings of amplitude may instead be mediated by mechanisms within the cerebellum.

Friday, 10:10. The dynamic memory storage: mechanisms and the passage of time.

Alberini, C.
New York University, Center for Neural Science

To become stored as a long-term memory newly learned information, which is in a labile state, undergoes a number of changes that make its trace (or engram) resilient to disruption. This process is defined as memory consolidation. Retrieval or reactivation of an apparently consolidated memory can render the memory labile again; this memory undergoes another process of stabilization, known as memory reconsolidation. Why does memory become labile after retrieval and reconsolidate? What is the contribution of the passage of time to memory consolidation and reconsolidation? Using inhibitory avoidance (IA) learning in rats, my laboratory is studying the mechanisms and functions of memory reconsolidation and how they evolve over time. We will discuss the dynamic nature of memory storage and how understanding these questions is important for potential clinical applications.

Friday,10:35. Enhancing, erasing, and tracing long-term memories by targeting PKMζ.

Sacktor, T.C.
SUNY Downstate Medical Center, Physiology, Pharmacology, and Neurology

Most molecular targets for manipulating memory focus on the signaling events that initiate memory formation during the brief time window of memory consolidation, or following the reactivation of memory, during reconsolidation. Targets for maintaining the long-term memory trace after consolidation have been largely unknown. Recently, however, the persistently active atypical PKC isoform, PKMζ, has been identified as a potential component of the molecular mechanism maintaining the long-term memory trace. Pharmacological or genetic inhibition decreasing PKMζ activity disrupts both new and established long-term memories, whereas increasing PKMζ enhances both new and established memories. Localizing the increases of PKMζ within specific circuits of the brain days to weeks after memory consolidation gives the first indication of how the physical trace of long-term memories are stored and can be erased and enhanced.

Friday, 11:00. Inhibiting PKMζ reveals dorsal lateral and dorsal medial striatum store the different memories needed to support adaptive behavior.

Pauli, W.M., Clark, A.D., Guenther, H.J., O'Reilly, R.C., Rudy, J.W.
University of Colorado, Psychology and Neuroscience

Evidence suggests that two regions of the striatum contribute differential support to instrumental response selection. The dorsomedial striatum (DMS) is thought to support expectancy-mediated actions, and the dorsolateral striatum (DLS) is thought to support habits. Currently it is unclear whether these regions store task-relevant information or just coordinate the learning and retention of these solutions by other brain regions. To address this issue, we developed a two-lever concurrent variable-interval reinforcement operant conditioning task and used it to assess the trained rat's sensitivity to contingency shifts. Consistent with the view that these two regions make different contributions to actions and habits, injecting the NMDA antagonist DL-AP5 into the DMS just prior to the shift impaired the rat's performance but enhanced performance when injected into the DLS. To determine if these regions support memory content, we first trained rats on a biased concurrent schedule (Lever 1: VI 40″ and Lever 2: VI 10″). With the intent of "erasing" the memory content stored in striatum, after this training we inhibited the putative memory-maintenance protein kinase C isozyme protein kinase Mζ (PKMζ). Infusing zeta inhibitory peptide (ZIP) into the DLS enhanced the rat's ability to adapt to the contingency shift 2 d later, whereas injecting it into the DMS had the opposite effect. Infusing GluR23Y into the DMS 1 h before ZIP infusions prevented ZIP from impairing the rat's sensitivity to the contingency shift. These results support the hypothesis that the DMS stores information needed to support actions and the DLS stores information needed to support habits.

Friday, 11:25. Synaptic and morphological effects of memory erasure and of memory reconsolidation failure in Aplysia.

Glanzman, D.L.[1, 2, 3, 4], Cai, D.[1], Chen, S.[1], Sun, P.[1], Pearce, K.[1], Roberts, A.C.[1]
[1]*University of California Los Angeles, Integrative Biology and Physiology*
[2]*David Geffen School of Medicine at UCLA, Neurobiology*
[3]*David Geffen School of Medicine at UCLA, Brain Research Institute*
[4]*University of California Los Angeles, Integrative Center for Learning and Memory*

Significant evidence indicates that even well consolidated memories can be rendered labile. A prominent example of the lability of memory is the disruptive effect of inhibiting protein kinase M (PKM), the catalytic fragment of atypical protein kinase C (PKC). For example, inhibition of PKM Apl III, the Aplysia homolog of mammalian PKMzeta, appears to erase the memory for long-term sensitization (LTS) in Aplysia (Cai et al. J. Neurosci. 2011). Furthermore, inhibition of PKM Apl III also disrupts the "memory" for the synaptic change that underlies LTS, long-term facilitation (LTF) of the sensorimotor synapse.
Another example of memory instability is the effect of reactivating a long-term memory. Specifically, reactivation of a memory can cause it to undergo additional consolidation (reconsolidation); during reconsolidation the memory is subject to removal by inhibition of protein synthesis. We found that reactivating the memory for LTS in intact Aplysia destabilizes the memory, as indicated by its susceptibility to disruption by treatment with a protein synthesis inhibitor (anisomycin; Cai et al. Curr. Biol. 2012). Reactivation of the synaptic memory involved in LTS, LTF, similarly subjects it to elimination by anisomycin.
An important question is whether memory erasure by inhibition of PKM, or by disruption of memory reconsolidation, involves the actual reversal of the physical changes that underlie long-term memory; or whether these two types of memory disruption represent retrieval failures. Accordingly, we examined changes in the morphological structure of sensorimotor synapses in vitro during memory erasure and disruption of memory reconsolidation using laser scanning confocal microscopy. LTF of sensorimotor synapses in dissociated cell culture involves the growth of additional presynaptic varicosities on the neurites of sensory neurons (Glanzman et al. Science 1990). Both inhibition of PKM Apl III, and disruption of synaptic reconsolidation by a reminder plus anisomycin, reversed this morphological change.

Friday, 1:15. Acute SSRI treatment enhances fear conditioning: a role for the extended amygdala.

Bauer, E.
Barnard College, Department of Biology

The bed nucleus of the stria terminalis (BNST), part of the extended amygdala, is known to mediate non-specific "anxiety-like" sustained fear responses. Its activity can also modulate subtle aspects of Pavlovian fear conditioning, such as stimulus-specificity and contextual fear. I will discuss this research as well as recent findings implicating the BNST in the acute effects of SSRIs on fear conditioning. Acute systemic administration of SSRIs potentiates anxiety and conditioned fear learning, but little is known about how specific amygdalar circuits contribute to these effects. When

fear conditioning was coupled with SSRI treatment we found enhanced expression of the immediate early gene Arc, a marker of cellular activity/plasticity, in several amygdala regions. Local infusions of fluoxetine into the BNST mimicked systemic injections by potentiating fear conditioning as well as Arc expression. These results highlight the need to look at the contributions of the extended amygdala in gating anxiety and learned fear.

Friday, 1:40. Learning not to fear: implications to PTSD and beyond.

Milad[1], M.
[1]*Massachusetts General Hospital, Harvard University*

In the past two decades, we have witnessed significant advances in understanding the neural correlates of fear learning and its subsequent inhibition in rodents. This knowledge is rapidly translated into the human brain using contemporary neuroimaging tools. In my talk, I will discuss some of the most recent findings in the domain of fear extinction in the human brain, and how such findings are translated to the psychopathology of posttraumatic stress disorder and other psychiatric disorders. In addition, I will present some recently published and unpublished data illustrating our efforts on 1) developing biological markers to predict fear learning, and 2) recent findings that could help enhance our understanding of why men and women may differ in the prevalence of anxiety and mood disorders.

Friday, 2:05. Thinking outside the "HPA Box": new targets for preventing stress-related enhancement of fear.

Goosens[1], K.A.
MIT McGovern Institute for Brain Research & Dept. of Brain and Cognitive Sciences

Although the body's stress response is adaptive in the short-term, its repeated activation can produce undesirable effects, such as enhanced vulnerability to affective mental illness. While changes following acute exposure to a stressor are well-characterized, much less is known about the biological factors regulating the effects of cumulative stress exposure. I will discuss recent findings from our laboratory showing that the peripheral hormone ghrelin is both necessary and sufficient for the enhancement of fear learning following repeated exposure to stress. Surprisingly, these ghrelin-mediated effects are independent of the hypothalamus-pituitary-adrenal (HPA) stress axis. We have also identified one of the downstream signaling molecules of ghrelin in amygdala neurons. Our findings strongly suggest that ghrelin is a novel biomarker for a maladaptive consequence of recurrent stress and anti-ghrelin strategies may have therapeutic value in the prevention of stress-sensitive psychiatric illnesses such as post-traumatic stress disorder.

Friday, 2:30. US Devaluation Effects in Flavor Preference Conditioning: Potential Neural Substrates.

Delamater, A.R., Scarlet, J.
Brooklyn College - CUNY, Psychology

Unconditioned stimulus (US) devaluation effects have been used extensively to determine if animals associate the conditioned stimulus (CS) with highly specific sensory features of the US. Prior work has established that the basolateral

amygdala (BLA), the orbitofrontal cortex (OFC), and possibly the gustatory cortex (GC) all play a role in mediating US devaluation effects when standard auditory and/or visual CSs are paired with distinctive USs in appetitive conditioning tasks. In the present studies we examined the role of these structures in a flavor preference learning paradigm where flavor cues were paired with nutrient USs that differed in their sensory features. We found that pretraining lesions of these structures failed to influence learning between flavor cues and the specific sensory features of their associated nutrients, as assayed with US devaluation tests, suggesting that the neural substrates mediating such learning may importantly depend upon CS modality.

Friday, 3:05. What does Pavlovian Fear Conditioning Condition?

LeDoux, J.
New York University, Center for Neural Science

Pavlovian Fear Conditioning is a widely used to study brain mechanisms in animals for the purpose of understanding the mechanisms of fear in humans. But to what does the "fear" in fear conditioning refer? There are more than three dozen words in English that relate to states of fear or anxiety (e.g. alarm, panic, worry, dread, horror, apprehension, concern, etc). In everyday speech we talk about being afraid of a wide range of objects or situations (animals, heights, open spaces, social settings, academic tests, falling in love, not falling in love, of fear itself, the eventuality of death, of not leading a meaningful life). Is there some underlying reality, some brain mechanism, that accounts for all these meanings and uses of fear. If not, should we be using the term fear conditioning so casually? Another issue is whether the fear in fear conditioning refers to fear at all? Do we really mean that we use fear conditioning to study the feeling of being afraid? I suspect that most researchers who use fear conditioning believe that they are studying the way the brain detects and responds to imminent threats to physical well being. The problem is that when we revert to describing our findings in terms of fear, all the hard fought battles of acquiring scientifically precise data are lost in the effort to make the results meaningful in a general sense. Research on threat processing in animals is really important for understanding so-called fear or anxiety disorders because they reveal the mechanisms that underlie behavioral and physiological responses that serve as debilitating symptoms, not because they illuminate how fear or anxiety is subjectively experienced.

Friday, 3:55. Nucleus accumbens involvement in Pavlovian Approach.

Horvitz, J.
City College, City University of New York, Psychology Department

Dopamine (DA) transmission within the nucleus accumbens (NAcc), and other striatal regions, modulates the efficacy of glutamatergic (GLUergic) throughput, and interacts with GLU NMDA transmission in synaptic plasticity. During behavioral learning, DA reward prediction errors are believed to promote synapse-strengthening by D1 receptor interactions with transmission at NMDA receptors on the same neuron. On the other hand, DA is believed to potentiate the expression of previouly-acquired reward-directed behaivor

by facilitating real-time GLU-transmission at AMPA receptors. We have recently examined the role of GLU transmission within the NAcc core on Pavlovian response acquisition and expression in rats. Results suggest that GLU acting at the NMDA receptor critically mediates the acquisition (but not expression) of food-directed Pavlovian approach. At the AMPA receptor, GLU transmission mediates expression of a previously-acquired Pavlovian approach response.

Friday, 4:15. The effect of stimulus duration distribution form on the acquisition and rate of conditioned responding.

Bonardi, C.
University of Nottingham, Psychology

Rats were conditioned to an auditory conditioned stimulus (CS) that was paired with food. The duration of the CS was either fixed on every trial, or drawn from an exponential distribution with the same mean value as the fixed duration. Higher levels of conditioned responding to the fixed than to the variable stimulus were observed, in both between- and within-subjects designs. This difference was maintained when stimuli trained with fixed or variable durations were tested under identical conditions. The cumulative distribution of a Weibull function was then fitted to the trial by trial response rates for each rat, to derive estimates of the speed of acquisition of conditioned responding. Differences in the pattern of acquisition to fixed and variable CS were found in certain metrics; a somewhat different pattern was found when I/T ratio was manipulated. The implications of these findings for theories of conditioning and timing are discussed.

Friday, 4:35. How associative mechanisms in the hippocampus guide decisions: Evidence from sensory preconditioning in humans.

Shohamy, D.
Columbia University, Psychology Department

Every day people make new choices between alternatives that they have never directly experienced. Yet, the neurobiological mechanisms that support such decisions remain unknown. Here we show that the hippocampus, traditionally known in humans for its role in building long-term declarative memories, biases the value of choice options that were never directly rewarded in the past. Using functional brain imaging (fMRI), we found that giving people monetary rewards led to activation of a network of memories, spreading the positive value of reward to non-rewarded items stored in memory. Later, people tended to choose these non-rewarded items. This value-based decision bias was predicted by activity in the hippocampus and by connectivity between the hippocampus and the striatum. These findings explain how the hippocampus supports the spread of value across associated items, enabling past experience of reward to guide new choices.

Saturday, 8:40AM. On the superiority of females: Evidence from appetitive conditioning.

Swithers, S.E.
Purdue University, Psychological Sciences

It is increasingly recognized that processes governing behavior across a variety of domains differ between males and females, and that hormonal differences may contribute significantly to sexually diergic behaviors. For example, ovarian-derived hormones have been identified as having a major influence on food intake and energy balance, as well as affecting performance on learning tasks in female rats. Recent work from our lab has identified circumstances under which learning associations between food cues and their consequences differs between males and females. Evidence suggests that females may more successfully acquire and use information about such associations to modulate energy balance. Further, such sex differences appear to result from organizational changes occurring during puberty which alter the impact of non-ovarian sources of estrogens on energy balance and/or learning about relations between food cues and their consequences.

Saturday, 9:00. Structural plasticity and cognitive function.

Gould, E.
Princeton University, Department of Psycholoogy

The hippocampus and medial prefrontal cortex (mPFC) are structurally plastic brain regions that play an important role in cognitive function. Exposure to negative or aversive experiences, such as stress and obesity, has been shown to reduce adult neurogenesis in the hippocampus as well as diminish dendritic complexity and the number of dendritic spines in both areas. Some, but not all, of these effects can be attributed to elevated glucocorticoid levels. These negative experiences also produce impaired performance on hippocampus- and mPFC-dependent cognitive tasks. Conversely, exposure to positive or rewarding experiences, such as sexual experience and running, enhances adult neurogenesis and promotes dendritic growth in the hippocampus and mPFC. Some of these structural changes may be the result of stimulated oxytocin release. Exposure to rewarding experiences also produces improved performance on cognitive tasks. Although experience-dependent structural change parallels change in cognitive function for both hippocampus and mPFC, the extent to which structural plasticity and cognition are causally linked remains unclear.

Saturday, 10:00. Developmental Changes in Forebrain Modulation of Cerebellar Learning.

Freeman, J.H., Goldsberry, M.E., Harmon, T.C., Ng, K.H.
University of Iowa, Psychology

Eyeblink conditioning has been used as a method for examining developmental changes in the neural mechanisms underlying cerebellar learning. The ontogeny of eyeblink conditioning is driven by developmental changes in interactions between the cerebellum and afferent pathways that transmit conditioned stimulus (CS) and unconditioned stimulus (US) information. Developmental changes in CS pathway input to the pontine nuclei and in

inhibitory feedback from the cerebellum to the inferior olive (US pathway) limit the induction of plasticity within the cerebellum. The septohippocampal system and amygdala modulate the acquisition of cerebellar learning in adult animals. Recent findings indicate that septohippocampal modulation of eyeblink conditioning emerges ontogenetically after conditioning starts to emerge, accelerating the learning curve. In contrast, amygdala modulation of eyeblink conditioning is evident as conditioning first begins to emerge. The findings suggest that although both the amygdala and septohippocampal system modulate cerebellar learning in developing rats, their contributions have different developmental time courses. The mature acquisition rate therefore requires a combination of developmental changes in the CS pathway, US pathway, and septohippocampal modulation.

Saturday, 10:25. Eyelid Conditioning during Sleep in Newborn Infants: Behavioral and EEG Measures of Learning.

Fifer, W.
Columbia University & New York State Psychiatric Institute

In human newborns, the capacity to learn and remember associations among internally and externally generated stimuli during sleep may be critical to adaptive functioning in the extra-uterine environment. We have now carried out a series of studies in sleeping neonates describing rapid changes in infant behavior and patterns of brain activation following a single-cue delay eyelid conditioning paradigm. Learning is observed in sessions lasting less than an hour while the newborn infant is still in the hospital. In our delay eyelid conditioning paradigm, a 1000 ms tone (CS) precedes and co-terminates with a 100 ms air puff (US). Periodic CS-alone trials allowed detection of conditioned responses, and US-alone trials permitted monitoring of unconditioned responses. High density EEG was collected with a 124-lead EEG sensor net. EEG spectral power and coherence, measures of cortical activation, and event related potentials are used to detect changes in cortical processing of the CS associated with acquisition of the conditioned response. In each study infants increase the frequency of eyelid responses to CS-alone trials, with over 90% of infants at least doubling their rate of responding. Control groups presented with the same stimuli but in an unpaired, semi-random sequence showed no increase in responding to the CS. ERPs show a more positive-going slow wave in frontal regions by the end of training in the experimental groups only, which may reflect memory updating . Moreover, EEG spectral power in the left central region increased across all frequency bands from the first blocks to the final blocks of the sessions which may relate to motor learning. Finally, a finding of increased 3-6 Hz coherence within frontal cortex and between frontal cortex and rest of head following learning points to cortical involvement within in other brain regions.

Saturday, 10:50. Applications of eyeblink conditioning to developmental neurobehavioral disorders.

Stanton, M.
University of Delaware, Psychology Department

Advances in the study of behavioral and neurobiological aspects of eyeblink

conditioning during development provide a powerful context for translational applications of this preparation to developmental disorders. This presentation reviews application of eyeblink conditioning in both rats and humans to research on Fetal Alcohol Spectrum Disorder and Autism. Some general conclusions that emerge from this work are (1) different disorders alter conditioning in different ways; (2) findings in animal models generally correspond to findings in humans; (3) experimental research with animal models and neuroimaging research in humans show clear potential to reveal mechanisms and guide interventions for these disorders, although these remain largely unexplored opportunities for researchers in our field.

Saturday, 11:15. Analyzing the role of adult-born hippocampal neurons in "pattern separation" using touch screen operant conditioning.

Drew, M.R.
University of Texas at Austin, Center for Learning and Memory

The dentate gyrus (DG) is one of a small number of mammalian brain regions that retain the ability to generate neurons in adulthood. In recent years there has been intense interest in elucidating the functional significance of adult neurogenesis with respect to behavior and underlying psychological processes. Theoretical studies have begun to coalesce around the hypothesis that adult neurogenesis enables pattern separation, which is the separation of overlapping patterns of perceptual stimulation into orthogonal neural representations. Consistent with this hypothesis, several recent studies found that suppressing adult neurogenesis impairs the ability of rodents to discriminate nearby but not far apart spatial locations. It is unknown whether this reflects a general role for neurogenesis in difficult discriminations, or whether the role of neurogenesis is confined to a particular class of discrimination problem. To characterize the role of adult neurogenesis in discrimination learning, we have begun assessing discrimination ability in mice using touch screens, which enable us to parametrically vary discrimination difficulty across several different perceptual domains. In this talk I report the results of some initial experiments characterizing acquisition of touch-screen responding and of a touch-screen spatial discrimination. We found that inducible, transgenic suppression of adult neurogenesis caused a time-dependent impairment in touch-screen spatial discrimination. The data are consistent with the hypothesized role for maturing adult-born neurons in pattern separation and encourage the use of touch screens to further analyze the mechanisms through which these cells contribute to discrimination learning.

Saturday, 11:35. Fear conditioning selectively and associatively alters the representation of sensory stimuli in primary sensory neurons in vivo.

Rosenthal, M.C., Kass, M.D., McGann, J.P
Rutgers University, Psychology

Traditional models of associative learning presume that sensory inputs to the brain's learning circuitry are approximately constant, though associative changes can occur in higher-order sensory structures.

However, here we find that discriminative olfactory fear conditioning induces associative, stimulus-specific changes in the neural representation of the CS+ at the primary sensory input to the brain. Odorant-evoked neurotransmitter release from olfactory sensory neuron (OSN) axon terminals was visualized through a cranial window in transgenic mice expressing the fluorescent exocytosis indicator synaptopHluorin. After context pre-exposure, mice underwent a baseline optical imaging session in which OSN synaptic output was visualized during the presentation of 5 different odorants. After recovery, mice were randomly assigned to undergo either 1) discriminative fear conditioning, where one odorant from the panel (CS+) was paired with mild footshock and another odorant (CS-) was presented without shock, 2) odorant exposure, where the two odorants were presented without shock, or 3) sensitization training, where footshocks were presented without odorants. This paradigm induced odorant-evoked freezing only to the CS+ and only in the fear conditioned group. Following training, the optical imaging session was repeated and results were compared to baseline. Remarkably, in the discriminative fear conditioning group, but not in control groups, the CS+ evoked neurotransmitter release from OSNs was significantly increased (81% on average) after conditioning, while that evoked by the CS- and by control odorants remained unchanged. In OSN populations that initially responded to both CS+ and CS- (based on shared chemical features), after conditioning their responses were only enhanced when evoked by the CS+. Emotional learning can thus alter the representation of sensory stimuli as early as the primary sensory neurons, including facilitating responses to local stimulus features based on global patterns with learned ecological significance. These results have broad implications for memory retrieval and learning about previously conditioned stimuli.

Saturday, 1:30. Effects of extinction trial spacing and retrieval - extinction manipulations on renewal of extinguished alcohol seeking.

McNally, G.P.*University of New South Wales, Psychology*

Four experiments investigated the effects of trial spacing or retrieval-extinction, on the context-specificity of extinction of alcoholic beer seeking. In Experiment 1, rats were trained for 7 days to respond for an alcoholic beer reinforcer in context A. This responding was then extinguished across four days in context B. For group Extinction, extinction training consisted of a single 1 hr session whereas for group Short-Long extinction training consisted of a short (10 min) then long (50 min) session. Rats were later tested in the extinction context (ABB) and the training context (ABA). There was evidence for ABA renewal that was significantly reduced by the spaced extinction, or retrieval – extinction, training. In Experiment 2, there was also a significant attenuation of ABA renewal when spaced extinction training consisted of long then short extinction sessions. Experiment 3 showed that the impact on renewal of these two trial spacing manipulations was equivalent. Finally, Experiment 4 showed that reversible inactivation of AcbSh prior to ABB test reinstated responding after normal and Long-Short but not Short –Long extinction training. Variations in extinction training trial spacing can therefore affect the

magnitude of ABA renewal and different trial spacing variations are associated with different neural substrates.

Saturday, 1:55. A computational perspective on erasing fear.

Gershman, S.
Princeton University, Department of Psychology

I discuss some new computational ideas about the nature of fear memories and their erasure. These ideas have inspired novel experiments that show some promise in preventing the recovery of fear.

Saturday, 2:20. Exploration of factors that promote or hinder fear memory updating.

Monfils, M.H.
University of Texas at Austin, Psychology

Although extinction generally presents as new learning, in a few notable exceptions it promotes updating of the initial memory trace instead; such exceptions include extinction early in development (Kim & Richardson, 2007), and immediately after fear acquisition (Myers et al., 2006). Instances in which extinction may reverse/update prior learning seem to have one thing in common: they operate within a discrete window of opportunity during which the memory in question is unstable/malleable/susceptible to disruption. We previously provided evidence for yet another window of opportunity to behaviorally update a fear memory: one that combines extinction and reconsolidation mechanisms (Monfils et al., 2009). Using a fear conditioning paradigm in rats, we demonstrated that presenting a single isolated conditioned stimulus (CS) prior to an extinction session results in what seems to be a permanent re-valuation of the CS as non-threatening, thereby preventing renewal, reinstatement, and spontaneous recovery (Monfils et al., 2009). Those results suggest that manipulations of the timing of only the first non-reinforced CS yield an effect that appears more in line with unlearning than typical extinction paradigms. This effect can seemingly be explained as a reconsolidation-updating mechanism, since it occurs only when the subsequent extinction training occurs within a specific reconsolidation window following the initial, isolated, CS presentation. Here we discuss cases that place boundary condition on the efficacy of the retrieval+extinction paradigm. Understanding the common factors that permit memory updating across currently known efficacy-windows will enhance our ability to successfully target and update memories more broadly.

Saturday, 2:45. Talk: Associative Bases of Causal Learning in Rats.

Miller, R.R., Polack, C.W., McConnell, B.L.
SUNY - Binghamton, Psychology

Are humans unique in their ability to interpret exogenous events as causes? We addressed this question by observing the behavior of rats for indications of causal learning. Within an operant motor-sensory preconditioning paradigm, associative surgical techniques found that rats attempted to control an outcome (i.e., a potential effect) by manipulating a potential exogenous cause (i.e., an intervention). Rats were able to generate an innocuous auditory stimulus. This stimulus was then paired with an aversive stimulus. Animals

subsequently avoided potential generation of the predictive cue, but not if the aversive stimulus was subsequently devalued or the predictive cue was extinguished (Experiment 1). Experiment 2 demonstrated that our aversive stimulus was in fact aversive and that it was subject to devaluation and that the cue-aversive stimulus pairings did make the cue a conditioned stimulus and that it was subject to extinction. Experiments 3 and 4 established that the decrease in leverpressing observed in Experiment 1 was goal directed instrumental behavior rather than purely a product of Pavlovian conditioning. To the extent that interventions suggest causal reasoning, it appears that causal reasoning can be based on associations between contiguous exogenous events. Thus, contiguity appears capable of establishing causal relationships between exogenous events. Our conclusions challenge the widely held view that causal learning is uniquely human and suggest that causal learning is explicable in an associative framework.

Saturday, 3:20. Mice Take *Calculated* Risks.

Kheifets, A., Gallistel, C.R.
Rutgers University

Animals successfully navigate the world despite having only incomplete information about behaviorally important contingencies. It is an open question to what degree this behavior is driven by estimates of stochastic parameters (brain-constructed models of the experienced world and to what degree it is directed by reinforcement-driven processes that optimize behavior in the limit without estimating stochastic parameters (model-free adaptation processes, such as associative learning). We find that mice adjust their behavior in response to a change in probability more quickly and abruptly than can be explained by differential reinforcement. Our results imply that mice represent probabilities and perform calculations over them in order to optimize their behavior, even when the optimization produces negligible material gain.

Saturday, 4:10. Climbing fibers encode information about the strength of an unconditioned periorbital airpuff stimulus at the single-cell and population levels.

Medina, J.
University of Pennsylvania, Department of Psychology

Climbing fibers originating in the inferior olive are thought to contribute to simple forms of motor learning like eyeblink conditioning by providing Purkinje cells of the cerebellar cortex with signals about the unconditioned periorbital airpuff stimulus. To be useful, these signals must carry information about graded features of the airpuff, like its strength; however, individual climbing fibers are typically described as being rather “binary”, responding to unexpected sensory events with an all-or-none burst of action potentials. Here, we use two-photon imaging of cerebellar cortex in awake mice to monitor the intracellular calcium signals evoked by climbing fibers in the dendrites of Purkinje cells, and measure their response properties to periorbital airpuffs of varying intensities. We find that information about the strength of the periorbital airpuff is encoded in the reliability, latency and amplitude of the calcium signal evoked by activation of

individual climbing fibers, and also in the level of coactivation in groups of climbing fibers.

Saturday, 4:30. Inhibitory after all: Contexts do become inhibitory during extinction.

Kutlu, M.G., Schmajuk, N.A.
Duke University, Department of Psychology & Neuroscience

The Schmajuk-Lam-Gray model (SLG, 1996) predicts that a salient context (CX) of extinction to become inhibitory and prevent the extinction of the association of the conditioned stimulus (CS) with the unconditioned stimulus (US). Although some data seemed to contradict that prediction (e.g., Bouton and King, 1983, Bouton and Swartzentruber, 1989), the model also predicted that the inhibitory CX-US association cannot be detected in a summation test with a long intertrial-interval (ITI) because attention to the CX decreases during the ITI. Remarkably, the model's predictions were recently confirmed by Polack, Laborda, & Miller (2012), who detected inhibitory CX-US associations following extinction with a short ITI. Recently, we confirmed additional SLG model's predictions regarding the inhibitory role of the context. Using a human predictive learning experiment we found that the inhibitory power of the CX can be detected (a) after a few extinction trials when attention to the CX is still high, (b) but not after many extinction trials once attention to the CX has decreased, and (c) even after many extinction trials by presenting Novel CSs which increase attention to the unattended CX.

Saturday, 4:50. Olfactory discrimination of oxygen based explosives and propellants by rats.

Kirkpatrick, K., Vilardo, M.
Kansas State University, Psychology

The present study trained rats to discriminate among three acids (Butyric, Acetic, and Propionic) and three ketones (Butanone, Acetone, and Hydrogen Peroxide). Some of these substances are components of or relatives of liquid explosives which are difficult to detect with normal scanning devices. Each of the compounds was assessed as a target and as a distracter odor, and the discriminability of each pair of substances was determined. In general, the rats displayed high discrimination ratios for all pairs of targets and distracters, despite close structural similarity among some of the compounds. This indicates that laboratory rats may be a useful model for detecting liquid explosives.

Poster Abstracts

P1. A Partial Reinforcement Schedule in Eyeblink Conditioning Reveals Facilitated Acquisition and Delayed Extinction in Anxiety Vulnerable College Students.

Allen, T.[1,2], Holloway, J.L.[2], Myers, C.E.[2,3,4], Servatius, R.J.[2,4]
[1]University of Northern Colorado, Psychological Science
[2]UMDNJ, Stress and Motivated Behavior Institue
[3]Rutgers University, Psychology
[4]New Jersey Health Care System, Neurobehavioral Research Laboratory

Individual differences in learning predictive relationships between stimuli and expressing avoidance may represent a diathesis for anxiety disorders. Learning differences in anxiety vulnerable individuals may be most evident when the predictive relationship between the conditioned stimulus (CS) and unconditional stimulus (US) is less than optimal. Previously, we reported that those expressing behavioral inhibition (BI) exhibited facilitated acquisition of conditioned eyeblink responses when the US was omitted on trials in which a conditioned response (CR) was present and when trained with associated yoked protocols. No significant differences in extinction were found in these two protocols. However, each subject received a different pattern and number of USs making direct comparisons difficult. Therefore, we chose to test the effects of an explicitly partial reinforcement paradigm in which all participants could be directly compared. All participants received 3 US alone trials, 60 acquisition trials, and 20 CS-alone extinction trials presented in one session. Conditioning stimuli were a 500 ms tone conditioned stimulus (CS) and a 50-ms air puff unconditional stimulus (US). The partial reinforcement group (n =34) was trained with a single pseudo-random schedule in which half of the acquisition trials were CS-US paired trials and half of the trials were CS alone (no more than 3 consecutive trials of either type); the continuous reinforcement group (n=29) received CS-US paired trials. All participants completed the Adult and Retrospective Measures of Behavioural Inhibition (AMBI and RMBI) and the Spielberger State/Trait Anxiety Inventory (STAI). Consistent with previous findings, those scoring high on the AMBI scale acquired an eyeblink CR to a higher degree than those scoring lower on this scale. Moreover, extinction was delayed in those scoring high on AMBI when trained with a partial reinforcement schedule. Enhanced sensitivity to acquired associations and slower extinction further support a learning diathesis model of anxiety disorders.

P2. Assessment of eyeblink responding in adolescents at risk for anxiety disorders: Comparisons of acquisition in delay and long delay contingencies.

Caulfield, M.D.[1,2], VanMeenen, K.M.[1,3,4], Servatius, R.J.[1,2,3]
[1]New Jersey Medical School, Stress and Motivated Behavior Institute
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[4]University of Medicine & Dentistry of New Jersey, Neurology & Neurosciences

A fuller understanding of the role of the cerebellum in human eyeblink conditioning is necessary in order to appreciate individual differences in associative learning. The cerebellum is clearly essential at optimal (400-500-ms) conditioned stimulus (CS) durations, which rely primarily on cerebellar structures. However, much less is known about the neural substrates underlying longer CS durations, which have been shown to recruit other brain areas in addition to the cerebellum to acquire the conditioned response (CR). Research in infants and older adults suggests optimal CS durations may vary with age. However, no studies to date assess acquisition in healthy adolescents. The present study compared acquisition of two delay durations (500-ms and 1000-ms) in adolescents following self-report of anxiety vulnerability on a battery of measures. Participants were pseudo-randomly assigned to a 500-ms or 1000-ms condition and presented with 60 paired CS-US trials (1000-Hz tone co-terminating with a 50-ms 5 psi corneal airpuff unconditional stimulus (US)) while eyeblink activity was recorded bilaterally with surface EMG sensors. The percent CR was calculated for each block of 10 trials. Preliminary data analysis (N=56, 14-18 years, M=15.5 years, 32% male) indicates that while the 500-ms group demonstrated significant learning over the training period, $F(5,85)=4.517$, $p<.005$, the 1000-ms group failed to acquire, $F(5,170)=1.142$, $p=.340$. Compared to low scoring individuals, overall acquisition of at-risk individuals is best in at the 500-ms condition and shows the greatest decrement at the 1000-ms condition suggesting a role for the hippocampus in modulating anxiety vulnerability.
Supported by the GSBS, Foundation of UMDNJ Society of Research Fellowship and the SMBI

P3. Modification of heart rate during eyeblink conditioning in differing human temperaments.

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The development of bradycardia throughout eyeblink conditioning in humans is more prominent in those with a higher degree of conditioned response (CR) acquisition, as well as individuals expressing an inhibited temperament and trait anxiety on self-report measures. In this study, our laboratory recruited male and female college students from 18 to 35 years old who completed a selection of self-assessed personality

measures that included the State/Trait Anxiety Inventory (STAI) and Adult/Retrospective Measures of Behavioral Inhibition (AMBI and RMBI, respectively). After completing the personality assessment, subjects were fitted with surface electrodes to collect electrocardiogram (ECG) and electromyogram (EMG) biopotentials during the conditioning session. A delay eyeblink conditioning paradigm was used consisting of a 500-ms conditioned stimulus (CS) co-terminating with a 50-ms corneal air-puff unconditional stimulus (US). Three US-alone presentations were used to assess the initial reactivity to the US, followed by 60 paired CS/US and 20 CS-alone trials with a pseudorandom intertrial interval of 20-40s. Preliminary results show elevated baseline heart rates in high AMBI, TAI, and SAI groups that replicate earlier findings by others. The same groups also displayed a marked and extended bradycardic response with increased heart rate variability during the three US alone presentations. Furthermore, these groups have shown a trend towards faciliated acquisition of the eyeblink CR. Increased vagal power, responsible for the enhanced bradycardia, may serve as a physiological basis for observed facilitated associative learning in those that express inhibited temperament and/or trait anxiety. Additionally, the origin of heart rate deceleration in the three groups may be partly attributed to an anticipatory response prior to the start of conditioning.

P4. Learned irrelevance is abolished in individuals with high behavioral inhibition, a vulnerability factor for anxiety disorders.

Miller, K.A.[1,2,3], Miller, D.[1,3], Allen, M.T.[1,4], Servatius, R.J.[1,2], Myers, C.E.[1,2]
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[2]DVA Medical Center, Neurobehavioral Research Laboratory
[3]Carthage College, Neuroscience
[4]University of Northern Colorado, Neuroscience

Several vulnerability factors have been identified as conferring risk for anxiety disorders such as PTSD. One class of vulnerability factors includes personality traits. Various psychometric measures have been used to measure behavioral inhibition (BI) and trait anxiety as markers to better identify individuals who are more susceptible to developing PTSD and other anxiety disorders. Another class of vulnerability factors is assessed via abnormal performance on cognitive tasks. Abnormal performances on cognitive tasks, including tasks of learning and memory, have also been identified in individuals with hippocampal dysfunction. For example, individuals with PTSD typically have reduced hippocampal volume and there is some evidence that this may pre-date onset of the disorder (i.e., be a vulnerability factor) rather than arise in the aftermath of exposure to trauma or development of the disorder. The aim of the current work is to collect measures of these vulnerability factors in healthy young adults, to establish the degree to which they do or do not co-occur in this population. To test this we used various psychometric self evaluation measures for BI and a hippocampal

dependent learned irrelevance (LIRR) task. In this sample, there was a clear LIRR effect in the low behaviorally inhibited individuals making more errors in the testing phase than those not pre exposed to the CS . However, the effect was reduced/abolished in the high RMBI - although there was a main effect of RMBI (with high BI making fewer errors overall), post-hocs on the interaction showed that the exposed and non-exposed high RMBI did not differ from each other or from the low RMBI non-exposed. From these data it is apparent that there is a relationship between BI and performance on cognitive tasks; however further research needs to be done to elucidate whether this is a cause and effect relationship.

P5. Behaviorally Inhibited Individuals Demonstrate Prolonged Bradycardia that Outlasts Presentation of Positive, Negative, and Neutral Images.

Holloway, J.L.[1,2], Sprycha, M.[2,3], Myers, C.E.[1,2,4], Beck, K.D.[1,2,4], Servatius, R.J.[1,2,4]
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[4]DVA Medical Center, Neurobehavioral Research Laboratory

Behavioral inhibition (BI) is a known risk factor for the development of anxiety disorders, but how this anxiety risk drives psychopathology is unknown. Prior work has identified associations between BI and social reticence, high stable heart rates in children, and enhanced amygdala activity to novel stimuli. Inhibited individuals also show facilitated conditioned eyeblink response acquisition, without demonstrating overt sensitivity to the conditioning stimuli. It is possible that more subtle, autonomic and neuroendocrine reactivity to neutral or mildly aversive stimuli may be promoting associative learning in these at-risk individuals. The present study was thus designed to examine how cardiac and neuroendocrine responsivity of inhibited individuals is affected when viewing low-arousal stimuli of positive, negative, and neutral valence. Images were chosen from the International Affective Picture System. Participants were pre-screened using the Adult Measure of Behavioural Inhibition and randomly assigned to valence group (POS, NEG, NEU) based on predetermined high and low BI scores. Each group was shown 60 images in their respective valence (30 novel, 30 repeated, pseudorandom order). Saliva samples were collected immediately before and after image viewing. Mild bradycardia to the images was of similar magnitude independent of BI score, while robust and sustained bradycardia was evident over the viewing session in high BI individuals. This reduction was most pronounced in group NEU over the session, and ameliorated in the POS and NEG groups. Inhibited individuals also had lower basal DHEA levels, and moderate increases in cortisol and alpha-amylase. The results indicate a complex relationship between prolonged vagal enhancement in inhibited individuals that appears to supersede image presentation, and corresponding HPA activity. In sum, learning about environmental stimuli could be driven by vagal reactivity in BI individuals, though modulated by HPA activity. These findings have implications for understanding the progression of anxiety psychopathology.

P6. UCS predictability and controllability influence UCR expression during Pavlovian fear conditioning in humans.

Hyde, S.O., Wood, K.H., Bowen, K.H., Shumen, J.R., Knight, D.C.
University of Alabama at Birmingham, Psychology

During Pavlovian fear conditioning, a conditioned stimulus (CS) is paired with an aversive unconditioned stimulus (UCS). The expression of a conditioned response (CR) in anticipation of the UCS is typically taken as evidence that the CS-UCS association has been learned, while the unconditioned response (UCR) is considered an automatic, unlearned reaction to the aversive UCS. However, learning-related changes in the UCR have been observed in prior conditioning research. For example, UCR amplitude is reduced when the UCS follows a CS compared to when the UCS is presented alone. The present study investigated the impact of UCS predictability and controllability on unconditioned skin conductance response and startle eyeblink electromyography responses during Pavlovian fear conditioning. During acquisition one tone (CS+: 10 sec duration; 20 sec ITI) coterminated with a loud (100 dB) white-noise UCS, and a second tone (CS-) was presented alone. To assess conditioned diminution of the UCR, the UCS was also presented alone. The study consisted of two groups of participants; one group (Control group) was able to control the duration of UCS presentations (UCS duration range: 0.5 to 6.0 sec) and a second group (Yoked group) received uncontrollable UCS presentations. The Control group had the ability to terminate the UCS by pressing a button. In contrast, UCS duration was not influenced by the participant's response in the Yoked group. Instead, UCS duration was determined by a participant in the Control group with whom they were yoked. UCR amplitude was diminished when the UCS followed the CS+ vs. presented alone. Further, UCR amplitude was diminished in Control vs. Yoked group participants. These results indicate that predictability and controllability of a UCS modulates UCR amplitude.

P7. The resurrection of the screaming lady: Fear reinstatement in (courageous) children and (wimpy) adults.

Newall, C.S.[1], Kwok, B.[1], Richardson, R.[2], Hudson, J.[1]
[1]*Macquarie University, Psychology*
[2]*University of New South Wales, Psychology*

Although fear reinstatement and renewal are commonly found in adults, studies using rodents have shown that both phenomena are absent early in life (Gogolla et al., 2009; Kim & Richardson, 2007; Yap & Richardson, 2007). The current study investigated whether fear reinstatement is also absent in children (7 to 12 years old). Thirty-nine children and 43 parents, who served as adult controls, were trained on the 'Screaming Lady Paradigm' (Lau et al., 2009). In this procedure, photographs of female faces with neutral expressions serve as the conditioned stimulus (CS) and the same face with a fearful expression and a shrieking auditory scream serve as the unconditioned stimulus (US). All participants were trained on differential fear conditioning

in which one face was paired with the scream (CS+) and another face was not (CS-). Following extinction, families were randomly assigned to either receive reinstatement (two brief presentations of the screaming lady) or not. Fear was indexed via self-report measures and preferential gaze of the CSs. Results revealed that adults and children exhibited comparable differential conditioning and extinction on all measures. However, adults but not children exhibited differential reinstatement on self-report measures of fear. Similar developmental differences were found with preferential looking to the CS+, although the results were marginal trends. Interestingly, children exhibited differential reinstatement when US expectancy was measured. This suggests that while children were more likely to expect the CS+ to be followed by a scream as a consequence of reinstatement, they were no longer afraid of the CS+. The extant evidence, including the current study, supports the possibility that extinction involves erasure early in life. Further behavioural and imaging studies are needed given that fear erasure in youths may have important clinical implications for the early intervention of childhood anxiety disorders.

P8. Using eye movement and pupil dilation measures to examine the role of awareness in fear conditioning.

Schultz, D.H., Balderston, N.L., Hannula, D.E., Helmstetter, F.J.
University of Wisconsin-MIlwaukee, Psychology

The role of explicit contingency awareness in fear conditioning is a topic of considerable debate. Several experiments suggest that CR expression is independent of awareness (Balderston et al., 2010; Knight et al., 2009; Schultz et al., 2010). However, other researchers have provided results inconsistent with this idea (Klucken et al., 2009; Weike et al., 2007). The inconsistency of such results across experiments and across the response systems usually measured in conditioning is problematic. Recently, several groups have reported memory effects on eye movement measures in the absence of explicit knowledge (Hannula et al., 2012; Ryan et al., 2004). The purpose of the current study was to manipulate contingency awareness while assessing implicit learning with eye tracking measures.

Participants were randomly assigned to one of two groups. The Easy condition was designed so participants would be aware of the relationship between the CS and shock. The Difficult group was designed so participants would not be aware of the contingencies. The conditioning session consisted of 12 CS+ trials and 12 CS- trials presented in a pseudorandom order. We measured eye movement and pupil dilation throughout the experiment in addition to skin conductance response and UCS expectancy.

The Easy group became aware of the contingencies as measured by UCS expectancy. The Difficult group did not become aware of the contingencies. Several measures of eye movement in the Easy group reflected learning. The Difficult group did not demonstrate learning on any of the eye movement measures. Pupil dilation data in the Easy group showed a conditioning effect. Pupil dilation data in the Difficult group showed a very short latency conditioning effect. We found some support for conditioning in the absence of awareness on the pupil dilation measure, but failed to observe a conditioning effect in

the unaware group with the eye movement measures.

P9. Comparability of MRI-compatible Infrared and Electromyogram Measures of Eyeblink Conditioning.

Innis, I.J., Kent, J.S., Bolbecker, A.R., Hetrick, W.P.
Indiana University Bloomington, Psychological & Brain Sciences

Human eyeblink conditioning (EBC) is a procedure used to measure associative learning and temporal processing. Because EBC requires the recruitment of the cerebellum and related brain regions, the procedure is used to investigate the functional integrity of these circuits and their behavioral output in disorders such as schizophrenia. The occurrence of an eyeblink in this procedure is typically recorded by measurement of the activity of eyelid muscles using electromyography (EMG) or changes in the infrared reflectance (IR) when the eyelid closes. However, these methods have not been adequately compared to determine their similarities and differences for characterizing the critical parameters used to indicate conditioning. We directly compared these recording techniques. Preliminary results indicate that the IR technique yielded shorter latencies and lower measured rates of conditioning compared to EMG.

P10. Sexual Conspecific Affective Response (SCAR): A Novel Animal Model for Sexual Abuse in Young Women.

Bowles, L.M., DiFeo, G.E., Shors, T.J.
Rutgers University, Psychology

Sexual abuse in adolescent girls and young women is unfortunately common and often leads to long-lasting deficits in thoughts and behaviors related to mental illness. In order to study the neuronal consequences of sexual abuse, we developed an animal model referred to as SCAR. The acronym stands for Sexual Conspecific Affective Response, which indicates behavioral, cognitive and neuronal changes that occur after repeated exposure to sexually aggressive and experienced adult males. In the first set of experiments, pubescent females were exposed to an adult male aggressor for thirty minutes every three days over the course of adolescence (PND 35- PND 57). During adulthood, the female's ability to learn an associative response was examined. Overall, adult females that were exposed to the sexually aggressive males during puberty did not perform as well as females that were not exposed to the male. Thus, the aggressive encounters during puberty were sufficient to induce long-lasting effects on processes of learning during adulthood. We also examined the effects of SCAR on the survival of new neurons in the hippocampus as a result of the training procedure. In previous studies, we find that learning keeps new neurons alive. However, adult females that were exposed to the aggressive adult males during puberty retained fewer new cells as a result of the training process. Since they did not learn as well, these results indicate long-lasting

effects of this procedure not only on cognition but also on the structural integrity of the adult braiin.
Supported by National Institutes of Health (National Institute of Mental / Health - 59970) and National Science Foundation (Integrative Organism / Biology - 0444364) to Tracey J. Shors (shors@rutgers.edu)

P11. Psychophysiological interactions of brain responses to aversive stimuli in patients diagnosed with Obsessive Compulsive Disorder: a functional MRI study.

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Obsessive-compulsive disorder (OCD) is a relatively common neuropsychiatric disorder with a lifetime prevalance of 2-3%. It's syptoms are characerized according to two features: 'obsessions'- recurrent intrusive thoughts and 'compulsions'- ritualistic behaviors performed in response to obsessions or anxiety. Understanding the mechanisms that mediate responses to averstive stimuli may lead to better understanding of the large-scale functional networks associated with OCD. In the current study, 15 healthy controls and 18 OCD patients underwent a partial-reinforcement classic conditioning paradigm and fMRI. During fear conditioning, 62.5% (10/16) trials (CS+) were followed by an elecric shock, while the remaining 6 CS+ trials were never paired with a shock (CS-). We examined the neural responses at the specific time window when: 1) the participants were expecting and receiving the shock (offset of the 10 reinforced CS+ trials), expecting the undelivered shock (offset of 6 CS+ trials that were not reinforced), and 3) the offset of the CS- that was never paired with the shock. When the shock was expected and delivered, relative to controls, OCD patients exhibited significant bilater hyperactivation in the lateral OFC, somatosensory cortex, and the insula. When the shock was expected but omitted, OCD patients showed exaggerated amgydala responsivity relative to controls. We next conducted psychophysiological interaction (PPI) analyses; the purpose of which were to identify whether the presence or absence of shock modulated the functional connectivity between seed regions and the rest of the brain. Our preliminary data revealed increased functional coupling between the somatosensory cortical area and thalamaus and orbitofrontal cortical regions in OCD patients. Increased functional coupling between the insula and hippocampus, the OFC, and dlPFC was also noted in OCD patients. These data suggest abnormal processing of aversive stimuli in OCD patients in a network of brain regions known to process sensory and fear-related information.

P12. Extinguishing Learned Fear by Imagination.

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Imagination can influence both emotion and arousal, but its effect on real-world fear memories is largely unknown. In this study, we investigated whether extinction training performed in one's imagination can reduce a fear response acquired in the real world. Participants underwent auditory fear conditioning. We used two tones as the conditioned stimuli. One tone (4s) was paired with an electric shock, 33% of the trials (CS+), and the other was never paired (CS-). There were three groups of subjects. One group underwent real-world extinction training (15 exposures of each tone without shock, in an intermixed order). The second group was cued to imagine the tones in the same presentation sequence (15 imaginary exposures of each tone). The third group was cued to imagine two neutral sounds from nature (e.g., rain and birdsong), this controlled for the general effects of imagination on arousal. All subjects were subsequently exposed to four unsignaled shocks to reinstate the fear memory, after which, all groups were re-exposed to the real tones (15 exposures each). Skin conductance responding was the measure of fear arousal, and functional magnetic resonance imaging (fMRI) was used to examine the underlying neural correlates. Consistent with previous research, the blood-oxygenation-level-dependent (BOLD) signal in the ventromedial prefrontal cortex (vmPFC) gradually increased during real-world extinction training. Interestingly, imagined extinction elicited overlapping vmPFC activation, while general imagination did not. Amygdala BOLD signal was also lower for these two extinction groups, compared to the imagination control group, upon re-exposure to the stimuli. These results suggest that directed imagination might be as effective as real-world extinction learning, perhaps by sharing or capitalizing on the neural mechanisms of standard extinction. In the clinic, controlled imagination might be an alternative or a complementary method to exposure therapy.

P13. Effects of Decreased Temporal Predictability during Human Pavlovian Fear Learning.

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University of Wisconsin-MIlwaukee, Neuroscience

Unpredictability is related to numerous anxiety disorders. Previous human fear learning research has shown a less predictable UCS can result in enhanced fear responses (Grillon , C., Baas, J.P., Lissek, S.L., Smith, K., & Milstein, J., 2004). Recently, Goosens (2011) varied the time of onset of the UCS during the CS period during fear conditioning and found increased responding in rats. There is currently very little known about the effect that manipulating the onset of the UCS might have on learning in humans. The present study was designed to examine the effects of UCS temporal unpredictability on shock expectancy learning and autonomic fear responding.
Volunteers were repeatedly shown one geometric figure (CS+) which was paired with shock (UCS), while another was presented alone (CS-). The Predictable (P)

group was exposed to standard delay conditioning during which the UCS coterminated with the 8 second CS+. In the Unpredictable (U) group, the UCS was presented at varying intervals (2s, 4s, 6s, 8s) after CS+ onset. UCS expectancy ratings as well as skin conductance response (SCR) were collected continuously. Group U showed increased overall fear as measured by significantly higher SCR on CS trials. The groups showed a distinctly different distribution of expectancy ratings across the 8 sec CS period. Group P was significantly more accurate at timing the onset of the UCS. Additionally, the P group learned not only which CS predicted the UCS, but also when the UCS would occur. The P group also showed significantly more accurate timing of of the UCS (as indicated expectancy ratings) in the late phase compared to the early phase of training. The results are considered in terms of the roles of attention, anxiety, and contingency awareness in human fear conditioning studies.

P14. Harm avoidant personality enhances transition from escape to avoidance on a computer-based paradigm.

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Avoidance behavior is a predominant symptom in all anxiety disorders. The propensity to acquire and express such behaviors may be an important vulnerability factor contributing to the etiology and pathogenesis of the disorders. To date, a full understanding of how avoidance behaviors are exhibited by humans is limited by the absence of relevant tasks. Here, we developed a computer-based task to study avoidance learning in human subjects, following a previously published task by Molet et al. (2006). Besides the option to prevent (avoid) the aversive event, we also included an option to escape, which enables the termination of the aversive event after its initiation. Such modification allowed us to observe the transition from escape to avoidance, a recognized feature of many anxiety disorders, which also parallels animal avoidance paradigms. We further analyzed the possible correlation between the escape/avoidance performance and harm avoidance personality, which is associated with individual differences in sensitivity to aversive stimulation and is a measure of anxiety proneness. Results suggest that the addition of an escape option facilitates avoidance learning in healthy young adults. Furthermore, although most of the subjects learned to escape the aversive event, only about half also demonstrated an avoidance response. The self-reported harm avoidance personality was a significant

predictor of the occurrence and the degree of such behavior.
This work was supported by NSF/NIH Collaborative Research in Computational Neuroscience (CRCNS) Program, NIAAA (RO1 AA018737) and SMBI.

P15. The Influence of Stress on Extinction Recall.

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Extinction learning is a form of inhibitory learning that allows an organism to associate a previously aversive cue with new, safe outcome. Extinction, however, does not erase a fear association but creates a competing association that may or may not be retained when again confronted with the cue. Examining the conditions under which extinction learning is retained and recalled is critical to the enhancement of treatments for anxiety disorders such as phobias and PTSD. The ventromedial prefrontal cortex (vmPFC) is crucial to the learning and recall of such safety learning. This brain region, however, is exceptionally sensitive to the effects of stress exposure. Studies in animals demonstrate that stress exposure could prompt the return of a conditioned fear expression, however, it remains unclear how stress might influence extinction recall in humans. Participants underwent a fear-conditioning paradigm, whereby one image was paired with shock on 40% of trials while the other image was never paired shock; extinction training directly followed. Skin conductance was measured throughout and served as our index of fear arousal. One day later, participants returned for an extinction recall test. Before this test, we either induced acute stress using the Cold Pressor task (participants submerged their arm in ice-water for 3 minutes) or did not induce stress (warm water). The efficacy of our stress induction was established by observing significant increases in cortisol relative to baseline for the Stress group only. We calculated a fear recovery index by examining the difference between conditioned responses during the last trial of extinction and that of the first trial of re-extinction. Participants in the stress group demonstrated lower extinction recall than those in the control group, suggesting that acute stress may impair the recall of extinction memory and may instead prompt the return of conditioned fear.

P16. Alterations in dopamine and opioid receptor mRNA levels in WKY rats: a model for anxiety vulnerability.

Cominski, T.P.[1,2], Jiao, X.[1], Kuzhikandathil, E.V.[2], Beck, K.D.[1,2], Pang, K.C.H.[1,2], Servatius, R.J.[1,2]
[1]VA Medical Center, Neurobehavior Laboratory
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The Wistar-Kyoto (WKY) rat serves as a model for anxiety vulnerability. Our lab has shown that WKY rats have altered anxiety-related behaviors when compared to Sprague Dawley (SD) rats. To complement our data on the behavioral alterations in WKY rats, we have begun to examine the underlying mechanisms that contribute to these behavioral differences, especially related to active avoidance behaviors. Previous research indicates that both the

dopamine system and the opioid system contribute to the etiology of anxiety disorders. The present study examined whether WKY rats display differences in these systems when compared to SD rats. Our hypothesis is that alterations in the dopamine system and/or the opioid system in WKY rats leads to the anxiety-related behavioral traits previously described by our laboratory; including behavioral inhibition and facilitated acquisition and impaired extinction of active avoidance behaviors. In this study, we examined dopamine receptor and opioid receptor mRNA levels using quantitative RT-PCR in brain regions involved in active-avoidance behaviors and open field activity in both WKY and SD rats. Our data indicate that WKY rats have lower dopamine receptor mRNA levels compared to SD rats in the cerebellum and higher levels in the basolateral amygdala, but remain unaffected in other brain regions. Kappa opioid receptor (KOR) mRNA levels were dramatically higher in the nucleus accumbens of WKY rats and more subtle differences in opioid receptor mRNA levels were detected in other brain regions. These data suggest that alterations in dopamine receptor and/or opioid receptor expression may contribute to the anxiety-related behavioral changes exhibited by WKY rats. An extension of this research is that alterations in dopamine receptor and/or opioid receptor levels may predispose an individual to the development of an anxiety disorder.

P17. Molecular level functional MRI of dopamine release in the ventral striatum.

Lee, T., Cai, L., Jasanoff, A.
Massachusetts Institute of Technology, Biological Engineering

Dopamine signaling is critical to brain systems controlling voluntary movement, learning, and the experience of reward. Although extensive studies of dopaminergic neural activity have been performed using electrophysiology and pharmacological approaches, very little information has been obtained about spatial characteristics of dopamine signaling in the brain. To address this issue, we recently developed a family of protein-based contrast agents that can detect dopamine in magnetic resonance imaging (MRI). Here we use these probes to perform molecular-level functional imaging of dopamine release during delivery of a widely-studied artificial reward, electrical stimulation of the medial forebrain bundle (MFB) in rats.
Rats were implanted with electrodes targeted to the MFB, and operant responses to MFB stimulation were verified behaviorally. Animals were then anesthetized, treacheotomized, artificially ventilated, and injected with 80 mg/kg L-DOPA in preparation for dopamine imaging with a 9.4 T Bruker scanner. During imaging with gradient echo T1-weighted contrast, the dopamine sensor BM3h-9D7 was infused into brain in order to fill large regions of the ventral striatum. Following 50 minutes of infusion, MFB stimuli were delivered in blocks of 16 s, alternating with 300 s epochs of rest. Statistical analysis using AFNI revealed significant stimulation-associated MRI signal changes across the ventral striatum, with the strongest responses observed in the medial part of

nucleus accumbens shell. Average time series data indicated signal changes of up to 2%, consistent with peak dopamine concentrations of approximately 10 µM binding to the sensor. These responses varied in a manner dependent on the stimulus parameters, and were not observed using an inactive form of the MRI sensor. Parallel measurements using electrochemical detection verified that dopamine concentrations determined by MRI were realistic, and confirmed that BM3h-9D7 binds dopamine in vivo. These experiments offer a novel and qualitatively unique spatiotemporal view of phasic dopamine signaling, and provide direct evidence for the spatial heterogeneity of dopamine release in ventral striatum.

P18. Dopamine is required for learning and forgetting in Drosophila.

Davis, R.L., Berry, J.A., Cervantes-Sandoval, I.
Scripps Research Institue, Neuroscience

Psychological studies in humans and behavioral studies of model organisms suggest that forgetting is a common and biologically regulated process, but the molecular, cellular, and circuit mechanisms underlying forgetting remain poorly understood. We recently discovered that chronic dopamine signaling to the adult mushroom bodies constitutes part of a molecular mechanism for active forgetting. Bidirectional modulation of a small subset of dopamine neurons after olfactory classical conditioning regulates the rate of forgetting of both punishing (aversive) and rewarding (appetitive) memories. Inhibiting synaptic release from these neurons after learning enhances memory expression, while activating these neurons after learning removes memory expression. Two of the dopamine neurons involved, MP1 and MV1, exhibit synchronized ongoing activity in the mushroom body neuropil in alive and awake flies before and after learning as revealed by functional cellular imaging. In addition, while the mushroom body-expressed dDA1 dopamine receptor is essential for the acquisition of memory, we show that the dopamine receptor DAMB, also highly expressed in mushroom body neurons, is required for forgetting. We propose a dual role for dopamine: memory acquisition through dDA1 signaling and forgetting through DAMB signaling in the mushroom body neurons. Thus, the brain is designed to learn information, but also to actively forget using dopamine signaling unless what is learned is so important that it overrides the forgetting signal.

P19. Differential effect of dopaminergic and noradrenergic drugs on active avoidance acquisition and extinction in an animal model of anxiety.

Jiao, X.[1], Pang, K.C.H.[1,2,3], Beck, K.D.[1,2,3], Stewart, A.L.[1], Smith, I.[1], Servatius, R.J.[1,2,3]
[1]*NJMS, SMBI*
[2]*New Jersey Health Care System, VA*
[3]*UMDNJ, GSBS*

The Wistar-Kyoto (WKY) rat has been studied as a model of behavioral inhibition (BI), exhibiting altered dopaminergic (DA) and noradrenergic (NE) function in the CNS. Recently, we demonstrate that WKY rats acquired avoidance (a core symptom of all anxiety disorders) faster than Sprague-Dawley (SD) rats, and they are more resistant to extinguish avoidance. Given an abnormal DA/NE system(s) being one of the vulnerabilities to develop anxiety disorders, we hypothesized that pharmacological

manipulation targeting of either the DA or NE pathway would affect avoidance acquisition and extinction learning selectively in WKY rats. In the present study, we evaluated the effects of nomifensine (a DA transporter(DAT)/NE transporter (NET) blocker), bupropion (a DAT blocker), and desipramine (a tricyclic antidepressant targeting NET) in WKY and SD rats using a discrete lever-press avoidance learning paradigm. The primary measures were: percentage of avoidance (leverpresses during the warning tone), avoidance expressed on initial trials, and the number of leverpresses during the safety period. In the first experiment, chronic treatment of nomifensine (10mg/kg/day) was administered both before and during acquisition and extinction training. In the second experiment, all 3 drugs were administered following acquisition and prior and during extinction training. Nomifensine did not reduce avoidance acquisition, instead, it actually facilitated avoidance acquisition of WKY rats and impaired extinction. Yet nomifensine, desipramine, and buproprion all facilitated extinction learning only in WKY rats when drugs were initiated following acquisition. These initial results suggest that the timing of treatment with regards to avoidance development, expression and extinction is critical in determining efficacy. Once established, increasing synaptic DA/NE level facilitates avoidance in WKY rats. These data extend our understanding of diathesis and the neurobiological mechanism underlying anxiety disorders.

P20. The Role of Midbrain Dopamine in Predictive Fear Learning.

Li, S., McNally, G.P.
University of New South Wales, Psychology

The firing of midbrain dopamine neurons during appetitive learning tasks conforms to the assumptions of associative learning theories. Some dopamine neurons also respond to aversive USs and CSs predictive of such USs. However, the role of dopamine in predictive fear learning, and its relationship to amygdala mechanisms for fear learning, remains unclear. Here we studied the role of dopamine in predictive fear learning using blocking designs and assessing fear via conditioned freezing and conditioned suppression. Blocking involved training rats to fear conditioned stimulus (CS) A in Stage I via pairings with shock. In Stage II, rats received pairings of CSA+CSB and shock. Blocking was shown by less fear to CSB than a control group that received Stage II, but not Stage I, training. Whilst microinjections of the D2 antagonist sulpiride into the VTA prior to Stage II conditioning prevented blocking using freezing as a measure of fear, they failed to do so when fear was assessed via conditioned suppression. Intra-VTA microinjections of the kappa opioid receptor antagonist nor-BNI also failed to prevent blocking as assessed via conditioned suppression, as did dopamine receptor antagonism in the basolateral and central amygdala subregions. Additional experiments studying the effects of dopamine receptor antagonism in other terminal regions, namely the nucleus accumbens and prefrontal cortex will be reported.

P21. Effects of dopamine D1/5 receptor activation on fear: Appetitive-aversive interactions in extinction.

Abraham, A.D., Lattal, K.M.
Oregon Health and Science University, Behavioral Neuroscience

The examination of dopamine's role in behavior has been primarily focused on reward, motivation and motor function. However, a growing literature indicates that dopamine is also involved in the formation and extinction of aversive memory. Previous research has shown that animals lacking dopamine D1 receptor signaling demonstrate impaired fear extinction and the distribution of dopamine D1/5 receptors in the central nervous system suggests overlapping circuits between reward memory formation and aversive memory extinction. Examining dopamine's role in fear extinction could allow for a better understanding of the etiology of anxiety disorders, such as post-traumatic stress disorder (PTSD), as well as providing a novel pharmacological target to enhance behavioral therapies for these disorders. Here, we show the enhancement of fear extinction with a post-extinction systemic administration of 10 mg/kg SKF 81297 (a dopamine D1/5 receptor agonist). Briefly, C57BL/6 mice received four unsignaled shocks (.35 mA footshock) on Day 1 in a novel context (12-min exposure), and were returned to the context on Day 2 for an extinction session (12-min). Following extinction, animals received SKF 81297 (1-10 mg/kg) and were placed in their home cage. On Days 3-5, mice were returned to the conditioned context (12-min) and tested for fear extinction retention. Animals that received SKF 81297 following extinction showed decreased freezing during test days. These effects were not mediated by non-specific locomotor activation and fear conditioning impairments with SKF 81297 administration indicated that the learning enhancements were specific to fear extinction. Additionally, experiments in conditioned place preference showed that pre-session (but not post-session) systemic administration of 10 mg/kg SKF 81297 induces conditioned place preference. These findings suggest a mechanism by which rewarding drugs could enhance the extinction of fear, and may indicate a target for understanding the co-morbidity between substance dependence and PTSD.

P22. The mathematical model of trace conditioning.

Kryukov, V.I.
St. Daniel Monastery, St. Daniel Monastery

There are three basic paradigms of classical conditioning: delay, trace and context conditioning where presentation of a conditioned stimulus (CS) or a context typically predicts an unconditioned stimulus (US). In delay conditioning CS and US normally coterminate, whereas in trace conditioning an interval of time exists between CS termination and US onset. The modeling of trace conditioning is a rather difficult mathematical problem and presents a challenge to the behavior and connectionist approaches mainly due to a time gap between CS and US. To account for trace conditioning, Pavlov (1927) postulated the existence of a stimulus trace in the nervous system. Meanwhile, there exist many other options for solving this association problem. Eight representative models of trace conditioning aimed at building a prospective model are being reviewed in a brief form. As a result, one of

them, comprising the most important features of its predecessors, can be suggested as a viable candidate for a unified model of trace conditioning. By means of mathematical analyses of the stochastic differential equation this model proved to be capable of explaining most of the experimental effects in the field. These effects are: (a) the boundary conditions for hippocampal involvement in Pavlovian conditioning, (b) an optimal values of trace conditioning parameters, (c) the explanation of some timing effects such as inhibition of delay and scalar property, (d) the hippocampal lesion effects, (e) the central role of theta-regulated attention, (f) how neurons and synapses operating on a millisecond time scale can encode information about trace intervals on the scale of seconds and tens of seconds. The model predicts a specific role of hippocampus, mFPC, amygdala, cerebellum, and sensory cortex in trace conditioning as well as potential use of the trace conditioning for detection early cognitive deficits.

P23. The mathematical model of trace conditioning.

Hegumen Theophan (Kryukov[1,] V. I.)
St. Daniel Monastery, St. Daniel Monastery

There are three basic paradigms of classical conditioning: delay, trace and context conditioning where presentation of a conditioned stimulus (CS) or a context typically predicts an unconditioned stimulus (US). In delay conditioning CS and US normally coterminate, whereas in trace conditioning an interval of time exists between CS termination and US onset. The modeling of trace conditioning is a rather difficult mathematical problem and presents a challenge to the behavior and connectionist approaches mainly due to a time gap between CS and US. To account for trace conditioning, Pavlov (1927) postulated the existence of a stimulus tracein the nervous system. Meanwhile, there exist many other options for solving this association problem. Eight representative models of trace conditioning aimed at building a prospective model are being reviewed in a brief form. As a result, one of them, comprising the most important features of its predecessors, can be suggested as a viable candidate for a unified model of trace conditioning. By means of mathematical analyses of the stochastic differential equation this model proved to be capable of explaining most of the experimental effects in the field. These effects are: (a) the boundary conditions for hippocampal involvement in Pavlovian conditioning, (b) an optimal values of trace conditioning parameters, (c) the explanation of some timing effects such as inhibition of delay and scalar property, (d) the hippocampal lesion effects, (e) the central role of theta-regulated attention, (f) how neurons and synapses operating on a millisecond time scale can encode information about trace intervals on the scale of seconds and tens of seconds. The model predicts a specific role of hippocampus, mFPC, amygdala, cerebellum, and sensory cortex in trace conditioning as well as potential use of the trace conditioning for detection early cognitive deficits.

P24. Let us reconsider the role that the Pavlovian CS plays in conditioned reinforcement.

Troisi, J.R.
Saint Anselm College, Psychology

Inspection of the vast majority of studies published in addiction, psychopharmacology, and behavioral pharmacology journals report that "conditioned reinforcers" can reinstate extinguished drug self-administration in rats. Interestingly, this reinstatement is not as robust as once thought, and when it occurs - it occurs under limited conditions. In fact, more recent investigations have shown that operant discriminative stimuli have a more profound effect on reinstatement of extinguished drug-reinforced responding. Perhaps the biggest problem in the reinstatement literature is the underlying notion that conditioned reinforcement is predicated on (if not reducible to) Pavlovian S-S relationships. Of course Skinner's new-response method showed that a Pavlovian CS can function as a secondary reinforcer; however, all instances of conditioned reinforcement do not involve S-S contingencies. Such contingencies are artifacts, rather than mediators, of operant activity and this may be important for understanding mechanisms of relapse. Contrasts between higher-order conditioning and the heterogeneous operant chain are made.

P25. Morphine Prevents the Development of Stress Enhanced Fear Learning in an Animal Model of Post-traumatic Stress Disorder.

Szczytkowski-Thomson, J.L.[1,2], Lebonville, C.L.[1], Lysle, D.T.[1]
[1]*University of North Carolina at Chapel Hill, Psychology*
[2]*Messiah College, Psychology*

Post-traumatic stress disorder (PTSD) is a chronic and debilitating anxiety disorder characterized by exaggerated fear and/or anxiety that may develop as a result of exposure to a traumatic event. The current study utilizes the stress enhanced fear learning (SEFL) animal model of PTSD to investigate the pharmacotherapeutic use of morphine as a preventative treatment for PTSD. Rats are exposed to a severe stressor (15 foot shocks) in one environment (Context A) and then subsequently exposed to a milder form of the same stressor (single foot shock) in a different environment (Context B). Animals that did not receive prior shock treatment exhibit fear responsiveness to Context B in line with the severity of the single shock given in this context. As with previous studies, animals that had received prior shock treatment in Context A exhibit an exaggerated fear response to Context B. Furthermore, animals receiving a single dose of morphine immediately following the severe stressor in Context A continue to show an enhanced fear response in Context B. However, animals receiving repeated morphine administration (three injections separated by 24 hours) after exposure to the severe stressor in Context A or a single dose of morphine at 48 hours after the severe stressor did not exhibit an enhancement in fear learning to Context B.

These results indicate that morphine treatment following a severe stressor may be useful in preventing or reducing the severity of PTSD in at-risk populations.

P26. Learning & Behavior Special Issue on Computational Models of Classical Conditioning.

Schmajuk, N.A., Alonso, E.
Duke University, Psychology & Neuroscience

Recently, we acted as Guest Editors for a Special Issue on Computational Models of Classical Conditioning of Learning & Behavior. In order to present the reader with a coherent issue rather than a disjointed collection of papers, we set three requirements for contributors to our project: models should be tested against a list of previously agreed phenomena; model parameters should be fixed across simulations; and authors should make available the simulations they used to test their models. These requirements of the project resulted in three major products: 1.The first is a list of fundamental classical conditioning results for which there is a consensus about their reliability, and that has acted to guide each of the papers that appear in this issue. 2. The second outcome of this project is that it provides the necessary information to evaluate each of the models. Wills and Pothos (2012) suggested that the competence of a model could be assessed by analyzing the number of successes in describing the experimental data using a fixed set of model parameters that apply to all the phenomena that the model is intended to address. They recommended adopting ordinal adequacy as the primary measure of a model success. 3. The third outcome is a repository of computational models ready to generate simulations. We hope that the Special Issue provides a way to find promising avenues for future model development.

P27. Opioids and stress: Activation of opioid receptors during a brief stressor enhances learning in males.

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The opioid system is most often associated with pain and related sensory mechanisms that are mediated by its activity in the periphery. However, opioids can also convey information about the environment to the central nervous system for cognitive processing. Endogenous opioids fall into three major classes: enkephalins, endorphins, and dynorphins, with corresponding receptor types, delta, mu, and kappa, respectively. Although they tend to induce similar analgesic effects when bound to their specific peripheral receptors, their central functions differ. For instance, mu and delta opioid receptor activation induces elevations in mood (Broom et al., 2002; Rubinstein et al., 1996), whereas kappa opioid receptor activation tends to induce states of dysphoria or depression (Bruchas et al., 2010). These differences in action in turn may mediate different responses to stressful life events. Here we hypothesized that endogenous opioids may enhance learning after stressful life experiences. To test this hypothesis, Sprague Dawley male rats were injected with an opioid receptor antagonist, naltrexone, or saline, and were then either returned to their homecages or exposed to 10 minutes of swim stress. 24h later, all

animals were trained with delay eyeblink conditioning, an associative learning task in which animals must learn to associate two environmental stimuli together. Overall, the male rats in the saline group that were exposed to the swim stress learned better than those that were not stressed. However, those rats that were injected with the opioid antagonist prior to the stressor did not learn better. These data indicate that activation of opioid receptors during a stressful event can increase learning in the near future. Presumably, this mechanism is centrally mediated, and if so, these results implicate endogenous opioids in the positive modulation of learning and the ability to make rapid associations about events in the environment.
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P28. Anxiety is not fear: Paired-housing predictably facilitates within-session extinction of avoidance behavior but does not impact first-trial avoidance responses in Wistar-Kyoto rats.

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[1]VA New Jersey Health Care System, Neurobehavioral Research Laboratory
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The perseveration of avoidance behavior, even in the absence of once threatening stimuli, is a key feature of anxiety disorders. This phenomenon can be observed the behaviorally inhibited Wistar-Kyoto (WKY) rats, who in comparison to outbred Sprague-Dawley rats, demonstrates the impaired extinction of an acquired lever-press active-avoidance behavior. Thus, the goal is to determine how to more readily extinguish avoidance in WKY rats. One means of reducing physiological responses to anxiety, and conditioned fear, in social species is the presence a conspecific animal. In male WKY rats, it has been found that social partnering, daily 30 minute interactions with a male conspecific, significantly impaired the acquisition and facilitated the extinction of classically conditioned fear, measured as freezing in response to an acoustic stimulus (Dasilva et al., 2011). Therefore, in the current study we tested whether pair-housed WKY rats would show slowed acquisition and facilitated extinction of active avoidance behavior in comparison to single-housed WKY rats. Male WKY rats were randomly assigned to single- and pair-housed conditions upon arrival. After one month of acclimation to their housing environment, rats were trained in lever-press escape-avoidance (E/A). Rats received 12 E/A acquisition sessions (intermittent footshocks preceded by auditory warning signals). These were followed by 9 extinction sessions (warning-signals only). Following no differences in acquisition across housing conditioning, between-session extinction of lever-press E/A appeared facilitated in pair-housed rats; however, the differences between sessions was attributable to significant differences in within-session extinction. Both housing conditions continued to respond with avoidance behavior on the first trial even in the last block of extinction sessions. Thus, paired-housing facilitated within-session extinction in WKY rats (suggesting a parallel to conditioned fear), but, importantly, did not affect the continued emitting of first-trial avoidance responses, a characteristic of WKY rats that is hypothesized to be an analogue of anxiety-related behavior.

P29. 22-kHz Ultrasonic Distress Vocalization and Social Transmission of Fear in Rats: Autoconditioning as Underlying Mechanism.

Kim, J.J., Kim, E.J., Kim, E.S., Covey, E.
University of Washington, Psychology

Social alarm calls alert animals to potential danger and thereby promote group survival. Adult laboratory rats in distress emit 22-kHz ultrasonic vocalization (USV) calls, but the question of whether these USV calls directly elicit defensive behavior in conspecifics is unresolved. The present study investigated, in pair-housed male rats, whether and how the conditioned fear-induced 22-kHz USVs emitted by the 'sender' animal affect the behavior of its partner, the 'receiver' animal, when both are placed together in a novel chamber. The sender rats' conditioned fear responses evoked significant freezing (an overt evidence of fear) in receiver rats that had previously experienced an aversive event (i.e., unsignaled footshocks) but not in naive receiver rats. Permanent lesions and reversible inactivation of the medial geniculate nucleus (MGN) of the thalamus effectively blocked the receivers' freezing response to the senders' conditioned fear responses, and this occurred in absence of lesions/inactivation impeding the receiver animals' ability to freeze and emit 22-kHz USVs to the aversive event per se. Based on these findings that prior experience of fear and intact auditory system are required for receiver rats to respond to their conspecifics' conditioned fear responses, we propose a mechanistic model of 'auto-conditioning' in the development of social signaling of danger by USVs.

P30. Corticosterone is necessary but not sufficient for stress-enhanced fear learning.

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Fear is normally proportional to the level of imposed threat. However, following a severe stressor, future fear learning becomes disproportionate to the actual threat received. The current set of experiments assessed the necessity of corticosterone (CORT) to this stress-enhanced fear learning effect (SEFL). In all experiments, the CORT synthesis inhibitor metyrapone, was used to determine the hormone's effects on SEFL. In Experiment 1, four doses of metyrapone (0, 50, 100, and 150 mg/kg) were administered 1 hour prior to a 15 shock stressor in male Long Evans rats. Metyrapone dose-dependently blocked the ability for the shock to directly condition fear to a context paired with shock, and also prevented the long-term sensitization of future fear learning (SEFL). In Experiment 2, 150 mg/kg metyrapone was injected 1 hour prior to a context test in the stressor context, and in Experiment 3, 150mg/kg was administered immediately after the stressor. When presented at any time point after the stressor, SEFL was not affected. In Experiment 4, 150mg/kg metyrapone was injected 1 hour prior to the stressor, and 10 mg/kg CORT was injected immediately before the stressor. SEFL was rescued if metyrapone-treated rats were given CORT prior to the stressor. In Experiment 5, western blotting was used to analyze the basolateral amygdala (BLA)

after SEFL, as well after metyrapone treatment for changes in the abundance of glutamatergic and GABAergic receptor subunits. SEFL increased the AMPA receptor subunit, glutamate receptor 1 (GluA1), and the δ subunit of the GABAA receptor compared to control rats. As with the behavioral experiments, metyrapone blocked these receptor changes. In conclusion, this data indicate that CORT is necessary for SEFL. Moreover, these data suggest other neurotransmitter systems that may be at play along with CORT. This study may highlight novel therapeutic interventions for harmful stress reactions and their associated disorders.

P31. Classical conditioning mechanisms explain the difference between seeing and doing in rats.

Kutlu, M.G., Schmajuk, N.A.
Duke University, Psychology and Neuroscience

We show that an attentional-associative model of classical conditioning (Schmajuk, Lam, and Gray, 1996) correctly describes experimental results regarded as evidence of causal learning in rats: (a) interventions attenuate responding following common-cause training but do not interfere on subsequent responding during observation, and (b) interventions do not affect responding after direct-cause training or (c) causal-chain training. According to the model, responding to the weakly attended test stimulus is strongly inhibited by the intervention in the common-cause case. Instead, in the direct-cause and causal-chain cases, the strongly attended test stimulus becomes inhibitory, thereby overshadowing the inhibitory effect of interventions. In agreement with the SLG associative model, but not with causal model theory, the data strongly support the notion that the attenuation of responding by interventions only following common-cause training is the consequence of well-known learning processes'latent inhibition, sensory preconditioning, conditioned inhibition, protection from extinction, and overshadowing.

P32. Social Defeat produces prolonged alterations in social interaction, but not on the generalization of contextual fear.

Dulka, B.N., Meduri, J.D., Jasnow, A.M.
Kent State University, Psychology

The experience of social defeat produces striking and prolonged changes social behavior, which requires the amygdala and its interaction with the hippocampus. This behavioral response generalizes across contexts and animals. Similarly, when rodents receive foot-shocks in one context and are tested in a different context at long delays after training, rodents freeze equivalently to the training and to novel contexts. Thus, rodents generalize contextual fear responses over time. Because response to social defeat generalizes across contexts and animals the objective of the present study was to determine the effect of acute social defeat stress on subsequent social behavior and the generalization of contextual fear. Using a resident-intruder paradigm, mice were subjected to two days of social defeat followed by social interaction testing and contextual fear conditioning/testing. Defeated mice displayed increased avoidance of novel conspecifics compared with control mice when tested at 24 hours and 30 days after defeat. However, despite moderate deficits observed in the extinction

of fear, social defeat had no significant effect on the generalization of contextual fear responses. These data suggest that the neural mechanisms underlying the generalization of fear across contexts are not modulated by prior social stress.

P33. Interactions between early life experience and adult social fear learning in rats.

Jones, C.E., Monfils, M.H.
The University of Texas at Austin, Psychology

Adverse early life experience can result in enduring changes in adult social interactions and emotional behavior. Affective and behavioral abnormalities that may emerge before puberty can be difficult to identify and, as a result, often go untreated until adolescence or early adulthood (Kessler et al., 2001).
Fear conditioning provides a useful model with which to study underlying neural mechanisms. In the current study, we applied a social fear-learning paradigm to adult rats that had been fear conditioned as juveniles. As adults, one rat from each cage of a triad was fear conditioned to a white noise CS. The next day, the conditioned rat was returned to the chamber accompanied by a second cage-mate while the noise was played in the absence of the foot-shock (fear conditioning by proxy'FCbP). Socially acquired fear was measured as freezing displayed by this second cage-mate to the CS alone on the following day.
Despite not showing a specific memory of the fear-inducing stimulus, as evidenced by lack of freezing to the first CS presentation during adult fear conditioning, early life fear conditioning at post-natal day 17 led to enhanced social fear learning as adults. Additionally, reconsolidation-based behavioral intervention during adolescence, where the fear memory was reactivated by the presentation of a single CS and subsequently extinguished (retrieval + extinction), retarded direct fear learning during adulthood and prevented enhanced social fear acquisition as adults. These results suggest that, in rats, adverse encounters early in life can influence how fears are acquired in a social setting and targeted behavioral intervention during adolescence can reduce this influence to normal levels.

P34. Impaired social interaction and fear learning after exposure to social defeat.

Meduri, J.D., Jasnow, A.M.
Kent State University, Psychology

In humans, excessive associative fear is a key symptom in many neuropsychiatric disorders, including specific phobias, social phobias, panic disorder and post-traumatic stress disorder (PTSD). The risk for developing subsequent PTSD, however, varies depending on the trauma experienced. For example, people exposed to interpersonal violence have a greater propensity for developing PTSD than people exposed to nonpersonal trauma. Several studies demonstrated that the experience of social defeat produces drastic and prolonged alterations in subsequent agonistic behavior. However, it is unclear how social stress modifies subsequent responses to other emotionally relevant stimuli. The present study uses social defeat as an animal model of trauma and stress to investigate the effects of social stress on subsequent social behavior, anxiety-like behavior, and fear learning and extinction. Mice were subjected to social

defeat and tested 24 hours later for social interaction. 24 hours after the social interaction test, mice were tested for anxiety-like behavior using an elevated-plus maze. One week post-defeat we used a standard cued fear conditioning procedure to examine the effects of prior social defeat on the acquisition, expression and extinction of fear. 30 days post-defeat, mice were tested for fear recovery and social interaction to examine the prolonged effects of social defeat on fear expression and agonistic behavior. Social defeat produced significant effects on social behavior both 24 hours and 30 days post-defeat. In addition, social defeat had no significant effect on the acquisition of fear conditioning but disrupted the within-session extinction and extinction retention. We demonstrate here that social defeat produces long-term alterations in both social behavior and subsequent cued fear extinction. These data suggest that exposure to social stress may act to reorganize fear circuits resulting in prolonged alterations in subsequent emotional learning.

P35. avoidance acquisition in wistar-kyoto (wky) and sprague dawley (sd) rats: shock expectancy or escape from fear?

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In our adaption of the procedures for discrete-trial signaled lever press escape/avoidance, the warning signal continues during shock delivery (continuous warning signal, as opposed to a discrete warning signal). A lever press has two response contingencies: termination of the warning signal and prevention (termination) of shock. Thus, there are two potential explanations for incremental increases in lever presses in the presence of the warning signal: termination of warning signal (i.e., escape from fear) or avoidance of the impending shock. To disambiguate the learning processes apparent in our protocol, we conducted an experiment in which: a) the 60 s warning signal continued in the presence of shock; lever presses terminated the warning signal and prevented shock, b) the warning signal terminated before the first shock, lever press responses terminated the warning signal and prevented shock and c) the warning signal terminated before the first shock, and a lever press prevented shock, but did not terminate the warning signal. A severe reduction in lever press responding in this latter group would provide strong evidence that lever presses are primarily motivated by fear of the warning signal, not necessarily the expectation of impending shock. Subjects were male and female Sprague-Dawley (SD) and Wistar-Kyoto (WKY) rats. To control for initial reactivity, rats within strain and sex were matched for acoustic startle responses and randomly assigned to the three training procedures. Training (20 trials a session) was conducted every other day for 15 sessions. For females, no differences were noted for strain or training conditions. For SD males, inability to remove the warning signal slowed learning; however they still attained a 50% avoidance rate by the last sessions of training. For male WKY rats, no differences were noted between training conditions. All groups, except for SD-M rats, exhibited greater than 80% avoidance by the last session of training. The generally high level of

avoidance achieved by rats without the ability to control warning signal duration strongly supports avoidance of shock (expectancy) as the motivation for lever presses in this protocol. However, male SD rats exhibited a balance between avoidance and escape and may be selectively motivated by escape from fear.

P36. Multimodal Navigation in Virtual Space.

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For accurate perception and understanding of reality information from multiple sensory modalities must be processed, translated into a common neural code and then integrated together into a unified experience. In order to study these multisensory integration processes we developed a rat virtual reality apparatus that allows for precisely controlled presentation of visual and auditory information in virtual environments. First, we demonstrated that rats can readily learn to avoid edges in virtual worlds and can therefore be constrained to finite two-dimensional environments. Next, we compared the relative contributions of auditory and visual information in a beacon navigation task and a spatial learning task, modeled after the Morris water maze. We used traditional navigational measures, such as latency and distance to reward, as well as target quadrant occupancy in the spatial learning task. In addition we measured the rate of reward tube checking as a measure of reward expectancy. Our findings show several expected results, such as visual dominance in beacon and spatial navigation. However, we also present several unexpected findings, principally related to the measurement of reward expectancy, which shows a very different multisensory interaction pattern from traditional navigational measures. Our findings are consistent with the notion that reward expectancy reflects a temporal learning process and that the auditory modality is dominant in the temporal domain. Overall, the use of multimodal rodent virtual reality provides a fertile new avenue of research with the potential to answer fundamental questions about the underlying neural mechanisms of multisensory integration across both time and space.

P37. Reduction and enhancement of Pavlovian retroactive cue interference as a function of training in multiple contexts.

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Pavlovian retroactive cue interference refers to a reduction in conditioned responding to a target cue (X) at test when pairings of another cue with the outcome (e.g., A-O) are interposed between the target cue-outcome pairing phase (e.g., X-O) and testing on X. Two conditioned suppression experiments with rats were conducted to

determine whether renewal of retroactive cue interference (i.e., the recovery of responding to the target cue when testing occurs outside of the context of interference training) is similarly modulated by context switching manipulations that alter renewal effects observed in retroactive outcome interference (e.g., extinction). Experiment 1 found that training the interfering association in multiple contexts decreases renewal of retroactive cue interference. Experiment 2 found that training the target association in multiple contexts increases renewal of retroactive cue interference. The possibility of similar associative mechanisms underlying both cue interference and outcome interference is discussed.

P38. Attenuating the contextual specificity of latent inhibition.

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Recent data indicate that extinguished fear returns when the testing conditions differ from those of treatment. Moreover, extensive extinction training, extinction in multiple contexts, spacing the extinction trials, and spacing the extinction sessions, all reduce the return of fear. Additionally, extensive extinction and extinction in multiple context summate, and spacing of the extinction trials and of the extinction sessions summate to further reduce the return of fear. Here we evaluated whether these techniques also attenuate the release from latent inhibition produced by testing outside of the preexposure context and whether they summate to produce further attenuation of release from latent inhibition. In two experiments, with rats as subjects in a lick suppression preparation, we assessed the effects of massive CS preexposure, CS preexposure in multiple contexts, spacing the CS-preexposure trials, and spacing the CS-preexposure sessions in reducing the release from latent inhibition that results from a context shift. Fear responding was attenuated by all four manipulations. Moreover, extensive CS preexposure in multiple contexts, and conjoint spacing of the CS-preexposure trials and sessions were more effective in reducing the release from latent inhibition than each manipulation alone. Thus, techniques effective in decreasing the return of fear following extinction are also effective in decreasing the release from latent inhibition in an animal model of anxiety.

P39. Latent inhibition affects the associability of CS duration.

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Exposing an animal to a stimulus with no fitness outcome retards its ability to learn about this stimulus' association if subsequently paired with a reward or punishment. Such latent inhibition of learning is currently well accounted for by associative learning models. These explain that a reduction in the associability of the preexposed CS affects learning regarding the link between the physical CS identity and an unconditioned stimulus (US). However, it remains unresolved as to whether this reduction in associability also affects learning about the temporal

properties of the CS, for example its duration during delay conditioning. We present the results from several latent inhibition experiments suggesting that latent inhibition of timing does occur (at least in between-subjects comparisons). However, timing effects are less clear-cut within-subjects, suggesting there may be some generalization of learning about CS duration between novel and preexposed CSs.

P40. Examination of the relationship between chronic nicotine induced tolerance and withdrawal-related deficits in contextual fear conditioning.

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Nicotine addiction is a complex disorder involving the interplay of multiple factors. The ability of nicotine to alter cognition through modulation of learning and memory processes emphasizes the importance of neuroplasticity in the maintenance of addiction. Acute nicotine enhances contextual conditioning in mice, tolerance develops to this effect with chronic administration, and withdrawal from chronic nicotine impairs contextual conditioning. Additionally, chronic nicotine administration has been shown to upregulate nicotinic acetylcholine receptors in the brain, a potential result of nicotine mediated receptor desensitization. While tolerance and withdrawal-induced learning impairments both occur following chronic nicotine administration, it is unknown if these neuroadaptive processes operate through the same biological and cognitive mechanisms. The present set of experiments attempt to elucidate whether chronic nicotine induced tolerance and withdrawal are dissociable events. C57BL/6J mice were implanted with osmotic minipumps that delivered constant nicotine or saline for various durations and then were trained and tested in contextual conditioning either during chronic nicotine administration or 24 hours after pump removal. Chronic nicotine had an enhancing effect on contextual conditioning in a dose- and time-dependent manner. Tolerance developed to this enhancing effect and the duration of chronic nicotine treatment required to produce withdrawal related cognitive deficits differed than that required to produce tolerance. Taken in conjunction with preliminary radioligand binding experimental data, these results suggests that tolerance and withdrawal are mediated by separate mechanisms and may contribute differently to the maintenance of nicotine addiction.
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P41. Acetylcholine and Learning: Are they related and does it matter for associating events across time?

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Decades ago, acetylcholine was considered intrinsic to processes related to attention and/or learning and memory. Much of this was based on its presumed role in dementia associated with Alzheimer's disease. However, in the last decade or so, this

relationship has been questioned and with good reason (Parent & Baxter, 2004). That said, only a few studies have addressed the involvement of acetylcholine in tasks that require an animal to associate stimuli separated in time, such as trace eyeblink conditioning. This type of task is dependent on the hippocampus and is severely disrupted in both patients with Alzheimer's disease and animal models of the disorder (Kishimoto, 2012; Waddell et al., 2008; Woodruff-Pak & Papka, 1996). In the present study, we hypothesized that animals with minimal Ach input to both hippocampi would not learn whereas those with input into one hippocampus could. The immunotoxin 192 IgG-Saporin was infused into the MSDB to selectively kill cholinergic neurons in Sprague-Dawley rats and then trained with trace eyeblink conditioning. A complete bilateral lesion (< 25% ChAT+ cells remaining) prevented early acquisition of the trace response ($p<.05$). Indeed, none of the animals so far trained reached a learning criterion of 60 % CRs during any session of training. In contrast, animals with a loss of ACh in just one hemisphere were able to learn the CR. Finally, animals with half the number of cholinergic neurons remaining were still able to learn trace eyeblink conditioning regardless of whether the damage was bilateral or unilateral. Thus, it would appear that the progressive loss of ACh coincides with the loss of learning potential, especially when that learning requires associations across time. This approach and the experimental results may model the progressive nature of Alzheimer's disease, in which the loss of neuronal function is slow but cumulative.

P42. The loss of presynaptic GABAB1A receptors results in increased rates of context fear generalization.

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Contextual fear conditioning involves pairing a novel context (conditioned stimulus) with several footshocks (unconditioned stimulus) that serve to condition fear to that context. Many studies have demonstrated that shifting contextual cues following context fear conditioning results in reduced freezing, (i.e., the context shift effect). At early time points rodents can discriminate between a training and novel context. However, these shifts in contextual cues become less disruptive as the retention interval between training and testing increases (context specificity is lost by 14 days post-training). In other words, the fear memory is no longer precise or context-specific, but has generalized to novel contexts. In an attempt to investigate potential mechanisms underlying the generalization of fear responses over time, we have identified presynaptic inhibition as playing a role in the precision of context memory. Specifically, we discovered that mice lacking a GABAB1 receptor subtype, GABAB1a, exhibit a loss of context discrimination compared to wild-type animals. Animals lacking GABAB1a receptors showed a significant, but not complete loss of context specificity 24 hours post-training. GABAB1a knock out mice exhibited a complete loss of context discrimination (i.e. generalization) by 5 days post-training. However, knock out mice exhibited normal context discrimination immediately (2 hours) following training, suggesting that GABAB1A receptors are necessary for the retention, but not

acquisition, of context discrimination. Our results indicate that presynaptic inhibition is required for the maintenance of context discrimination and identify GABAB1a receptors as a potential mechanism underlying context fear generalization. We are currently investigating the neural circuit within which these receptors function to regulate context discrimination.

P43. Identifying Psychological and Neural Factors Contributing to Poor Active Avoidance in Rats.

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Active Avoidance is an instrumental conditioning paradigm where subject learn to escape threats and prevent exposure to painful or dangerous unconditioned stimuli. In the laboratory, this is often studied using brief footshocks that can be prevented by shuttling between chamber sides. Pavlovian conditioning occurs early in training before subjects are exposed to the instrumental contingency, and instrumental learning may depend on this early Pavlovian step (i.e. 2-factor theory). Sidman active avoidance (sAA) requires rats to emit an avoidance responses (ARs) at regular intervals to prevent shock delivery. sAA is difficult for rats to learn, partly because there is no explicit warning signal. In fact, up to 30% of trained rats fail to acquire the AR. These Poor Avoiders display excessive fear reactions like freezing, and may model aspects of human pathological anxiety. Thus, we are exploring ways to explain Poor Avoidance and predict which individuals will fail to acquire the AR. To this end, we are analyzing several new measures together during sAA training, such as 22kHz alarm cries, freezing, shock-escape and brain expression of immediate-early genes (cFOS). We are also quantifying the percentage of shocks actually received by the rats, using new custom shock-sensors to evaluate the possibility that passive avoidance strategies contribute to Poor sAA. These new measures appear to identify Poor Avoiders as early as Session 1, well before traditional AA measures show any difference. Post-training cFOS expression was also significantly lower in specific regions of the amygdala and prefrontal cortex for Poor Avoiders, but not other areas. This suggests that Poor Avoidance may be a predictable trait that can be studied with sAA protocols to identify factors contributing to risk vs. resilience in human disorders.

P44. Thyroid Receptor β is Critically Involved in the Effects of Nicotine on Hippocampus-Dependent Memory, while Thyroid Receptor α1 is not.

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Cigarette smoking is common despite its adverse effects on health. Nicotine's effects on cognition may contribute to the development of addiction to tobacco products by enhancing maladaptive drug-context associations or by altering normal neural plasticity. Nicotine may also alter a variety of endocrine functions, including thyroid signaling. Thyroid signaling is critical for neural development and plasticity, and

modulation of this system could have long lasting implications on cognitive processes. Low thyroid hormone levels in adulthood can confer cognitive deficits, and animal models suggest nicotine can reverse some of these changes. Initial examination with Protein/DNA arrays (Panomics) identified hippocampal thyroid receptor (TR) activation during nicotine enhancement of hippocampus-dependent learning. The present work evaluates the functional contribution of TRs (β and α1) in the effect of nicotine on hippocampus-dependent memory using a contextual fear conditioning paradigm. It was hypothesized that TRs would be critical for the acute effects of nicotine on contextual fear conditioning, but the specific receptor types proposed to be important were unclear. To determine the role of TRβ and TRα1 in the effects of nicotine on memory, mice lacking the TRβ and TRα1 gene (KOs) and wildtype littermates (WTs) were administered acute nicotine prior to contextual fear conditioning. Twenty-four hours later, mice were returned to the training context and evaluated for context-evoked freezing for 5 minutes. TRβ WTs receiving nicotine froze more than WTs receiving vehicle alone, while KOs receiving nicotine did not differ from vehicle treated mice; demonstrating a critical role for TRβ in the effect of nicotine on hippocampus-dependent memory. In contextual fear conditioning, TRα1 WTs and KOs receiving nicotine froze significantly more than those receiving vehicle (for both genotypes), indicating this receptor type is not important for the pro-cognitive effects of nicotine.

P45. Differential patterns of learning-induced Arc protein expression within the CA3 and CA1 subfields of dorsal and ventral hippocampus

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Accumulating evidence suggests not only that dorsal and ventral subregions of the hippocampus differentially contribute to some forms of memory, but that the contribution of discrete subfields (CA1, CA3, dentate gyrus) within the hippocampus may also be dissociable. In the present study, we examined the regional distribution of learning-related Arc (activity-related cytoskeletal protein) expression following training in hippocampal-dependent trace fear conditioning. Arc has previously been shown to be tightly linked to the induction of neuronal plasticity, is expressed within various subfields in the hippocampus, and has been implicated as a biomarker of learning. We have shown that trace fear conditioning enhances Arc protein levels, and both trace conditioning and the associated learning-related enhancement of Arc can be blocked by infusing Arc antisense oligodeoxynucleotides (ODNs) or the NMDA receptor antagonist APV into dorsal or ventral hippocampus prior to training. Thus while NMDAr-dependent Arc expression in dorsal and ventral hippocampus appear to be critically involved in acquisition of trace fear conditioning, the extent to which Arc is differentially expressed within discrete subfields of the hippocampus following learning has yet to be characterized. Different groups of subjects were trained in our auditory trace fear conditioning paradigm or served as home-cage, handled control subjects.

Consistent with earlier findings, the present results suggest an increase in Arc expression in dorsal and ventral hippocampus following trace fear conditioning. With respect to the regional distribution of Arc, expression was significantly higher in CA3 relative to CA1 in dorsal hippocampus, whereas expression was notably greater in CA1 relative to CA3 in ventral hippocampus. When considered together with previous data regarding learning-related Arc expression and the known anatomical connections between the hippocampus and amygdala, these data suggest that regionally specific patterns of NMDAr-dependent Arc expression within discrete subfields of dorsal and ventral hippocampus may play dissociable roles in learning.

P46. Pre-testing inactivation of ventral, but not dorsal, hippocampus attenuates expression of trace fear conditioning over extended training-testing intervals.

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It was once widely accepted that damage to the hippocampal system resulted in a graded retrograde amnesia for some types of information learned prior to the surgical or traumatic event. These data were interpreted to suggest that hippocampal-dependent memories are encoded primarily in the hippocampus itself as well as by neocortical networks, but initially rely on hippocampal integrity for retrieval. Furthermore, according to this view, the memory trace is reorganized over time such that the neocortex eventually becomes capable of supporting recall without the hippocampus. Recent data, however, suggest that the time-limited involvement of the hippocampus in memory consolidation is likely more complicated than once thought. Specifically, emerging data suggest that disruption of the hippocampus can produce retrograde amnesia at both recent and remote time points—i.e. a flat gradient. These discrepancies suggest that patterns of retrograde amnesia depend heavily on the learning task in question and the specific manipulation employed; and moreover that there may be different temporal profiles for the dorsal and ventral hippocampal subregions. However, to date there has yet to be a systematic investigation of the relative contributions of dorsal and ventral hippocampus in maintaining trace fear conditioning over time. In the present study, rats were trained using an auditory trace fear conditioning paradigm, and were tested 1, 7, 28, or 42 days later. DH or VH was temporarily inactivated prior to testing using the GABA-A agonist muscimol, and the performance of these subjects was compared to that of subjects receiving pre-testing saline infusions. The results revealed a marked dissociation: pre-testing inactivation of VH impaired recall at all time-points whereas pre-testing inactivation of DH failed to impair recall at any time-point. Collectively, these data suggest that VH, but not DH, remains a neuroanatomical locus for expression of trace fear conditioning over an extended period of time.

P47. Automated detection of movement and location of an earthworm.

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Studies of learning in earthworms date back at least to Yerkes' work in 1912; some might argue that Darwin's final book (1881) on the importance of earthworms to vegetative mould included learning studies. Classical and instrumental learning have both been examined; we recently demonstrated that earthworms are capable of avoidance and escape learning. Nearly all of the prior studies have utilized visual observation of the worms' responses. We present an account of our efforts to automate the process.

First we describe a sensitive electronic switch based on the principle of the darlington transistor, that allows the presence of the worm contacting two sensors to be detected readily. By crawling across two sensors, the worm closes an electrical circuit; the minute electrical current that flows along the worm's skin is amplified via the darlington circuit, allowing a relay to close. This system works well as a means of detecting the arrival of the worm at a pair of sensors, but because the worm leaves a trail of moisture behind itself, the senors often remain activated even after the worm is no longer in contact with the sensors.

Various investigators have tried using “running” wheels to detect locomotion of the worm. We have done so as well, with varying degrees of accuracy, using infrared phototransistors to monitor movement of the wheel. Because the earthworm typically weighs less than 0.5 g, balance and friction are critical; worms sometime crawl around the wheel without causing it to rotate, and thus without the recording of data. We describe angled variations on the running wheel that appear to reduce this problem. Our ultimate goal is to develop an automated system of response recording such that learning studies can proceed in earthworms in a manner free of the problems inherent in visual observation.

(Order of authors 2 through 4 is alphabetical. Support from Albion College Neuroscience Program, Dept, of Psychological Science, Faculty Development Committee, and Foundation for Undergraduate Research, Scholarship, and Creative Activity.

P48. Preventing spontaneous recovery of fear through counterconditioning.

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Previous studies have shown that the successful avoidance of an aversive outcome can activate brain areas generally associated with the experience of a reward (Kim et al., 2006). Likewise, during extinction of fear, the expected aversive stimuli is avoided, suggesting that fear extinction memories could be encoded in brain areas involved in reward learning. We hypothesized that training rats to associate a fear-provoking stimulus with reward delivery (counterconditioning) would result in a more durable fear extinction memory than fear extinction training alone. All rats received auditory fear conditioning. Some rats received extensive auditory extinction

training, whereas other rats received moderate extinction training followed by Pavlovian reward training with the same tone. Spontaneous recovery of fear was measured in both groups. Our data revealed that rats trained to associate the previously fearful tone with a reward delivery exhibited no spontaneous recovery of fear, suggesting that the extinction memory is more persistent when rats learned to associate the tone with a positive value. Our ongoing work uses in vivo physiology and molecular markers of activity to identify brain circuits that participate in both fear extinction and reward learning. We believe this approach could be used to improve the treatment of disorders thought to result from a failure to extinguish fear memories, including anxiety disorders and Post-Traumatic Stress Disorder (PTSD).

P49. The Rodent Lateral Orbitofrontal Cortex is Necessary for Between but not Within Session Pavlovian Extinction.

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Objective: Extinction learning in Pavlovian learning tasks depends upon a number of neural regions e.g. the amygdala. The orbitofrontal cortex (OFC) is a cortical structure that is functionally connected to subregions of the amygdala, yet its role in extinction learning has not been directly assessed. OFC lesions impair performance on reversal learning tasks, which require the simultaneous acquisition of new and the extinction of old, cue-outcome associations. Thus there is good evidence to suggest that the OFC plays a role in extinction. The present study directly assessed the role of the OFC in Pavlovian extinction. Methods: Long Evans rats received 16 presentations of a 15s click stimulus followed by a pellet reward per day for 9 sessions. Cannulae were then surgically implanted targeting the lateral OFC. After 3 more days of acquisition, all animals received 3 days of extinction with an infusion of muscimol (n = 7) or saline (n = 8), followed by 3 days of extinction with no infusions. Extinction sessions were identical to acquisition except that no pellets were delivered. Response frequency at the site of pellet delivery was measured.
Results: Over the first 3 infusion days saline control animals appropriately decreased responding between and within each session. In contrast, muscimol infused animals appropriately reduced responding within each session, but returned to a high level of responding at the start of each day. In the absence of drug infusions, animals that had previously received muscimol showed an appropriate reduction in responding between days. Conclusions: Functional inactivation of the rodent lateral OFC selectively impairs between but not within session extinction. The possible role of the OFC in consolidation and/or the representation of context will be discussed.

P50. Extinction of trace fear conditioning requires the retrosplenial cortex but not the amygdala.

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The amygdala plays a central role in the consolidation, reconsolidation, and extinction of standard delay fear conditioning (DFC). The role of the amygdala in trace fear conditioning (TFC),

however, is currently unclear. TFC, unlike DFC, requires cortical participation for acquisition, which might change the role played by the amygdala. Our lab has previously demonstrated that the amygdala is required for both TFC and DFC acquisition, but it is currently unknown whether the amygdala is necessary for TFC reconsolidation or extinction. First, we tested whether TFC reconsolidation requires the amygdala. DFC or TFC animals were given a CS retrieval trial followed by intra-amygdala infusion of the protein synthesis inhibitor anisomcyin or vehicle. Both DFC and TFC animals showed disrupted fear memory at a remote test after anisomycin infusion, suggesting that reconsolidation of TFC memory also requires amygdala plasticity. We then tested whether TFC extinction requires the amygdala. Here, we blocked NMDA or AMPA receptors in the amygdala during TFC or DFC extinction training and tested extinction memory the following day. DFC animals given either inhibitor showed poor extinction memory whereas TFC animals showed normal extinction despite NMDAR or AMPAR antagonism, suggesting that successful TFC extinction learning may not require the amygdala. Western blots on tissue from trained animals identified the retrosplenial cortex (RSC) as a site showing increased extinction-related pERK expression following TFC, but not DFC extinction. We tested whether the RSC plays a role in TFC extinction by inhibiting intra-RSC NMDA receptors during TFC or DFC extinction. Preliminary results demonstrate that TFC extinction is disrupted by RSC NMDAR antagonism whereas DFC extinction is unaffected. Together, our results indicate that the amygdala and RSC play dissociable roles in DFC and TFC extinction; the amygdala is required for DFC, but not TFC extinction whereas the RSC is uniquely required for TFC extinction.

P51. CaMKII regulates proteasome-dependent increases in GluR2 in the amygdala during fear memory reconsolidation.

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Several studies have shown that retrieval of a context fear memory results in memory "destabilization" in the amygdala and dorsal hippocampus, which requires de novo protein synthesis in order to reconsolidate. Both changes in AMPA receptor phosphorylation and composition and ubiquitin-proteasome mediated protein degradation have been shown to be important in this destabilization process (Jarome et al. 2011; 2012; Lee et al. 2008; Rao-Ruiz et al., 2011); however, very little is known about how these destabilization mechanisms are regulated. Recently, we have shown that CaMKII regulates increases in proteasome activity in the amygdala following fear conditioning (Jarome et al., submitted); however, it is unknown how protein degradation is regulated downstream of NMDA receptors during memory reconsolidation. In the present study, we examined whether CaMKII controls changes in protein degradation and AMPA receptor composition following memory retrieval through its regulation of proteasome activity. Using an in vitro proteasome activity assay, we found that all three types of proteasome activity were increased in amygdala synaptosomal membrane fractions 90-min after context retrieval and this increase in

proteolytic activity correlated with transient increases in the levels of AMPA receptor subunit GluR2 at 90-min. Only proteasome trypsin-like activity was increased at hippocampal synapses 90-min after retrieval and this correlated with increases in GluR2/3 at 7-hrs. Infusion of the specific CaMKII inhibitor myr-AIP or the proteasome inhibitor Blac into the amygdala following memory retrieval completely reversed this increase in proteasome activity in the amygdala, suggesting that increases in proteasome activity may be downstream of CaMKII. Interestingly, only blocking amygdala proteasome activity directly, but not indirectly, abolished increases in hippocampal proteasome activity. Additionally, blocking proteasome activity directly or indirectly abolished increases in GluR2 in the amygdala. These results suggest that CaMKII may regulate memory destabilization following retrieval through its regulation of proteasome activity and that increases in protein degradation are necessary for retrieval-induced changes in AMPA receptor composition.

P52. Corticotropin-releasing factor in the basolateral amygdala impairs fear extinction.

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The neuropeptide corticotropin-releasing factor (CRF) is released during periods of anxiety and stress and modulates learning and memory formation. One region with particularly dense concentrations of CRF receptors is the basolateral nucleus of the amygdala (BLA), a critical structure for both Pavlovian fear conditioning and fear extinction. While CRF has the potential to modulate amygdala-dependent learning, its effect on fear extinction has not yet been assessed. Moreover, while the BLA contains high concentrations of CRF receptors, the cellular distribution of these receptors remains unknown. In the present study, we first used double immunofluorescent staining to determine that CRF receptors are located on both principal excitatory neurons as well as GABAergic interneurons of the BLA. We next examined the modulatory role of CRF on both within-session extinction and fear extinction consolidation. Intra-BLA infusions of high doses of CRF impaired the expression of fear conditioning. Low doses of CRF, however, affected neither the expression of fear conditioning nor within-session extinction learning. When low-dose CRF animals were tested twenty-four hours later, drug free, they showed impairments in extinction memory. These results suggest that enhanced CRF levels within the BLA at the time of fear extinction learning actively impair the consolidation of long-term fear extinction.

P53. A retrieval-extinction procedure reduces recovery of fear in adolescent rats.

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Adolescent rats exhibit a marked recovery of extinguished fear, an impairment of extinction retention which is not evident in pre-adolescent or adult rats. A single nonreinforced exposure to the conditioned stimulus (CS; a retrieval trial) given shortly before extinction has been shown in some circumstances to reduce the recovery of

fear after extinction (e.g., to reduce renewal). The present experiments investigated whether a retrieval-extinction procedure would reduce the recovery of extinguished fear in adolescent rats. Adolescent rats (postnatal day 34-37 at extinction) were trained to fear a white noise paired with shock (in context A). The following day, rats received one nonreinforced CS presentation (a retrieval trial) or equivalent context exposure (no retrieval) in a second context (B) before being returned to their home cage for 10 min. Fear was then extinguished in context B via 30 nonreinforced CS presentations. Animals in the No Retrieval group received 31 CS presentations during the extinction session. In the first experiment, the No Retrieval group exhibited a recovery of fear in the extinction context (ABB) and higher levels of fear in the training context (ABA renewal). A retrieval trial shortly before extinction reduced overall levels of fear in both test contexts (i.e., it improved extinction retention and reduced renewal). In the second experiment, we replicated this effect and also showed that a retrieval trial 10 min after extinction produced a similar reduction in overall levels of fear as retrieval before extinction. These findings suggest potential manipulations to reduce the recovery of extinguished fear in adolescence.

P54. Cycloheximide induced retrograde amnesia for reconsolidation and extinction is dependent on cue exposure duration in rats.

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It is becoming well established that extinction involves new learning, rather than a breakdown of the original association. In support of this, recent research has demonstrated that extinction learning is susceptible to an amnestic agent when presented shortly after an extinction session. Similar results have been demonstrated using a previously stored reactivated memory, where forgetting occurs if the amnestic agent is presented immediately following a reactivation treatment. That both reactivating an old memory (i.e., reconsolidation) and extinction learning involve reexposure to the conditioning stimuli raises the question of when does reconsolidation shift to extinction. Evidence suggests that the duration of the exposure is important in determining which competing learning becomes dominant, and thus susceptible to amnesia. Data presented here using passive avoidance in rats demonstrate retrograde amnesia induced by the protein synthesis inhibitor Cycloheximide for an old reactivated memory when given a brief (15 sec) and moderate (6 min) cue exposure duration, but amnesia for extinction with a longer duration (12 min) leaving the original memory intact. Results are discussed as further evidence that extinction is new learning, that reconsolidation and extinction may require protein synthesis, and that the cue exposure duration is an important factor for obtaining the outcome of retrograde amnesia for extinction. Follow-up work is evaluating whether these amnestic effects follow a state-dependent retrieval failure account of retrograde amnesia.

P55. Memory retrieval and the extinction of Pavlovian conditioning.

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We studied the effect of retrieval-extinction on the relearning of Pavlovian conditioned fear. In Experiment 1a, rats received auditory fear conditioning (unconditioned stimulus [US] = 0.8 mA, 0.5 s footshock). Two days later, rats received a re-exposure to the conditioned stimulus (CS) 10 min prior to CS fear extinction. On the following day, rats were reconditioned via CS-footshock (0.3 mA, 0.5 s) pairings. There were similar profiles of fear extinction and recovery (reacquisition) regardless of whether extinction was preceded or not by memory retrieval. In Experiments 1b and 1c, we varied the initial conditioning US intensity whilst holding constant the reconditioning US intensity to study whether the retrieval-extinction effect may be revealed using a weaker US in training. There was evidence for faster reacquisition when extinction was preceded by memory retrieval. Experiments 2a and 2b studied whether this effect would generalise to reacquisition of context fear conditioning. Rats were trained to fear a context. Two days later, they received a brief re-exposure to the context 10 min prior to context fear extinction. On the following day, rats were reconditioned to fear the context and were tested the next day. Again, we systematically manipulated the training and retraining US intensities. There were similar profiles of responding during context fear extinction. Interestingly, retrieval prior to extinction could retard, have no effect, or augment re-acquisition of context fear depending on the retraining US intensity. Retrieval-extinction appeared to render rats more sensitive to manipulations at reconditioning - resembling naive subjects being conditioned the first time. In contrast, rats that underwent conventional extinction were selectively sensitive to manipulations at original conditioning despite US intensity variations at reconditioning. These experiments suggest a potential avenue to reconcile the diverse effects of retrieval-extinction manipulations on fear recovery reported in the literature.

P56. Retrieval-induced enhancements and decrements in performance.

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The simple act of retrieving a memory has potential to modify that memory as it is updated in response to a changing environment. Many studies show that longer or repeated re-exposures to a previously reinforced stimulus (e.g., CS), result in greater behavioral extinction. Other studies have shown that retrieval may enhance memory expression when re-exposure is brief. Here, we investigate retrieval conditions that lead to enhancements or decrements (e.g, extinction) in performance using contextual fear. We generally find that certain manipulations during retrieval such as prolonged re-exposure to a fearful context or pharmacological enhancements of transcription in the infralimbic cortex (e.g., histone acetylation) lead to robust response loss on subsequent tests. Surprisingly, like long context re-exposure, we found that relatively short durations also lead to greater response loss while intermediate

durations have little effect on behavior. Enhancements of fear expression relative to control were also seen under select retrieval conditions as well as when transcription was enhanced in the prelimbic cortex or amygdala. However, control and follow-up experiments revealed that these enhancements could largely be attributed to handling, impaired extinction, second order conditioning and other processes. These basic findings are consistent with retrieval-induced associative (e.g., extinction) and/or non-associative processes that do not rely on reconsolidation accounts to produce enhancements and decrements in behavior.

P57. Extinction, applied after retrieval of an auditory fear memory, increases Zif268 and rpS6P in prefrontal cortex and lateral amygdala.

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Retrieval of consolidated memories induces a labile phase during which memory can be disrupted or updated. We previously showed that fear memory retrieval leads to increased level of phosphorylated GluR1-receptors (pGluR1), a well known calcium-permeable AMPA receptor (CP-AMPAr) in the lateral amygdala. When a second CS is presented 1 hour after the initial retrieval, the receptors undergo dephosphorylation, possibly suggesting that destabilization of the memory trace underlies the lack of fear reemergence observed after Ret-Ext (Monfils et al., 2009). Clem and Huganir (2010) showed that a central component of Ret-Ext induced erasure of fear is the synaptic removal of CP-AMPAr in the lateral amygdala, a metabotropic GluR1 receptors-(mGluR1r)dependent mechanism leading to memory destabilization and long-term depression (LTD) at LA synapses. They showed that reconsolidation update and CP-AMPAr-mediated-LTD share a requirement for mGluR1r activation. mGluR1r-LTD has been associated with increased phosphorylation of the mammalian target of rapamycin (mTOR) downstream molecule ribosomal protein S6 (rpS6P; Antion et al., 2008). In the present study, we investigate the effect of Ret-Ext on the expression of specific and relevant molecular correlate of memory destabilization and reconsolidation. We tested the effect of Ret-Ext on the validated marker of reconsolidation zinc finger transcription factor (Zif268) and rpS6P expression by immunolocalization in prelimbic cortex (PRL), infralimbic cortex (IL) and lateral amygdala (LA). Our results show that retrieval alone increases Zif268 expression in PRL, IL and BLA confirming that memory reconsolidation is engaged after retrieval in our conditions. Ret-Ext induced a significant increase of Zif268 compared to retrieval and no effect was observed after extinction alone. Ret-Ext, but not retrieval or extinction alone, increased the expression of rpS6P in PRL, IL and BLA. Together, these data suggest that extinction, if applied after retrieval, is incorporated in a memory reconsolidation process.

P58. Attentional deficits in mouse offspring born small or large for gestational age are due to a double dissociation between inattention and impulsivity.

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Inappropriate gestational sizes at term (either small or large for gestational age, SGA and LGA respectively) increase the risk of mental disorders of cognition and attention, namely attention deficit/hyperactivity disorder (ADHD), autism, and cognitive delay. However, it is not known whether this is due to environmental factors associated with SGA and LGA, or directly linked to abnormal gestational growth. To test this, we tested adult male mice from normal maternal diets, SGA born to dams fed a low protein diet, and LGA born to dams fed a high fat diet on a series of operant tasks assessing reward and attention. We first examined animals on a version of Pavlovian conditioned approach (PCA) developed for mice. In PCA, approaching a cue that predicts reward, rather than approaching the reward itself, has been associated with inattention and addiction in outbred rats. SGA offspring displayed an increased propensity to approach the cue, suggesting that they are particularly at risk of distraction by environmental stimuli. After PCA, animals were trained on FR1. LGA were slightly delayed at acquiring FR1 over the first 5 days but performed equivalently after additional training. Animals were then trained on a progressive ratio task to assess motivation. LGA offspring terminated responding significantly earlier than controls, indicating deficient motivation under challenging conditions. Following this, we tested animals on a 5-choice serial reaction task, modeled after similar 5-choice tasks used to assess ADHD. Both SGA and LGA offspring had fewer correct trials, but due to increases in omitted trials (inattention) in SGA versus increases in incorrect and premature trials (impulsivity) in LGA. However, extensive overtraining mitigated these differences. Overall, SGA and LGA in our model are directly linked to attentional deficits, but these are due to dissociable errors in salience/inattention in SGA offspring versus motivation/impulsivity in LGA offspring.

P59. Sex Differences in the Generalization of Contextual Fear.

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There is a high prevalence of anxiety disorders among adults and, females are 60% more likely to suffer from an anxiety disorder than males. One hypothesis for these findings may be that females exhibit higher rates of fear generalization than males. It has been demonstrated that the generalization gradient for contextual cues flattens over time whereas retention of the learned response remains intact in male subjects. The current experiment was designed to investigate the possibility of sex differences in the generalization of contextual cues. 184 male and female Long-Evans rats were trained and tested in a passive avoidance procedure to examine sex differences in the forgetting of stimulus attributes, as inferred from flattening of the generalization gradients. Rats were tested at different retention intervals (1, 3, 5, or 7 days) in either the same context as training

or in a significantly altered context. At 1 day, male and female rats displayed equivalent levels of reduced fear when tested in a novel context, as expected (i.e., the context shift effect). Males continued to express reduced fear in a novel context across all retention intervals, whereas females exhibited comparable levels of fear in either context after 3 days. Overall, females showed no significant differences in the expression of fear between contexts at the 3, 5, and 7 day retention intervals. These results demonstrate the generalization gradient for contextual cues flattens at a faster rate in female rats. Current work in the lab is attempting to elucidate the role of estrogens in the generalization of fear.

P60. DIFFERENTIAL ONTOGENY OF OBJECT AND PLACE NOVELTY IN DEVELOPING RATS.

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Rats display a preference for exploring novel objects (object novelty). Although novel object recognition is clearly exhibited on postnatal day (PD) 20-23 (Reger, Hovda, & Giza, 2009), the reporting of the ontogenetic profile of place novelty recognition in developing rats has been inconsistent in the recent literature (e.g. Kruger et al., 2012; Ainge & Langston, 2012). Here, we report that object novelty is present in both PD21 and PD26 rats, while place novelty emerges sometime between PD21-26. Rats were habituated to the arena in three 10 min sessions. The first test session was either object or place novelty (5 min exploration, 5 min delay, 3 min testing session) on PD20-21(n = 20) or PD25-26 (n = 21), followed by the second test session with the opposite task the following day (PD22 or 27). Novelty ratios (time spent exploring the novel object/total time spent exploring both objects) were contrasted by matched-pair t-test with chance performance (50%). Performance was not affected by task order. Object novelty ratios exceeded chance and did not differ across age (combined ratio = 74.5% +/- 2.3%). Place novelty ratios increased significantly with age ($p < .021$) and exceeded chance in PD25-27 rats (64.3% +/- 3.4 %) but not PD20-22 rats (51.7% +/- 4%). These findings are discussed in relation to other studies of incidental spatial learning in developing rats (ibid.; Schiffino et al., 2011).

P61. Development of Amygdala Modulation of Cerebellar Learning.

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Auditory fear conditioning in rat pups can be established as early as postnatal day (P)16, whereas auditory eyeblink conditioning emerges ontogenetically after P17. The amygdala modulates the rate of acquisition of eyeblink conditioning in adult animals and may also play a role in the ontogeny of eyeblink conditioning. The current study examined the effect of amygdala inactivation on acquisition of delay eyeblink conditioning in rat pups trained on P17-19 or P24-26. Pups were trained twice daily, with 4-hour intervals between sessions, for a total of 6 sessions. Sessions 1-5 consisted of 45 paired CS-US training and 5 CS-alone trials. Prior to each of these sessions, pups received bilateral central amygdala infusions of either bupivacaine (0.3 ul each side, 1.2%) or vehicle. On

session 6, no infusion was given and pups were presented with 50 CS-alone trials. All six sessions were video-taped, and automated scoring of freezing responses was completed with frame by frame comparisons. As observed in previous studies, P24-26 saline-treated pups showed a higher percentage of eyeblink conditioned responses (CR) than P17-19 pups. Both the P24-26 and P17-19 pups that received bupivacaine showed impairments in eyeblink CR acquisition as compared to age-matched controls. Finally, there was a higher level of freezing observed in saline-treated animals than animals that received intra-amygdala infusions of bupivacaine. The findings indicate that the amygdala modulates acquisition of eyeblink conditioning early in ontogeny, as eyeblink conditioning starts to develop.

P62. The prelimbic cortex contributes to the down-regulation of attention towards redundant cues.

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Previous research suggests disruption of activity in the prelimbic (PL) cortex produces deficits in tasks requiring preferential attention towards cues that are good predictors of an event. By manipulating cue predictive power, we clarify this role using Pavlovian conditioning. Experiment 1 showed pre-training excitotoxic lesions of the PL cortex disrupted the ability of animals to distribute attention across stimuli conditioned in compound. Experiment 2a demonstrated that these lesions did not affect the ability to block learning about a stimulus when it was presented simultaneously with another stimulus that was previously paired with the outcome. However, experiment 2b revealed that PL-lesioned animals learnt about this blocked cue faster than sham-lesioned animals when this stimulus alone was paired with reinforcement, suggesting these animals did not down-regulate attention towards the redundant cue during blocking. Experiment 3 tested this hypothesis using an unblocking procedure designed to explicitly reveal a down-regulation of attention during blocking. In this, sham-lesioned animals were shown to down-regulate attention during blocking. PL-lesioned animals did not exhibit this effect. We propose that observed deficits are the result of a specific deficit in down-regulating attention towards redundant cues, indicating the disruption of an attentional process described in Mackintosh's (1975) attentional theory.

P63. Psychophysics of associative learning: Quantitative properties of the distribution of associative strengths.

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We studied the psychophysics of associative learning. Participants were exposed to a variant of Crump et al. (2007)'s streamed-trial procedure, during which streams of 100-ms stimuli were presented. They had to judge the contingency between a target cue and an outcome by choosing "yes" or "no" when asked if the cue was more likely (experiment 1) or less likely (experiment 2) to appear following the outcome. Furthermore, the participants had to indicate how confident they were of their judgment

(not sure, sure, or very sure). The contingencies presented, as measured by the ΔP index, were -0.8, -0.4, 0, 0.4, and 0.8. We assumed that, 1) when a target cue and the outcome are paired, an association between the two is created, and that the strength of that association can be characterized as a random variable with a mean, μ, and a standard deviation, σ; and 2) that each confidence rating corresponds to a different response criterion above which the participant chooses "yes", and below which he chooses "no". A signal detection theory analysis was applied to the results, in order to study the shape (Is it Gaussian?), variance (Is it equal across distributions?), and mean (Is it a linear function of the contingency?) of the distributions obtained from each of the five random variables for each of the two experiments.
Keywords: Associative Learning; Psychophysics; Signal detection theory; Confidence rating; Streamed-trial procedure

P64. Posterior parietal cortex and surprise in Pearce-Hall associability changes.

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Prediction error plays an important role in associative learning. In some models (e.g., Pearce & Hall, 1980), the ease by which a cue enters into new associations, termed its associability, is proportional to the magnitude of that error. Previous research from our laboratory delineated a brain circuit critical for increasing cue associability after the induction of prediction error through the surprising omission of expected events. That research suggested separable brain systems for changing the associability parameter and for using that information in new associative learning. Here, we found that inactivation of the posterior parietal cortex (PPC) at the time of surprise prevented the associability enhancements normally found in the Serial Prediction Task (Wilson, Boumphrey & Pearce, 1992). In the first phase of this task, animals received serial light-tone compounds on a 50% food reinforcement schedule to establish a strong light-tone association. Next, prediction error was induced in "Surprise" rats by omitting the tone on the nonreinforced trials, while "Consistent" rats continued to receive the light-tone compound on all trials. Before each session in this phase, some rats in each training condition received bilateral infusions of 1,2,3,4-tetrahydro-6-nitro-2,3-dioxo-benzo[f]quinoxaline-7-sulfonamide (NBQX), a competitive AMPA-type glutamate receptor antagonist, and others received only vehicle infusions. Finally, the associability of the light was tested by examining the rate of learning with direct light-food pairings in the absence of any infusions. NBQX infusions at the time of surprise reversed the facilitating effects of prediction error on learning about the light in test. We discuss implications of these results for associability circuitry in light of prior evidence that performance in this task is impaired by NBQX inactivation of a major PPC afferent, the basal forebrain substantia innominata, at the time of test, but not by NBQX inactivation of that region at the time of surprise (Holland & Gallagher, 2006).

P65. Facilitation of Within-Compound Associations.

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Interspersed presentations of complex stimuli, XB and AB, have been used to produce inhibitory relationships between unique elements of those compounds, X and A (Espinet, Iraola, Bennett, & Mackintosh, 1995). Subjects seemingly learn that Stimuli X and A are mutually exclusive events. Additionally, if Stimulus A is subsequently paired with an aversive stimulus (i.e., footshock), then X will function as a conditioned inhibitor for that aversive stimulus. In a fear conditioning preparation with rats, we replicated the finding that many XB and AB discrimination trials followed by reinforcement of A results in the observation of conditioned inhibition between X and a transfer excitor, whereas few discrimination trials do not (Experiment 1). In Pavlovian conditioned inhibition training one can observe either conditioned inhibition or second-order conditioning depending on the number of training trials, we sought to determine whether a similar distinction would occur using Espinet pretraining. In Experiment 2, we found that few Espinet pretraining trials resulted in a facilitative X-footshock relationship. Experiment 3 investigated the role of within-compound associations in this facilitated responding to X. This series provides further support for the view that, as the number of training trials increases, within-compound associations shift from serving a facilitative role to serving in an inhibitory-like role.

P66. Effect of apparatus configuration on cocaine-induced conditioned place preference in mice.

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Drug-seeking behavior is often induced with environmentally associated cues and studied with a conditioned place preference (CPP) procedure. Two common types of CPP apparatus configurations have either one or two compartments, yet few experiments have compared the effects of these differing approaches. This study examined the relevance of apparatus configuration on the acquisition and extinction of cocaine-induced CPP. Different groups of C57BL/6 mice received CPP trials in a one- or two-compartment tactile floor apparatus. Two-compartment chambers were identical to one-compartment but included a clear divider splitting the chamber area in half with the opposing CS flooring/side visible. CPP acquisition consisted of animals being placed on their CS+ or CS- paired floor following a cocaine (+) or saline (-) injection. CPP was strongest in the two-compartment compared to one-compartment groups. In addition, preference was greatest when cocaine was paired with alternating rather than consistent chamber sides. Behavioral differences demonstrated with apparatus configuration did not correspond to differences in retrieval-induced cFos activation in several brain regions. In contrast to effects on acquisition, extinction of CPP was strongest with a one-compartment procedure. These findings suggest that a two-compartment configuration facilitated acquisition of a

cocaine-induced CPP while attenuating CPP extinction. The application of different CPP configurations highlights important distinctions between acquisition and extinction and may be useful in determining the underlying substrates and relevant stimuli for each process in cocaine abuse.

P67. Behavioral and neural analysis of the priming of fear memory.

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We recently showed that a single pairing of light with a weak footshock, insufficient to support fear memory formation, primes future learning such that a second pairing presented within a time window from about 1 hour to 3 days results in a robust and long-lasting fear memory. We also showed that the priming of future learning depended on PKA activity in the amygdala. Several questions remain about the nature of the apparent priming effect, including whether or not evidence of long-term memory would be observed if we measured a different fear response and whether there are distinct cellular events that are associated with the priming of memory after a single trial or the formation of long-term fear memory (LTM) after two spaced trials. Results showed that rats trained with a single light-shock pairing did not show any evidence of LTM when freezing behavior is measured. This affirms our previous findings with fear-potentiated startle and supports our conclusion that with these parameters a single light-shock pairing serves to facilitate future learning. Next, we further examined the cellular events engaged after a single training trial or after two spaced trials. There was a significant increase in the phosphorylation of ERK/MAPK in the amygdala which was only observed after a single training trial, while there was increased phosphorylation of the GluR1 subunit of the AMPA receptor, CREB, and p70s6 kinase after both the first and second training trials. In a separate experiment, rats were trained with a single trial or two spaced trials and the expression of GluR1 protein in distinct cellular compartments was measured using subcellular fractionation. Preliminary results show there was an increase in synaptosomal GluR1 expression in the amygdala in rats given two-training trials compared to rats given a single training trial or two unpaired trials. These data are consistent with the notion that LTM formation depends on an increase in synaptic expression of GluR1-containing AMPA receptors. Collectively, these results indicate that a single light-shock pairing primes future learning and that the priming and induction of LTM depend on somewhat unique cellular changes.

P68. Fear Generalization and the Order Effect in Mice.

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As an environment is explored, the hippocampus must attend to the details and either create a contextual representation from scratch, or recall and reinstate a representation of a previously-encountered context, in order to guide behavior. This process occurs within the extent of the behavioral experience, yet the relevant aspects of the context and their influence on discrimination between two similar or very distinct contexts is not yet fully understood. In the present experiment, we conditioned

mice to fear a context (A), and the following day tested their fear to two of the following three contexts: the same context (A), a highly similar but distinct context (B), or a very distinct context (C). We found that the freezing for each context varied along a generalization curve, with generally the highest fear to A, intermediate fear to B, and lowest fear to C. However, we discovered a profound order effect on test day, whereby the first context experienced has elevated freezing, while the second context has reduced freezing, independent of which context was being tested. Though we systematically examined the effects of varying: type of transport to and from the context chamber, extended habituation to an unshocked context before acquisition, using discriminable odors between contexts, and adding a week between acquisition and test, we saw no influence on the order effect. We conclude that the robust nature of the order effect in mice likely relates to an evolutionary benefit to treating the first context experienced after a shock with more caution, and hence more fear, than a context experienced following a safe environment.

P69. Appetitive behavioral traits and stimulus intensity influence maintenance of conditioned fear.

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When pairing a conditioned stimulus (CS) with an unconditioned stimulus (US) a variety of conditioned responses (CR) may develop. Following training, CR may occur in the presence of the CS, US, or when subjects are re-exposed to the training context. When fear conditioning rats with a foot-shock US, the intensity of the shock influences the amount of cue- and context-induced freezing exhibited following training (Baldi et al., 2004). In addition, recent evidence suggests that rats that develop predominantly CS-directed responses differ from those that develop predominantly US-directed responses during appetitive training (Morrow et al., 2011). In the current study, we investigated how subjects' behavior in an appetitive training paradigm, i.e. their propensity to display CS-directed vs US-directed responses, predicts differences in freezing behavior following fear conditioning, as a function of US intensity. In addition, we employed a typical extinction paradigm as well as extinction within a reconsolidation window opened by a single CS-exposure (described in Monfils et al., 2009) to attenuate cue-induced fear responses. We report that both the individual's propensity to engage in orienting behavior, as well as US intensity, impact the maintenance of conditioned fear responses after extinction.

P70. Using Response Stereotypy to Detect the Emergence of a Habit.

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Initially, goal-directed operant behavior is sensitive to outcome value, but becomes insensitive to value changes as behavior becomes habitual with extended training. We examined the relationship between the features of ongoing behavior and insensitivity to outcome value. Subjects were trained on a VI 30s schedule for 25 days before being given an outcome devaluation test during an extinction session. Rates of responding increased

and temporal variability decreased over training. We tracked 6 specific indicators of stereotypy over the course of extended training, and these indicators predict the degree of perseveration during outcome devaluation. This approach may allow for online monitoring of behavior as it transitions between goal-directed and habitual modes of action.

P71. Enhancing the rescue effort: Effortful learning increases neurogenesis through an increase in cell survival.

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Learning rescues new neurons from death in the adult dentate gyrus (Gould et al., 1999; Shors et al., 2011). Providing that learning does occur, animals that require more training trials to learn retain more new neurons (Dalla et al., 2007; Waddell & Shors 2008; Curlik & Shors 2011). These data suggest that effort may be a critical factor in the rescue effort. In previous studies, we determined that training with a physical skill task using an accelerating rotarod increases the number of surviving neurons (Curlik et al., in prep). In the present study, adult female Sprague-Dawley rats were trained on the same type of accelerating (4-40 RPM) rotarod procedure over a 4 day period (4 trials per day). To increase the amount of effort expended during the training procedure, cold water was placed under the rod. If animals were to fall off the rod during training, they would very briefly experience the cold water. This way, the animals were more motivated to remain on the rod during the trial. Indeed, female rats training in this way learned the task very well (p's < .05), with latencies to stay on the rod approaching the upper limit of 600 seconds. As a consequence, many new neurons were rescued from death. Animals trained for the 4 days retained nearly twice as many newborn hippocampal cells as those that were not trained ($p < .05$). These data indicate that learning an effortful physical skill task drastically increases the number of newborn neurons rescued from death in the adult female rat's hippocampus. These results suggest that engaging in a mental/physical activity that requires effort, such as learning a new sport or dance, as well as other types of complex motor skill training, increases the numbers of new neurons that are retained in the adult hippocampus. If practiced and accumulated over time, such an increase in neuronal number might prevent some of the cognitive decline that occurs during normal aging as well as age-related diseases, such as Alzheimer's and dementia.

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P72. Involvement of medial and lateral entorhinal cortex in delay eyeblink conditioning paradigm of latent inhibition in rats.

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The entorhinal cortex (EC) is a primary source of input to the hippocampus. In a prior study, we found a double dissociation between hippocampal and entorhinal functions: EC lesions eliminated latent inhibition (LI) of classical eyeblink conditioning, but did not interfere with spatial learning in a water maze. In contrast, hippocampal lesions hindered spatial learning but did not affect LI. LI refers to the retardation in learning of a conditioned stimulus (CS)-unconditioned stimulus (US) association following the repeated non-reinforced presentations of the CS alone. The current study focused on the involvement of the EC in LI by examining the contribution of its two major divisions, medial entorhinal cortex (MEC) and lateral entorhinal cortex (LEC). Recent studies found that neurons in LEC exhibit very little spatial selectivity, whereas MEC neurons are spatially tuned and are involved in path integration, suggesting that the two divisions process qualitatively different types of information. In the present study, male Sprague Dawley rats received either an MEC or an LEC ibotenic acid lesion or sham surgery. Following recovery, a delay eyeblink conditioning paradigm was used to assess LI. During the pre-exposure phase, rats received either 30 trials of CS alone (82dB, 500ms white noise, 25 - 35s ITI) or were placed in the conditioning box for the same duration without CS presentation. Pre-exposure was immediately followed by paired CS-US conditioning (100 trials per session for four sessions) with co-terminating CS and US (10V, 10ms stimulation) and an average inter-trial interval of 30 sec. Our results indicate that lesions of the LEC abolish latent inhibition while lesions of MEC doesn't impact this latent learning suggesting that the two regions of the entorhinal cortex may encode and process different information characteristics in eyeblink conditioning paradigm of latent inhibition.

P73. Cerebellar Cortical Administration of the Cannabinoid Agonist WIN55,212-2 Impairs Acquisition of Delay Eyeblink Conditioning in Rats.

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Eyeblink conditioning is established by paired presentations of a conditioned stimulus (CS) such as a tone or light and an unconditioned stimulus (US) that elicits the blink reflex. Delay eyeblink conditioning involves the CS terminating with the onset of the US and has been demonstrated to require intact cerebellar circuitry. CS and US information are conveyed to the cerebellar interpositus nucleus and cortex. The cerebellar cortex, particularly the molecular layer, contains the highest density of cannabinoid receptors (CBR1) in the mammalian brain. The CBR1s are located on the axon terminals of parallel fibers, stellate cells, and basket cells where they inhibit neurotransmitter release.

Research from our lab indicates that WIN55,212-2 injected subcutaneously impairs acquisition, retention, and extinction of delay eyeblink conditioning. The hypothesis proposed from these studies is that WIN55,212-2 impaired eyeblink conditioning by blocking LTD induction within the cerebellar cortex. However, these studies have used systemic CB1R administration and localization of the effect has not been demonstrated. The current study infused different concentrations (0.1 µg/µL, 1 µg/µL, or 10 µg/µL) of WIN55,212-2 into the cerebellar cortex during acquisition of delay eyeblink conditioning. The rate of spontaneous or non-associative blinks was not affected by any of the concentrations of the drug. However, both 1 µg/µL and 10 µg/µL infusions impaired the rate of acquisition of delay eyeblink conditioning. The deficit in the 10 µg/µL group did not statistically differ from a group that had received subcutaneous injections of WIN55,212-2 from a previous study. Following cessation of administration both groups of rats learned to control levels. The CBR1 antagonist SR141716A was administered 30 mins prior to WIN55,212-2 and blocked the effect of WIN55,212-2. Additionally, WIN55,212-2 administered into the anterior interpositus nucleus did not impair the rate of learning. These results indicate that infusions of WIN55,212-2 into the cerebellar cortex, but not the deep nuclei, mimic impairments from systemic administration. Cannabinoid receptor agonists may therefore impair associative motor learning by disrupting plasticity mechanisms within the cerebellar cortex.

P74. Selective transgenic manipulation of the entorhinal cortex inputs to hippocampal CA1 during fear memory formation and retrieval.

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[1]Massachusetts Institute of Technology, PILM

It has been recognized that the expression of memory depends importantly on the context in which memory is formed and retrieved. The learning of the context seems to require the integration of multiple sensory cues into a unified configural representation. Recent studies with rodents demonstrated that the hippocampus and its surrounding medial temporal lobe areas, including the entorhinal cortex (EC), are crucial to this process. However, little is known about the neural circuit within the hippocampus that is involved in contextual learning and retrieval. The hippocampus gets information from the EC through at least two major routes: EC layer II to DG and CA3; and EC layer III to CA1. To differentiate these inputs, we created a triple transgenic mouse line in which synaptic transmission can be selectively blocked at the EC layer III axon terminals in an inducible and reversible manner, while leaving the intrahippocampal trisynatpic route intact. To elucidate the roles of the EC layer III input in contextual memory formation and retrieval, we subjected the mice to Pavlovian fear conditioning paradigms. When the mice were conditioned with a single shock in a novel chamber at 10 or 60 seconds after being placed on day 1 and re-introduced into the same chamber on day 2, the mutant and control animals displayed the same amount of freezing levels, suggesting EC III input may not be necessary for the association

between context and shock. However, when the mice were preexposed to a chamber for 10 minutes on day 1 and then shocked in the same chamber at 0, 10, 20, or 60 seconds after being placed on day 2, the mutant that were shocked at 10 or 20 seconds on day 2 displayed a significant reduction in freezing after being returned to the same chamber on day 3. This indicates that the retrieval of the familiar context was slower in the mutant during the time prior to the shock, suggesting the EC III input may play a pivotal role in a rapid retrieval of a previously formed presentation of the context, which may involve a pattern-completion dependent mechanism in the entorhinal-hippocampal circuit.

P75. Possible Strain Difference in the Basolateral Amygdala to Prelimbic "Emotional Bottom-Up" Circuit.

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The inbred Wistar Kyoto (WKY) rat strain can serve as a model for anxiety disorder vulnerability. The WKY rat exhibits several unique behaviors representative of anxiety vulnerability including: behavioral inhibition (decreased open field activity), hyperarousal (increased startle magnitude), and sensitivity to avoidance (accelerated acquisition of active avoidance). Abnormalities in the basolateral amygdala (BLA) to prelimbic (PL), "emotional bottom-up" circuit, is believed to underlie several of the anxiety like behaviors observed in WKY rats. Few studies have explored the electrophysiology of this pathway, with the majority pertaining to extinction in outbred Sprague Dawley (SD) rats. Therefore, understanding the differences in the electrophysiological properties of the BLA to PL circuit in SD and WKY rats may provide unique insight into the vulnerability to develop anxiety-like behaviors. In this study, strain differences in evoked field potentials, paired pulse facilitation, and long-term potentiation from the BLA to the PL cortex were compared between WKY and SD rats under urethane anesthesia. Preliminary data show that evoked field potentials have similar magnitudes between strains. Paired pulse facilitation was observed between 50 – 150, but WKY rats had a greater magnitude of facilitation than SD rats. In contrast, WKY rats were resistant to LTP induction using theta-burst high frequency stimulation in the BLA. These preliminary results suggest that differences in synaptic plasticity of the BLA to PL pathway may underlie anxiety vulnerability modeled by the WKY rat. The manner in which differences in synaptic plasticity within this circuit could result in WKY rats being vulnerable for developing anxiety-like behaviors will be discussed.

P76. 5-HT2C receptor antagonist SB 242084 improves interval timing performance.

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Previous studies of a transgenic mouse that overexpresses striatal dopamine receptor D2R (D2R-OE) have shown that the overexpression leads to deficits in motivation and timing (Drew et al., 2007). We also observed an upregulation of serotonin subtype 2C (5-HT2C) receptor in striatum of D2R-OE mice and found that the selective 5-HT2C receptor antagonist SB 242084 alleviated the motivational deficit as evidenced by an increase in the effort mice were willing to expand to obtain reward (Simpson et al., 2011). A similar increase in motivation occurred in control mice suggesting that the 5-HT2C receptor might be a useful target for modulating motivation. Some of our earlier work suggested that the timing deficits are at least partially rescued by enhancing motivation (Drew et al., 2007, Ward et al., 2009), therefore, in the present study, we investigated whether SB 242084 would enhance timing in both D2R-OE and control mice. In order to assess interval timing independent of rate of lever pressing vigor, SB 242084 was given to mice performing on a temporal bisection procedure. Mice were taught to press one bar following a 6-s tone and a different bar following a 24-s tone in order to earn a reward. D2R-OE was less accurate than controls. Systemic administration of SB 242084 improved timing precision and accuracy in both D2R-OE and control mice. This could be due to the 5-HT2C receptor antagonist having a direct pro-cognitive effect (e.g. altered memory or attention) or an indirect effect on cognition via modulation of motivation. More generally, these results show that 5-HT2C antagonists such as SB 242084 may have a therapeutic potential for treatment of cognitive and motivational disruptions in schizophrenia patients.

P77. Cocaine-induced Cognitive Deficits are Ameliorated by Histone Deacetylase Inhibition.

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Much work has demonstrated that repeated psychostimulant exposure results in long-lasting disruption of reward circuitry. As deficits in executive function result from drug use and as predispose individuals to initial and continued substance abuse, a better understanding of the neural mechanisms underlying these deficits may reveal novel pharmacological targets to facilitate cessation and prevent long-term effects of drug-exposure. We used a model of working memory dependent associative learning to investigate the effects of binge-cocaine administration on cognitive function in C57BL6 mice. Trace fear conditioning differs from delay and contextual conditioning in that the CS and US are separated by a trace-interval, recruiting prefrontal cortex and hippocampus to the task of CS-US association. Additionally, work in humans and rodents, demonstrates

that this task relies on both working memory and attention, two important components of executive function. Thus, we examined the effects of binge-cocaine administration (20 mg/kg cocaine, 3 times per day for 5 days) on cued and contextual components of trace and delay fear conditioning. Binge administration produced robust deficits in trace conditioning without affecting delay or contextual conditioning. Examination of the time course of this effect revealed that it persisted for at least 14 days after drug administration. Additionally, administration of a single dose of cocaine per day for 5 days produced a smaller but similar deficit in trace conditioning, and 1 day of binge cocaine administration failed to produce deficits in any forms of fear conditioning. These results demonstrate that robust deficits in cognitive function follow repeated cocaine exposure. Further, we used cognitive enhancing histone deacetylase inhibitors to reverse cocaine-induced learning deficits. Collectively, these results demonstrate a robust model of psychostimulant exposure-induced cognitive deficits and elucidate a pathway which may serve as a target for cognitive enhancing cessation therapies.

P78. Neural activity related to awake-state sharp wave-ripple -complexes is essential in hippocampal learning.

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Hippocampal electrophysiological oscillations play a key role in regulating memory trace formation, which is thought to proceed in two consecutive stages, encoding and consolidation. It is assumed that during sharp wave-ripple complexes (SPW-Rs), i.e. bursts of synchronous cell firing in the hippocampo-entorhinal region, recently encoded material is replayed and the memory trace is consolidated into long-term memory as a result of synchronized activity. During SPW-Rs, hippocampal cell firing closely follows that which took place during the initial experience, most likely reflecting replay of that event. In fact, disrupting hippocampal SPW-Rs using electrical stimulation after training on a spatial task retards learning in rats. However, it is still uncertain, whether ripples, as such, are also the means of information transfer between the hippocampus and the neocortex. Here, adult rabbits were trained in trace eyeblink conditioning, a hippocampus-dependent associative learning task, and a light was presented to them during the inter-trial interval, when awake, either following SPW-Rs or irrespective of ongoing neural state. Learning was particularly poor when the disrupting light was presented following SPW-Rs. Together with the fact that the hippocampal SPW-Rs themselves were left intact by the light presentation, it seems that learning depends on neuronal activity related to but not limited to hippocampal SPW-Rs.

P79. Fear conditioning modulates intrinsic excitability of lateral amygdala neurons.

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New learning such as fear conditioning modulates intrinsic excitability in

hippocampus and prefrontal cortex. Although the role of amygdala in fear acquisition is well established, it is not known whether fear learning modulates intrinsic excitability of amygdala neurons. To test this hypothesis, 2 groups of rats were trained on fear conditioning. Rats from the "Trained-1hr" group were decapitated immediately following conditioning, brains removed, and coronal slices containing lateral amygdala (LA) were made. "Trained-24hr" rats were treated similarly as the "Trained-1hr" except that a CS probe was presented 24 hrs after conditioning to quantify fear memory, rats were sacrificed immediately afterwards and slices were made. To measure changes in intrinsic excitability, somatic intracellular recordings from LA pyramidal neurons were obtained. All neurons were held at -65 mV and current-voltage relation, postburst afterhyperpolarization (AHP) and spike frequency adaptation were measured. No change in the intrinsic excitability of LA neurons from Trained-1hr group was evident as AHP (-8.53 mV) and spike frequency adaptation (4.43 spikes) were similar to that of LA neurons from naïve rats (4.15 spikes, -8.56 mV). This lack of intrinsic plasticity following fear conditioning could be because modulation of intrinsic excitability is time-dependent and hence, was not evident immediately following conditioning. To test this hypothesis, we compared intrinsic excitability of LA neurons from Trained-24hr group to naïve rats. Spike frequency adaptation was reduced in LA neurons from Trained-24hr rats (5 spikes) when compared to LA neurons from naïve rats. In addition, LA neurons from Trained-24hr rats had reduced AHP (-6.99 mV) than those from naïve rats. These data indicate that fear conditioning leads to a modulation of intrinsic excitability of LA neurons in a time-dependent manner. Furthermore, these changes could serve as a substrate for metaplasticity, whereby modulation of intrinsic excitability facilitates future LA dependent learning.

P80. Optogenetic silencing of prelimbic mPFC during the trace interval impairs trace fear conditioning.

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The association of the conditional stimulus (CS) and unconditional stimulus (UCS) across an empty trace interval in trace fear conditioning (TFC) requires the hippocampus, amygdala, and prelimbic area of the medial prefrontal cortex (PL; e.g., Gilmartin & Helmstetter, 2010; Gilmartin et al., 2012). In contrast, delay conditioning, in which no gap separates the stimuli, is largely supported by the amygdala. Presumably the additional circuitry in TFC serves to bridge the gap, allowing a representation of the CS to overlap with the UCS. PL may serve this role. Unit recording studies revealed learning-related increases in firing during the trace interval in PL, but not hippocampus (Gilmartin & McEchron, 2005a,b). Inactivating PL with muscimol during TFC impairs learning (Gilmartin & Helmstetter, 2010). However, pharmacological inactivation of PL cannot address whether trace interval activity per se is necessary for associating the CS and UCS. Here we directly test the role of trace interval activity using viral-mediated expression of a light-sensitive proton pump (AAV9/CAG-ArchT-GFP), which when activated by light (532nm), prevents firing in neurons expressing the pump. Histological

analysis confirmed that virus expression was limited to PL. Light-induced silencing of PL units was confirmed by recording unit activity in 2 rats. Eight rats were injected with virus in PL and implanted with bilateral optic fibers. All rats were trained with 6-trial TFC. Half of the rats received light delivered to the fiber implants during the 20-s trace interval on each trial, while the other half received 20s of light during the ITI. Rats that received ITI light delivery showed intact freezing to the CS at test the next day. Rats that received trace interval light delivery exhibited impaired CS freezing. Contextual freezing was intact. These findings suggest that PL activity during the trace interval is necessary for the association of the CS and UCS in TFC.

P81. Secretin in the Cerebellar Cortex Modulates Acquisition and Extinction of Eyeblink Classical Conditioning.

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[1]*University of Vermont, Psychology*

Eyeblink conditioning (EBC), a well-studied form of classical conditioning supported by plasticity in the cerebellum. EBC involves trials in which a tone conditioned stimulus (CS) precedes an eyelid stimulation unconditioned stimulus (US). The conditioned response (CR) is an eyeblink to the CS. Both Purkinje cells (PCs) in cerebellar cortex and neurons in the interpositus nucleus (IPN) receive CS and US inputs. The interaction between cerebellar cortex and IPN modulates EBC. PCs are powerfully regulated by basket cells (BC), a cortical inhibitory interneuron. The axon terminals of BCs have the highest concentration in the brain of the voltage-gated K+ channel α-subunit, Kv1.2. Previous research shows that PCs express and release secretin, surface Kv1.2 in BC terminals is reduced by secretin and secretin increases IPSCs in PCs, which is blocked by GABAA antagonists. We have shown that infusing either a Kv1.2 blocker or secretin into lobulus simplex in cerebellar cortex facilitates conditioning presumably by increasing inhibition of PCs, thereby reducing inhibition of IPN. The current experiments expand on these findings. In Experiment 1, rats received infusions of the secretin receptor antagonist, 5-27 secretin, or vehicle into lobulus simplex immediately prior to Sessions 1-3 of EBC. Rats that received 5-27 secretin showed slower acquisition. In Experiment 2, rats received infusions of secretin or vehicle into lobulus simplex immediately prior to Sessions 1 or 2 of extinction. Rats that received secretin prior to Session 1 of extinction showed slower extinction. In Experiment 3, rats will receive infusions of 5-27 secretin or vehicle into lobulus simplex prior to Sessions 1 or 2 of extinction. We predict that rats that receive 5-27 secretin prior to Session 1 of extinction will extinguish faster. Our working model is that cerebellar cortical secretin modulates EBC by reducing surface levels of Kv1.2 at BC terminals, thereby increasing inhibition of PCs.

P82. The role of the hippocampus during long delay eyeblink conditioning in Sprague-Dawley rat.

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The effects of hippocampal lesions on delay and trace eyeblink conditioning (EBC) have been well studied. Animals with a hippocampal lesion exhibit faster learning of a delay EBC paradigm (500ms). In contrast, acquisition of trace EBC is impaired in animals with a hippocampal lesion. Hippocampal lesions also impair long delay EBC (1400ms), but this has not been as extensively investigated as delay and trace EBC. The current study investigates the role of the hippocampus in long delay EBC in Sprague-Dawley (SD) rats. SD rats were randomly assigned to either paired or explicitly unpaired delay EBC training at a 500, 1000, 1500, or 2000-ms inter-stimulus interval (ISI). In order to assess the effect of a hippocampal lesion during long delay training, SD rats either received a saline or Ibotenic acid lesion followed by either paired or explicitly unpaired training at 1500ms ISI. Paired groups received 100 trials per day for three days in which the CS (82-dB white noise), co-terminated with a 10-ms US, (10-V stimulation) with an inter-trial interval (ITI) of 20-40s. Explicitly unpaired groups received 100 CS alone and 100 US alone exposures per day for three days with an ITI of 8-25s. Preliminary data at 1500ms demonstrates that rats acquire the conditioned response (CR); the number of CRs was greater in paired training than during explicitly unpaired training suggesting associative learning occurs at this long interval. Accounting for pseudoconditioning, acquisition at 1500 ms was slower than 500 ms. We are currently assessing the effects of hippocampal lesions on long delay EBC learning in the SD rat.

P83. Contributions of prefrontal cortex, hippocampus, amygdala, and accumbens to the expression of active avoidance.

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We recently developed a simple avoidance task in which rats, trained to press a bar for food, learned to avoid a tone-signaled footshock by stepping onto a nearby platform (Bravo-Rivera et al, 2011, SFN). Remaining on the platform for the duration of the 30-sec tone protected them from the shock, but also prevented their access to food. In addition to avoidance, rats showed low to moderate levels of freezing to the tone. Here we used pharmacological inactivation to address the neural circuitry involved. After 10 days of avoidance training, rats were infused with saline or GABAA agonist muscimol in the prelimbic cortex (PL), basolateral amygdala (BLA), ventral hippocampus (vHPC), or nucleus accumbens core (NAc), and tested for avoidance. Inactivation of each of the four structures blocked avoidance responses, which returned the following day when tested drug-free (p's<0.05). However, inactivation had different effects on freezing

depending on the structure. Inactivation of BLA and vHPC blocked freezing, consistent with the loss of fear to the tone. In contrast, inactivation of PL or NAc did not reduce freezing. In fact, in 64% of the rats, freezing to the tone increased by > 50% compared to the previous day. Loss of avoidance with a concurrent increase in freezing suggests that inactivation eliminated the avoidance program. Our results suggest that BLA and vHPC contribute an essential fear signal, which drives avoidance. In contrast, PL and NAc contribute an avoidance program which inhibits freezing, perhaps through the CeL (Lázaro-Muñoz et al, 2010). In the absence of PL and NAc, rats resort to freezing as an auxiliary defense mechanism. Cortico-striatal connections have been implicated in psychiatric disorders involving excessive avoidance, such as PTSD and OCD.

P84. Amygdala arc expression following declarative memory consolidation: A trace-cued-fear conditioning analysis.

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It has been well documented that the amygdala plays a key role in fear-related memories. More specifically, many studies utilizing auditory fear conditioning have established that the amygdala is important for both acquisition and consolidation of Pavlovian fear. However, unlike delay and contextual fear conditioning, trace-conditioning, which has been suggested to be a good platform for examining declarative memories, has not been heavily investigated. In trace-conditioning, there is a separation in time between the CS and US; additionally, it is dependent on the hippocampus and medial prefrontal cortex. Analyses of amygdala's involvement in trace-fear conditioning have generated opposing findings. The following analysis utilized amygdala expression of activity-regulated cytoskeleton-associated protein (Arc/Arg 3.1), an immediate early gene believed to be important for synaptic plasticity, to determine the amygdala's role in consolidating trace-cued- fear conditioning. Adult C57BL/6 mice were randomly assigned to one of three groups: trace-conditioned, backward-conditioned and cage-controlled. Mice in the trace-conditioned group were presented with a tone (30s; 68db), followed by a stimulus-free interval (45s; trace) and a mild foot shock (2s; 0.6mA). Backward-conditioned mice were presented with a mild foot shock (2s; 0.6mA), followed by a stimulus-free interval (45s; trace) and a tone (30s; 68db). This group was a control for neuronal stimulation--mice did not learn the trace-tone-association, but received training-induced stimulation. Cage-controlled mice did not receive any conditioning, thus were a control for learning- and training-induced neuronal stimulation. Trace- and backward-conditioned mice were collected 1h following conditioning; cage-controlled mice were also collected at this time. Consistent with analyses of Arc expression in the amygdala following delay-cue-fear conditioning, our findings suggest that Arc protein expression is up-regulated in trace-conditioned mice 1h following training, compared to backward-conditioned and cage-controlled mice. These data suggest that the amygdala plays a modulatory role in

fear-related declarative memory consolidation.

P85. Parametric investigation of retrieval and extinction timing intervals in fear memory attenuation.

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Exaggerated and persistent fear is a common occurrence in psychiatric disorders. It is important to find ways to manipulate associative fear memories such that they no longer cause debilitating fear responses in pathological cases. Our earlier work has shown that a behavioral protocol that combines principles of reconsolidation and extinction could lead to a persistent reduction in fear responses; yet, the precise conditions under which this protocol may be effective remain to be determined. The present study examined the effect of manipulating the timing between different retrieval and extinction cues, and the relationship of these intervals to the inter-trial intervals used during conditioning. In the first experiment, we assessed whether a mere difference between the first and subsequent inter-CS intervals is sufficient to inhibit return of fear (rather than the first retrieval interval being longer than the inter-CS intervals). Our second experiment examined the importance of the length of the interval between the isolated retrieval trial and the extinction session and addressed whether similarity between conditioning and retrieval intervals was a requirement for persistent fear attenuation. Our results suggest that preventing and/or reducing the magnitude of the return of fear is contingent upon the extinction ITI being shorter than the interval between the retrieval trial and extinction, but also requires that the interval between the first and second CSs be sufficient long to allow memory destabilization

P100. Job Postings

Are you or your department hiring a faculty member, post-doc or technician? Post your job here. If you would like to talk to candidates put your name and contact information on the poster.

Local Information

There is a wealth of information about local restaurants and attractions at **www.destinationjerseycity.com** and of course if you cross the river the choices are endless **www.nycgo.com**

Restaurants & Bars near hotel (thanks to Meghan Caulfield) :

Iron Monkey (American - Bar/Restaurant) – 0.3 Miles Walking. Good Burgers/Entrees. Rooftop bar and dining.

Light Horse Tavern (American - Bar/Restaurant): 0.5 Miles Walking. Restored 1850's tavern with nice atmosphere. Upscale American style dining ranging from Burgers to Steaks to Seafood. Also good for Brunch on weekends.

Satis Bistro (Modern/European): 0.5 Miles Walking. Upscale bistro, a bit eclectic. Very nice casual fine dining atmosphere.

Skinner's Loft (Bar/Restaurant): 0.7 Miles Walking. Good Burgers & Entrees. Rooftop dining. Good brunch on weekends.

Thirty Acres (American - BYOB). 0.8 Miles Walking. Hip and casual with nice atmopshere. Changing menu that focuses on seasonal availability. Liquor store next door.

Zeppelin Hall (German Style Beer hall). 1.0 Miles Walking. A lot of indoor/outdoor seating and entertainment at night. Big screen televisions. Also has free parking.

Surf City (Bar). 1.0 Miles Walking. Wouldn't bother eating here but a nice bar that overlooks the harbor and has NYC views. Also has free parking.

Barcade (Bar). 0.7 Miles Walking. Features vintage arcade games that can be played for quarters and a large craft beer selection.

Liberty State Park:

Can be accessed by a foot bridge on Jersey Avenue. Beautiful views of NYC. Also great to run/walk/bike/picnic. Ferry access to Statue of Liberty and Ellis Island (shorter lines than NYC side).

PATH Trains:

Exchange place trains found right outside the hotel only go to World Trade Center. There you can get on the New York City Subway system.

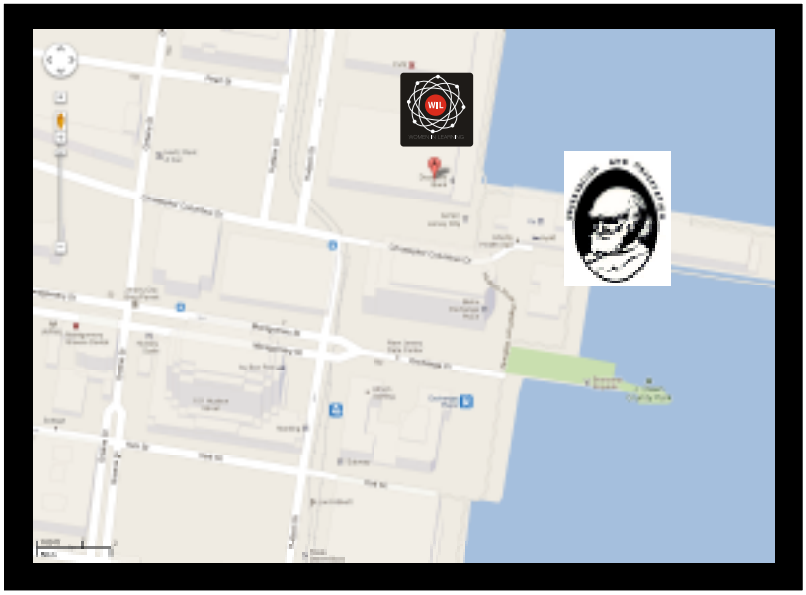
To get to the West Village/Chelsea/Midtown area on a PATH train you need to use the 33rd Street Line. You can get this train by taking a Hoboken Bound train and changing in Hoboken or Newport on weekdays. On weekends and nights, you have to take a Newark Bound train to Grove Street and then take a Hoboken/33rd Street Train. Alternately, you can walk to Grove Street (0.6 miles) and take the train from there.

Women in Learning (WIL)

For the support and advancement of women in science.

2nd Annual Luncheon:

Markers Restaurant, Jersey City, NJ
Saturday, September 22
12:00 - 1:15 p.m.
Special Guest: Dr. Elizabeth Gould



Women in Learning (WIL) provides a forum in which students and post-docs in the field of Learning Theory, Behavior, Memory and Neuroscience can seek advice, support, and guidance on the advancement of female researchers from a notable female researcher who has already carved a path in the field. WIL is open to anyone interested in supporting the advancement of women in science.

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Society of Computational Modeling of Associative Learning

SOCMAL

Pavlovian Society Meeting
September 23rd 2012
Jersey City, NJ

8:00-8:05	John Moore: Welcome
8:05-8:30	Randy Gallistel: Learning from a Rationalist Perspective
8:30-9:00	Eduardo Alonso: Extending the TD model
9:00-9:30	Andrew Delamater: A Multilayered Connectionist Approach to Pavlovian Learning
9:30-9:45	**Break**
9:45-10:15	Sam Gershman: A theory of memory reconsolidation
10:15-10:45	Randall Jamieson: Instance based learning and retrospective revaluation
10:45-11:15	Munir Kutlu: Solving Pavlov's Puzzle
11:15-11:45	Elliot Ludvig: Animal learning meets reinforcement learning: Associationism for the 21st century
11:45-12:15	Justin Harris: Timing without a clock
12:15-12:30	Nestor Schmajuk: General Discussion

1. Randy Gallistel. Rutgers U.
Learning from a Rationalist Perspective
Learned behavior is a consequence of domain-specific information-acquisition mechanisms. Implicit in the structure of these mechanisms are mostly, but not entirely, mathematical principles. Dead reckoning (path integration) is an example: it is a computation specific to acquiring knowledge of location. Implicit in it is the principle that position is the integral of velocity. Cue competition is another example: It is specific to the determination of what predicts and retrodicts what. Implicit in it is the principle that basal uncertainty (the amount of source information) limits the amount of information that cues may communicate. Circadian food anticipation is an example of a non-mathematical built-in principle, the principle that the day-night cycle has a 24-hour period. Other examples will be given as time allows.

2. Eduardo Alonso City University London
Extending the TD model
We present a set of new algorithms that extend the Complete Serial Compound Temporal Difference model to work with different contexts, stimulus compounds, and configural cues. These algorithms permit prediction of phenomena for which simple elemental solutions are insufficient, such as certain complex discriminations and context-related effects. In addition, we will make a demonstration of a freely available cross-platform simulator that allows the user to input trial-based designs, computes and displays predicted associative strength as numerical and graphical outputs per trial and per stimulus component, as well as simulated responses. It also implements different time steps and variable stimulus durations, includes a functionality to export the results to data processors, and provides a user-friendly graphical interface.

3. Andrew Delamater Brooklyn College – CUNY
A Multilayered Connectionist Approach to Pavlovian Learning
The question of how events become represented by the brain has become increasingly important in the study of Pavlovian learning, not only at psychological but at neural systems levels of analyses as well. Traditionally, this issue was intertwined with the "what is learned" question, and a large amount of research has focused on issues concerning what aspects of the unconditioned stimulus (US) get encoded within an associative structure. In contrast, less work has been directed to the question of how conditioned stimuli (CS) are represented. Nevertheless, a range of phenomena (e.g., acquired equivalence and distinctiveness, common coding, patterning, conditional discrimination learning, occasion setting) suggests that such representations might undergo dynamic changes over the course of a conditioning treatment. It will be argued here that a multi-layered connectionist approach can quite naturally and perhaps realistically capture how the brain might solve these sorts of problems, and, indeed, might point to more inclusive ways of conceptualizing even more traditional problems of associative structure.

4. Sam Gershman. Princeton University

A theory of memory reconsolidation

Retrieval can render render memories labile, allowing them to be modified or erased by behavioral or pharmacological intervention. This phenomenon, known as reconsolidation, defies explanation in terms of classical associative learning theories, prompting a reconsideration of basic learning mechanisms in the brain. I propose that two mechanisms interact to produce reconsolidation: an associative learning mechanism of the form posited by classical theories, and a structure learning mechanism that discovers the units of association by segmenting the stream of experience into statistically distinct clusters (latent causes). Simulations demonstrate that this model can reproduce the major experimental findings from studies of reconsolidation, including dependence on the strength and age of memories, the interval between memory retrieval and extinction, and prediction errors following retrieval. In addition, I present new experimental data confirming the theory's prediction that performing part of extinction prior to retrieval attenuates reconsolidation.

5. Gunes Kutlu Duke University

Solving Pavlov's Puzzle

We introduced a new “real-time” model of classical conditioning that combines attentional, associative, and "flexible" configural mechanisms. In the model, attention to both conditioned (CS) and configural (CN) stimuli are modulated by the novelty detected in the environment. Novelty increases with the unpredicted presence or absence of any CS, unconditioned stimulus (US) or context (CX). Attention regulates the magnitude of the associations CSs and CNs form with other CSs and the US. We incorporate a flexible configural mechanism in which attention to the CN units increases only after the model has unsuccessfully attempted to solve a problem with CS-US associations. In consequence, CSs become associated with the US and other CSs in fewer trials than CNs. Because the CSs activate the CNs through un-modifiable connections, a CS can become directly and indirectly (through the CN) associated with the US or other CSs. In order to simulate timing processes, we simply assume that a CS is formed by a temporal spectrum of short-duration CSs that are activated by the nominal CS trace. The model accurately describes a large percent of the basic properties of classical conditioning using fixed model parameters and simulation values in all simulations.

6. Randall Jamieson. U. of Manitoba

Instance based learning and retrospective revaluation

I present an instance-based model of associative learning based in a classical theory of human memory. I show that the model accommodates retrospective revaluation at the first, second, and third orders of association. The model is a unique bridge for understanding connections between research on associative learning and human memory.

7. Elliot Ludvig. Princeton University

Animal learning meets reinforcement learning: Associationism for the 21st century

In this talk, I suggest that the formalisms of reinforcement learning (RL) are a natural extension of animal learning theory that offer a rich theoretical framework for building future associative models. RL is a branch of artificial intelligence that aims to create interactive agents that learn to optimize rewards in their environments. RL algorithms are typically simple and incremental, making them particularly suitable as computational models of associative learning. In addition, they are normatively grounded, allowing for clear theories of what is being computed, and often backed by theoretical guarantees about their functionality. Models derived from RL algorithms, such as TD learning, already provide successful computational accounts for many conditioning phenomena, including some that are particularly challenging for standard associative learning models such as timing, revaluation, and invariance. I end with some speculations about areas of RL research that might be best exploited for future models of associative learning.

8. Justin Harris. U of Sydney

Timing without a clock

When an unconditioned stimulus (US) is consistently presented at a fixed time during or after presentation of a conditioned stimulus (CS), conditioned responses (CRs) tend to peak close to the approximate time of the US. Models of conditioned that have been designed to capture this timing of CRs use some form of clock to mark the passage of time. In so-called "timing models", this clock is an explicit component of the learning mechanism; among "real-time" associative models, the clock mechanism is built into a dynamic representation of the CS. In this presentation, I will describe how a recent elemental associative model without a purpose-built pacemaker can nonetheless capture aspects of response timing.