SYNAPSE 2014 Abstracts (Listed in the order that they were received)
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01 Kinley-Cooper SK, King BS, Ruscio MG
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Effect of Social Environment on Neurogenesis and Estrogen Receptor Alpha in the Hippocampus of the California Mouse (*Peromyscus californicus*)
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Adverse social environments, such as isolation, have a variety of detrimental effects across vertebrate species. We aimed to elucidate the neuroendocrine mechanisms underlying behavioral deficits associated with isolation by quantifying neurogenesis and estrogen receptor throughout the central nervous system of the California mouse, *Peromyscus californicus*. Adult neurogenesis is affected by social environment in several species of rodents. Estrogen receptor alpha (ERa) concentration is associated with a variety of social behaviors, as well as degree of sociality across species. Furthermore, circulating estrogen influences rates of neurogenesis. California mice are monogamous and bi-parental, therefore we predict that alterations of social environment should have particularly acute effects. After housing male and female California mice in paired or isolate housing for 4 or 24 days, brains samples were collected. Using fluorescent immunocytochemistry we quantified, BrdU expression, double labeled cells (BrdU + neuronal marker), as well as double labeled cells for ERa with BrdU. Within the dentate gyrus of the hippocampus (DG), isolated animals had significantly more BrdU labeled cells than paired animals. There was an interaction with sex and duration. There were a limited number of cells that co-localized BrdU +ERa, and no significant differences across groups. However, there was an increase in single labeled ERa cells in the DG in the 24 day conditions relative to the 4 day conditions. Both BrdU and ER are significantly affected by social housing. If estrogen does affect neurogenesis in this species, it is through an indirect mechanism or a mechanism that does not involve ERa in the hippocampus.

02 Dougherty SP, Thompson K, Kim, Christopher, & Rasin MR
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Foxp2 Cortical Conditional Knockout (cKO) Increases Critical Values of Apical Dendrites
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Forkhead box protein P2 (Foxp2) is a nuclear transcription factor that has been shown to be mutated in a particular family, known as the K-E family. Foxp2 is implicated in speech and language disorders, as well as other higher level cognitive and motor functions in mammals and birds that learn songs. Little is understood about Foxp2's regulatory mechanisms; however, Foxp2 has been associated with the RNA-binding protein HuR. In previous experiments, HuR has been implicated in gross columnar structure of the cortical plate and proper orientation and morphology of individual, pyramidal neurons within the neocortex. HuR has also been shown to be involved in dendritic complexity. As Foxp2 is a part of HuR's mRNA cargo, we were interested in determining the effects of temporally-regulated Foxp2 mRNA translation on dendritic complexity. We have found that a Foxp2 cortical conditional knockout (cKO) is associated with greater apical dendritic complexity within the sensorimotor region of the neocortex, relative to wild type (WT) apical dendrites. Furthermore, similar to the HuR cKO phenotype, the Foxp2 cKO is associated with overall columnar misalignment and individual neuronal deficiencies.

03 Osborne JI, Bentzley BS, Cope ZA, Vazey E, Roth BL, Aston-Jones G
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Exploring Adaptive Gain Theory through Economic Demand
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Adaptive gain theory suggests that the explorative-exploitive behavior observed in response to changes in task demand and utility is correlated with the tonic firing of the locus coeruleus. We employed a within-session behavioral-economic procedure designed to assess changes in demand for cocaine as a function of cocaine price (lever responses/mg of cocaine). At high prices, the utility of performing a behavior wanes and motivation no longer supports the increased effort needed to obtain the reward. The maximum price that maintains increases in response rate is known as Pmax. We hypothesized that increased tonic discharge of locus coeruleus-noradrenergic (LC-NE) neurons would cause animals to disengage from the task at a lower Pmax. LC-NE neurons were tonically activated using the excitatory hM3Dq DREADD (Designer Receptors Exclusively Activated by Designer Drugs). After cocaine self-administration training, animals were randomized to receive one of three doses of the selective DREADD agonist, clozapine-N-oxide (CNO; 0, 0.1, or 1 mg/kg, ip) 30 min prior to testing in the within-session behavioral economic procedure. A decrease in Pmax in response to CNO would provide evidence for a causal role of the LC in modifying behavior in response to changing task demands and utility. A trend toward CNO decreasing Pmax was observed (n=5, $p<0.10$). Additional animals are currently being tested.

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Keywords: control, norepinephrine, attention

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Music genre preference and tempo alter alpha and beta waves in human non-musicians.
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Music is a worldwide form of entertainment that has apparent social, emotional, and cultural effects. To examine the effects of music genre and tempo on brain activation patterns, this study measured alpha and beta wave amplitudes using EEG recording. Two genres (rock and jazz) and three tempos (100, 120, and 140 BPM) were presented to 10 non-musicians, and the EEG results were analyzed through Fast Fourier Transform (FFT). To avoid confounds involved with using multiple songs with multiple tempos, a small sample of songs per genre were kept constant and tempo was artificially modified. When participants listened to their preferred genre, alpha wave amplitudes were significantly higher than when participants listened to their unpreferred genre ($F(1,7) = 6.616$, $p = 0.037$, $\alpha = 0.05$). Although a main effect of tempo on beta waves was not observed, there was a significant positive linear trend that indicates higher beta amplitudes for 140 BPM than for 100 BPM ($F(1,8) = 7.742$, $p = 0.024$, $\alpha = 0.05$). The findings of this study indicate that genre preference and music tempo do affect alpha and beta wave activation in non-musicians listening to preselected songs. Based on the nature of alpha and beta waves, the results suggest that preferred genres of music elicit a more relaxed mental state, which may translate to a better mood. In addition, increasing tempos tend to increase activation, which may explain why it is popular to listen to upbeat music before exercising (faster music excites the brain and therefore the body).

05 Marina Leon, Candler Paige, E. Alfonso Romero-Sandoval
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Assessment of Potential in Vitro Toxicity of Nanoparticles (Mannosilated Polyethylenimine) on THP-1 Macrophages

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We propose to develop a preventive cell targeting gene therapy using the human-tested, non-viral polyethylenimine (PEI) nanoparticle, jetPEITM-Macrophage (mPEI). The nanoparticle mPEI contains mannose-conjugated linear polyethylenimine that enhances binding to monocyte derived cells that exclusively express mannose receptors. The goal of the current study was to examine the potential cytotoxicity of the nanoparticle mPEI on human THP-1 macrophages. We hypothesize that mPEI will not cause cytotoxicity to THP-1 macrophages. We used two different cytotoxicity assays: the Trypan blue test and the lactate dehydrogenase (LDH) release assay. We examined the potential cell toxicity in non-stimulated and lipopolysaccharide (LPS)-stimulated THP-1 macrophages on the presence or absence of mPEI. We performed two observations in triplicates and the experiments were conducted twice for a total of six observations for each experiment. Ethanol produces concentration-dependent cell toxicity in the Trypan blue test. On the other hand, the presence of 2% Triton produces a cell concentration-dependent LDH leakage. We did not observe any significant cell death with mPEI in the presence or absence of LPS in THP-1 macrophages using either the Trypan blue test or the LDH assay. These results suggest that mPEI does not produce cytotoxicity in THP-1 macrophages. We are in the process of testing cell penetration rate and gene induction efficiency of mPEI. These studies will support the use of mPEI as a vector for a cell directed gene therapy that might be used to reduce peripheral neuritis or inflammatory process that typically produce neuronal sensitization.

06 Garzón, M & Lom, B
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BPA Decreases Tyrosine Hydroxylase Expression in Developing Xenopus laevis brains
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BPA (4,4'-(propane-2,2-diyl)diphenol) is used in the manufacture of polycarbonate plastics, such as canned food lining. BPA can leach into food and beverages causing unintended human consumption. As an endocrine disruptor with estrogen-like properties, concerns have been raised about BPA's effect at levels lower than those used in traditional toxicological studies. BPA is known to decrease a population of dopaminergic neurons that express tyrosine hydroxylase (TH), a rate-limiting enzyme for dopamine biosynthesis. We investigated the effects of BPA at low concentrations on TH expression by exposing stage 10 Xenopus laevis embryos to 0-300 nM BPA for 96 hours. The tadpoles were fixed, analyzed for gross morphological features, then cryosectioned and stained for TH immunoreactivity. Measurements of eye diameter and anterior-posterior length revealed that BPA did not significantly alter gross morphology. Similarly, BPA did not significantly alter brain length, width, or cross-sectional area. However, TH expression in the posterior tuberculum decreased with BPA exposure, demonstrating a significant decrease at 1.5-30 nM. In subsequent experiments, tadpoles exposed to similar concentrations of BPA for 96 hours and then reared for an additional 96 hours in the absence of BPA showed TH expression similar to controls ($p>0.05$). Thus, BPA exposure in early development appears to decrease TH+ expression in the brain in a reversible fashion without influencing gross morphological features.

07 Flemming B, Henson A, Brehmer T & Steinmetz KR
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Cortisol Level and Sex Differences Associated with Changes in Emotional Memory Retrieval
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Variations in memory between stimulus types (items vs. backgrounds) may be attributable to sex differences, cortisol levels, the arousal level of the stimulus, and the nature of the memory (false memories vs. true memories). The current study examined these potentially influential variables. Participants encoded scenes that included a negative or neutral item placed on a neutral background. After a 30-minute delay, half of the participants completed a stressful task, while the remaining half completed a similar control task. Immediately following these tasks, both groups of participants underwent a recognition memory test in which they were asked to recognize negative and neutral items separately from their backgrounds. Salivary cortisol was collected at five points over the course of the experiment. Variations occurred such that 1) memory was better for high arousal items than for low arousal items, while there was no significant difference based on arousal for backgrounds, 2) for both groups, higher levels of cortisol at retrieval were associated with more false alarms for negative information, 3) memory for females was better overall, specifically for items, with no gender difference for memory of backgrounds 4) anxiety level was positively correlated with item memory and negatively correlated with background memory. These differences in memory may be modulated by the differential activation of the hypothalamus-pituitary-adrenal (HPA) axis and the limbic system in response to stressful situations. The influence of anxiety level and sex differences on retrieval and memory are presented.

08 Stalker, C & St. Peters, M
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Examing Post-Traumatic Stress Disorder Gender Differences in Animal Models
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A predator scent stressor animal model was used to test for cognitive deficits associated with those who have post-traumatic stress disorder. Previous researchers have used this model to demonstrate that male rats are an effective model for the emotionality symptoms of PTSD shown in humans. A research study was done to test for cognitive deficits between genders associated with PTSD. The subjects, eight rats: four male and four female of those two groups, were then separated into two more groups. One group of rats was exposed to a traumatic event, used cat litter, in order to produce PTSD in approximately 1/3 of the exposed rats. The other group of rats was the control group. All of the rats were tested in an attention task to test cognition. The male and female rats each had a high and low responder to the attention tasks that had PTSD: one high and low responder for each gender. The controls did not have PTSD. Results thus far suggest this is a good model for the cognitive deficits and gender difference associated with PTSD.

09 Kennedy L, Sims C, Nichols D, & Shenal B
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A correlational study of dementia types and age
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Although modern medicine has delayed mortality rates of pathogenic diseases, infections, and various bodily diseases, we have yet to discover a treatment to cure and prevent diseases of the brain. Because our bodies are now outliving our brains, the prevalence of dementia diagnoses is rising. Our clinical research, conducted at the Veterans Affairs Medical Center in Salem, focused on patients in the Memory Assessment Clinic (MAC) suffering from dementia. The four variations of dementia observed included Mild Cognitive Impairment (MCI), subcortical (Parkinson's, vascular dementia), cortical (Alzheimer's disease, frontotemporal dementia) and mixed (a combination of subcortical and cortical). Based on the four subtypes of dementia, we hypothesized that the severity of diagnosis would correlate positively with the age of patients in the following order: MCI, subcortical or cortical, and mixed dementia, the

most severe of these, affecting the eldest population. After creating a database, a relationship was observed between the subtype and the patient's age supporting our hypothesis. The average age of MCI population was 77 (n=14), the weighted average age of cortical and subcortical was 77.5 (n=10), and mixed dementia patients averaged 83.2 years (n=18). Application of this data is important in clinical venues to understand common population diagnoses to improve patient care.

10 Lucke-Wold BP, Logsdon AF, Turner RC, Huber JD, Rosen CL
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The Endoplasmic Reticulum Stress Response: a Bridge Between Acute Neurotrauma and Chronic Neurodegeneration
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The Department of Defense has labeled blast-induced traumatic brain injury (bTBI) as the 'hallmark injury' of modern warfare. Blast-induced neurotrauma can lead to increased risk for development of neurodegenerative disease such as chronic traumatic encephalopathy (CTE). Although the process of disease development is unknown, endoplasmic reticulum (ER) stress has been implicated in both acute injury and chronic neurodegeneration. We sought to investigate the underlying mechanism of injury using our clinically relevant blast model. We propose that the ER stress response is continually activated during CTE progression, and that manipulation of the pathway will improve behavioral outcomes and decrease tau hyperphosphorylation. We examined the contribution of the ER stress response on neural injury over time in young adult male rats and human CTE specimens using western blot analysis and immunohistochemistry (IHC). All three arms of the ER stress response were significantly elevated in the entorhinal cortex of human CTE brains using IHC ($p<0.05$). Additionally, inositol requiring enzyme 2 alpha, a marker of ER stress, was co-localized with hyperphosphorylated tau in both human CTE brains and repeat blast samples from Sprague Dawley rats. Caspase-12, a marker of apoptosis, was elevated at 24 h post-blast and was co-localized with C/EBP homology protein (CHOP). The p-eIF2 alpha phosphatase inhibitor, salubrinal, was used to significantly decrease CHOP ($F(2,15) = 9.172$, $p < 0.01$) and decrease impulsive behavior on elevated plus maze after blast injury ($p < 0.05$). Understanding how ER stress contributes to CTE will improve diagnostic accuracy, and contribute to novel therapeutic targets for neurotrauma and neurodegenerative diseases.

11 Flowers, J
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The Effects of Amphetamine and Ethanol on Condition Place Preference in an Animal Model
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The current study was designed to investigate the reinforcing properties of amphetamine and ethanol using conditioned place preference in a rodent model. Sixteen male Long Evans Hooded, rodents were assigned to AMPH, EtOH, AMPH+EtOH or saline drug groups. On testing days EthoVision software recorded the amount of time spent in each chamber: preferred (non-drug paired), neutral or non-preferred (drug-paired). The study tested the hypothesis that rats would prefer individually administered drugs when compared to dual administration. This was done by comparing within groups the time the rats spent in the non-preferred chamber in the pretest and posttest. While results showed the amount of time spent in the non-preferred chamber did increase from pretest to posttest, independent sample t tests did not show the difference to be significant. A repeated measures ANOVA comparing all drug groups showed that the difference between the AMPH and saline groups time spent

in non-preferred chamber approached significance. This shows a trend that AMPH, EtOH and AMPH+EtOH do have reinforcing effects when compared to no drug.

12 Becker-Krail D & Lavin A
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Improving Cognition in Dysbindin-1 Null-Mutant Mice, a Genetic Model for Schizophrenia
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Estimated to affect 24 million individuals worldwide, schizophrenia is a heritable neuropsychiatric disorder characterized by a range of symptoms from hallucinations and delusions to social withdrawal and cognitive deficits. Recent studies have linked these schizophrenia related deficits in cognition with diminished expression of the dystrobrevin-binding protein-1 (dsybindin-1). The lab has previously shown that a lack of dysbindin-1 reduces glutamate release in the prefrontal cortex (PFC) through decreases in the ready releasable pool of synaptic vesicles, decreased rates of endo- and exocytosis, and diminished expression of the L- and N-type Ca2+ channels. Fingolimod, a drug historically used to treat multiple sclerosis, is known to increase endogenous levels of brain derived neurotrophic factor (BDNF), and in turn, it has been shown that BDNF increases N-type Ca2+ channels. To explore a potential means of restoring glutamate release, and perhaps improving the cognitive deficits, we investigate the effects of fingolimod using a dysbindin-1 null mutant mouse. The mice were divided into two groups: saline or fingolimod treatment (7 days intra-peritoneal injection). We tested cognition across three genotypes (WT, HET and MUT) using a social interaction/working memory task. For both groups, we assayed BDNF concentration in PFC homogenate and analyzed levels of intracellular [Ca2+] in a crude PFC synaptosome preparation using a fluorescent calcium assay. Relative to WT mice, non-treated dysbindin-1 MUT mice demonstrated impairments in social interaction, decreased working memory, and lower levels of PFC presynaptic intracellular [Ca2+]. However, fingolimod treated null MUT mice show increased social interaction with novel mice, improved working memory, higher PFC [BDNF], and an increase in PFC presynaptic intracellular [Ca2+]. These results show promise for counteracting social and cognitive impairments associated with schizophrenia, and shed light on the possible role of dysbindin-1 in symptom pathogenesis.

13 James CJ & Meyer-Bernstein EL
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Circadian Gene Oscillation in the Presence of a Simulated Tide in the Starlet Sea Anemone, *Nematostella vectensis*
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Animals display endogenous rhythms in physiology and behavior that are governed by a self-sustaining biological clock. The most widely studied of these biological clock outputs, circadian rhythms, have a period of approximately 24 hours and are synchronized to the environmental photoperiod. In intertidal marine organisms, non-photic environmental cues governed by the changing tide, such as hydrostatic pressure and salinity, can also influence rhythmic behavior. Unlike circadian rhythms the mechanism underlying these circatidal rhythms remains unclear. We have observed circatidal behavior in the starlet sea anemone, Nematostella vectensis when exposed to a 12.4 hour simulated tide in the laboratory. To determine whether known circadian clock genes also underlie circatidal behavior, we have analyzed gene expression in N. vectensis individuals simultaneously exposed to an oscillating tide and

photoperiod. Genes were quantified at various time points, and compared to gene expression under the influence of a photoperiod alone. The addition of a simulated tidal cycle to a photoperiod appears to alter rhythms of circadian gene expression significantly. Daily peaks in gene expression for cryptochrome and cyclin B were shifted by 10-12 hours, suggesting a potential role of these genes in entrainment to a tidal cycle. Clock, a central transcription factor in the circadian clock, appears to be unaffected by the simulated tide. These results suggest that a subset of known circadian genes may be contributing to multiple frequency clock outputs, and further describe the molecular underpinnings of biological clocks.

14 O'Hara, K & Gendle, M
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Magnesium Supplementation and Test Anxiety
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Many students in college suffer from test anxiety. Current pharmacological treatments for test anxiety (such as benzodiazepines) produce significant side effects such as drowsiness and cognitive impairment. Therefore, there is a significant need for anxiolytic agents that do not produce such effects. One candidate compound is elemental magnesium. Magnesium is vital to the function of NMDA receptors in the hypothalamic-pituitary-adrenocortical (HPA) axis, which mediates responses to stress. Episodes of transient high anxiety (such as during final exams) are associated with temporary hypomagnesic states that result from increases in urinary magnesium excretion. This double-blind study assessed the possibility that oral magnesium citrate could reduce test anxiety during finals, presumably through the reversal of stress-induced hypomagnesic states that impair NMDA receptor function and dysregulate the HPA axis. A total of 122 university undergraduates were enrolled, each completed two pretest measures of anxiety, the AMAS-C and the Westside Test Anxiety Scale. Five days before their first final exam, each participant randomly received a five-day course of oral magnesium citrate (300 mg/day) or matched placebo. On the night before their first final exam, all participants completed the Spielberger State Anxiety Inventory. The level of self-reported anxiety on the night before the participantsâ€™ first final exam did not differ between the placebo and magnesium groups (p = 0.69). A number of possible factors could have produced this null finding, and future research needs to be conducted before the specific cause of this null result can be identified.

15 Cantwell K, Boger H, Umphlet C, Ledreux A, Granholm AC
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Neuroprotective Effects of Rasagiline in a Double Lesion Model of Parkinson's Disease
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Most published preclinical work with the monoamine oxidase inhibitor, rasagiline, and disease modification in Parkinson's disease (PD) has focused on the classical models of PD, including unilateral 6-OHDA (a dopamine neurotoxin) lesions in rats, and mitochondrial permeability transition pore (MPTP) lesions in mice. However, these models do not take into account cognitive dysfunction which occurs often in PD, such as diminished executive function and cognitive flexibility. We have recently utilized a model for slow, progressive loss of both locus coeruleus noradrenergic neurons (LC-NE) and substantia nigra dopaminergic neurons (SN-DA) in rats, mimicking both the cognitive and motor function impairments observed in PD. We hypothesize that rasagiline and its metabolite, aminoindan, will have neuroprotective effects on cognitive and motor symptoms in a double lesion PD animal model. Six

month old Fischer 344 male rats were administered DSP-4 (a norepinephrine toxin), followed by bilateral intrastriatal 6-OHDA injections 7 days later. Three weeks following the double lesion, an Alzet pump was implanted subcutaneously, delivering either rasagiline, aminoindan (3 mg/kg/day) or saline. Rats were tested in cognitive and motor function tasks three weeks into the drug treatment. Grip strength and balance, evaluated using the prehensile traction task, were not improved by either rasagiline or aminoindan treatment. However, rats with double lesions treated with both drugs exhibited increased velocity and motor activity when tested in a spontaneous locomotion task. Further, rasagiline and aminoindan treatment enhanced performance in a novel object task, suggesting that these treatments may increase behavioral flexibility and working memory following an LC-NE and SN-DA double lesion. We conclude that while rasagiline and aminoindan do not increase balance or grip strength, they do enhance spontaneous activity, exploratory behavior, and cognitive function such as working memory. Supported by a grant from TEVA Neuroscience.

16 Tracey E, Pereira A, Hughes M, & Korey C
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Sensory neuron plasticity during claw transformation in the snapping shrimp, *Alpheus angulosus*
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Neural asymmetry is reflected throughout vertebrate and invertebrate families, while instances of neuro-regeneration are much more rare. Both phenomena are exceptionally drastic in crustaceans, like those of the genus Alpheus, or snapping shrimp, that present with radical phenotypic differences in their front claws. Snapping shrimp are distinct from other crustaceans because if one claw is removed, the "handedness" often switches in an extreme example of neuroplastic regeneration. We have previously described the morphological changes that occur in the regenerating claw during transformative molts. To begin examining how these shrimp are able to rewire their nervous systems, we examined setae, or sensory hair, distribution changes throughout claw transformation. While total number of setae remains constant during development, the proportions of setae subtypes change predictably in the areas of the claw most altered by transformation. Setae are fully redistributed by molt two, long before pristine morphology is achieved. This finding suggests that basic neuron organization is conserved between claw types, but it may also be indicative of major changes in cell fate and neural wiring. It also suggests that an intact sensory system is key to the transformative process. This work is the first step in creating a complete visual atlas of claw sensory projections in the snapping shrimp and detailing the differences between the claw types. Creating the normal network map of sensory projections will begin to provide clues to what regions of the thoracic ganglion process the sensory inputs from each claw. This will provide the developmental framework required to examine the molecular mechanisms that underlie this radical regrowth and plasticity.

17 Aninweze A, & Birgbauer E
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The Effect of Ibuprofen on Growth Cone Collapse of Chicken Retinal Axons
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Damage to the CNS and the spinal cord is irreversible. There is minimal nerve regeneration at the site of the injury, but it is not enough to reverse the injury. Recently, Fu et al (2007) found out that ibuprofen promoted nerve regeneration at the site of injury in dorsal root ganglion cells of mice. Furthermore, they proposed that ibuprofen causes nerve regeneration by inhibiting RhoA. In the retinal axons of chicken, the lysophospholipid LPA causes axonal growth cone collapse by activating the RhoA pathway.

If ibuprofen promoted axonal regeneration through RhoA inhibition in dorsal root ganglion cells of mice, growth cone collapse of chicken retinal axons by LPA should be inhibited by ibuprofen. We used ibuprofen at 500µM and 50µM, which were similar to concentrations used by Fu et al, and below the lethal dose, to test inhibition of growth cone collapse by LPA. Using time lapse microscopy, live events were recorded as the retinal axons were treated with ibuprofen and/or LPA. At concentrations of 500µM of ibuprofen, some growth cone collapse occurred before the LPA treatment. Furthermore, treatments done with LPA showed significant growth cone collapse even when pretreated with ibuprofen. Our results showed that ibuprofen did not prevent growth cone collapse, which did not correlate with Fu et al's findings, suggesting a more complex role for ibuprofen in nerve regeneration.

18 Vakamudi, Harini B, Kohn, Jordan, Johnson, Zachary P, & Wilson, Mark E.
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5-HTTLPR polymorphisms and predisposition to anxious and depressive tendencies as measure by blood cortisol and behavioral paradigms.
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The short (s) polymorphism of the serotonin transporter gene (SERT, 5-HTT) has been implicated as a risk factor for depressive or anxious tendencies, particularly in the presence of a significant stressor or significant early life stress. The implications of the polymorphism for differential symptomology and treatment efficacy is an impetus for further research into 5-HTTLPR. Rhesus macaques have been a viable model in gene-environment paradigms, due to the behavioral and genetic similarities between humans and non-human primates. We genotyped 20 unrelated female Rhesus macaques of known lineage and collected blood samples to establish basal cortisol levels. We collected additional blood samples in response to the human intruder paradigm at various time points. The subjects were also observed in their respective social groups to measure anxious, aggressive and affiliative acts initiated and at separate time points. Using a one-way ANOVA, we observed relationships between genotype and cortisol and genotype and frequency of anxiety, duration of anxiety, and affiliative acts initiated. However, of the significant results, affiliative acts initiated was the only variable to present with the expected mean value of the L/L homozygote replicate relative to that of the S-allele carriers. Coupled with the lack of significant correlations between affiliative and aggressive acts, cortisol, and anxiety, the results allude to the importance of environmental variables, particularly early life stress (maternal neglect or abuse) and chronic stress (subordination, in examining the relationship between 5-HTT and anxious and depressive tendencies. Future studies may benefit from including significant early life stress and chronic stress variables in the statistical analyses.

19 Hawkins CB, Griffin WC, Lopez MF, Haun HL, May CE, Luderman L, Becker HC
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The Effect of Topiramate on Drinking Behavior and Brain Ethanol Concentrations in a Binge-like Model of Alcohol Consumption
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As a chronic relapsing disorder, alcoholism presents not only serious health concerns to abusers, but also national economic costs that arise from health care expenses, crime, and loss of productivity. Because of the widespread occurrence of alcoholism, the increasing knowledge of risk factors, and the known mechanisms of action in the body, many drugs have arisen as possible methods to curb abusive behavior. In this study, we investigate one drug in particular, topiramate, or Topamax. Aside from its

role as an anticonvulsant, topiramate is known to cause a reduction in dopamine release in the mesolimbic pathway. Because of dopamineâ€™s role in rewarding behavior and its believed role in the reinforcing effects of alcohol consumption, topiramate shows potential as a drug that can reduce drinking. When measuring alcohol consumption, mice were given access to ethanol for two hours/day for three days and four hours of access on the fourth day. In this model, mice generally drink to a point of intoxication, demonstrating a binge-like consumption found in humans. We found that the administration of topiramate prior to a drinking session significantly reduced the consumption of ethanol as compared to mice solely treated with saline ($p<0.001$). A neurochemical analysis of cerebrospinal fluid collected during microdialysis, also showed a decrease in the brain ethanol concentration of topiramate treated mice ($p<0.001$). Ultimately, topiramate may show promise as a pharmaceutical means of not only combating abusive behavior and avoiding symptoms of withdrawal, but also reducing the urge to drink in those suffering from alcoholism.

20 Kassem GL, Cummins ED, Peterson DJ, Brown RW
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The Effects of AT010 on Behavioral Compensation After Cerebral Ischemia in the Rat
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Release of glutamate in cerebral ischemia results in an excitotoxic reaction in the central nervous system resulting in neuronal cell loss. Providing neuronal protection via N-methyl D-asparate (NMDA) receptor blockade in response to cerebral ischemia may result in preservation of function following ischemia. The present study was designed to test compound AT010, an NMDA signaling antagonist, on behavioral compensation and infarct size in a cerebral ischemia model in the rat. Animals were surgically implanted with a filament via the external carotid artery, providing an occlusion of he medial cerebral artery for 60 min. Approximately 30-45 minutes prior to surgery, the compound AT010 (3uM or 10uM) or saline was iv administered at 1% of body weight. All animals were behaviorally tested on behavioral tasks that analyzed postural reflex, limb placement, righting reflex, adhesive removal, and behavioral motor function at 3, 7, and 14 days post-ischemia. In addition, animals were tested on the Morris water maze, a spatial memory task 28 days post-ischemia. Regardless of dose, composite neurological scores for all motor and sensory tasks were higher for animals given AT010 compared to saline at 7 and 14 days post-ischemia. Water maze results revealed significant improvement of animals administered the higher dose of AT010 (10uM) on acquisition and probe trial performance, although no effect was revealed for the lower dose (3 uM). Finally, analysis of brain tissue samples revealed no significant effect on infarct size. These results indicate that compensation occurred throughout the undamaged brain areas, likely through synaptic communication changes as a result of drug treatment.

21 Stanion, JV & Rice, OV
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Effect of selective dopamine D3 receptor antagonist PG1037 on ethanol consumption in mice
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Binge drinking is a prevalent form of alcohol abuse, especially in adolescents and young adults. It is characterized by bringing blood ethanol levels to ≥80 mg/dl within two hours of the first drink. Alcohol abuse overall is a primary health concern worldwide, is implicated in over 60 different types of diseases and injuries, and has many serious economic consequences as well. Addictive, highly appetitive substances such as ethanol have been found to be reinforcing due to their effects in the mesolimbic

dopamine pathway of the brain. Blocking specific dopamine receptors using chemical antagonists can significantly reduce motivation for addictive substances. The goal of the current experiment is to assess whether the selective dopamine D3 receptor antagonist PG-1037 will affect binge ethanol consumption in mice. Using a restricted-access binge-drinking model, 40 male C57BL/6J mice were given 2-hour daily access to a solution of 2% ethanol in nonalcoholic beer 30 minutes after receiving an intraperitoneal injection of either 0, 3, 10, or 30 mg/kg PG-1037 in deionized water. An acute dose-dependent reduction in binge drinking behavior was observed at 10 mg/kg on test day 1 and at 30 mg/kg on test days 1 and 2. A decrease in water consumption was also observed at 30 mg/kg on test days 1 and 2, but no significant differences in water consumption were noted at 10 mg/kg. A decrease in ethanol consumption with no change in water intake at 10 mg/kg suggests that an effective dose will be in an associated range. The selective D3 antagonist PG-1037 may have useful applications in drug abuse and addiction treatment at appropriate doses.

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Effects of Ethanol on the Discrimination of Amphetamine Using a Water T-Maze
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The current experiment tested the hypothesis that a water T-maze is a faster method of training on the drug discrimination task compared to traditional operant methods. The experiment also tested the hypothesis that the combination of AMPH and EtOH would reduce choice response accuracy on drug discrimination task. In this study 10 male, Long-Evans hooded rats were trained to discriminate 2 mg/g of AMPH from saline. After discrimination training a dose response was conducted to determine the range of doses that generalize to the training dose. EtOH dose of 1.5 g/kg was then combined with AMPH for a second dose response. The results of this study showed the effects of ethanol interfered with interoceptive cues of amphetamine and led to a reduction of choice response accuracy for each dose when compared to AMPH alone. The addition of EtOH attenuated the discriminative stimulus properties of AMPH.

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Altering Cognitive and Brain States Through Cortical Entrainment
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Electroencephalographic (EEG) imaging depicts rhythmic oscillations of neural activity. Various ranges throughout the frequency spectrum of EEG oscillations have been associated with different brain states and cognitive processes. Oscillation from roughly 12-24Hz is referred to as beta, and activity in this band is implicated in arousal and attention. Theta, ~4-7Hz, is observed in deep sleep and periods of relaxation. EEG activity of a particular frequency range can be induced, or entrained, in a subject via exposure to rhythmic auditory or visual stimuli. A pilot study was performed to investigate the neurological effects of entrainment using binaural auditory beats (BAB) in a simple visual target detection test. BAB's are an auditory illusion in which the frequency difference between two tones presented to either ear is perceived as a beating, and it is this frequency that is entrained to. It was found that entrainment to either the beta or theta frequency ranges using BAB stimuli increased the power of each respective range, as well as decreased latency of onset in the Theta range. The second phase of this study will examine the effect of these stimuli on vigilance and attention, in addition to EEG

measures, in a one-n-back style paradigm as used by Lane et al. 1997. Participants will be exposed to the same stimuli used in the pilot study, which were designed to entrain activity to the beta and theta ranges. This study is the second of three proposed studies which investigate the effects of BAB stimulation on neurological activity and cognition.

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Exploring Parameters for a Single-Dose Conditioned Place Preference to EtOH in C57 Mice
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Rewarding properties of alcohol (EtOH) are purportedly mediated in part by the synthesis and release of beta-endorphin (β-E). We study this relationship by employing transgenic mice with varying levels of beta-endorphin expression. However, finding a reliable method for demonstrating rewarding effects of EtOH in wild-type control (C57BL/6J) mice has been problematic. Our lab has developed a modified protocol of the CPP paradigm, namely, a single-dose exposure to the drug during conditioning. We expected to see a place preference in the B6 (control) mice, a preference in HT (50% β-E expression) mice, and no preference in the KO (lacking β-E) mice. Adult, male and female experimentally naïve mice were tested for place preference after a single injection of EtOH (1.5 g/kg, administered intraperitoneally). We found a strong place preference to EtOH in female HTs, but no preference in the HT males, suggesting a role of sex in the preference to EtOH. We also found no preference in the KO mice (both sexes). No preference was found in the WT mice; however, the trend of the data suggests that future studies may be able to demonstrate a preference in the B6 mice, thus supporting the role of β-E in ethanol reward.

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The Effects of Environmental Enrichment on Adolescent Nicotine Sensitization in a Rodent Model of Schizophrenia
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Our lab has shown that neonatal treatment with quinpirole, a dopamine D2/D3 agonist, to rats resulted in an increase in dopamine D2-like receptor sensitivity that persists throughout the animal's lifetime without a change in receptor number, consistent with schizophrenia. Approximately 80-85% of schizophrenics smoke cigarettes, and there is no delineated mechanism for this observation. Our lab has also shown more robust sensitization and accumbal dopamine release in response to nicotine in adolescent rats neontally treated with quinpirole compared to controls. This study analyzed whether environmental enrichment, known to reduce sensitization to psychostimulants, may also reduce or block enhanced sensitization to nicotine in this model. Male and female rats were treated with either quinpirole (1 mg/kg) or saline from postnatal day (P)1-21. After weaning at P21, animals were raised in either environmentally enriched or isolated housing throughout the experiment. Beginning on P33, animals were ip administered either nicotine (0.5 mg/kg free base) or saline 10 min before placement in a square locomotor arena and behavioral activity measured every second day from P33-49. Results revealed that animals given neonatal quinpirole treatment and reared in an enriched environment demonstrated more robust sensitization to nicotine than all other groups. Animals given neonatal quinpirole or saline treatment followed by nicotine in adolescence and raised in isolated housing conditions were equivalent, but demonstrated more robust sensitization compared to enriched rats

neonatally treated with saline and administered nicotine in adolescence. Results here show that environmental enrichment enhanced nicotine sensitization in rats neonatally treated with quinpirole, which is in contrast to the blockade of sensitization to nicotine which has previously been shown in normal animals. Importantly, these results show that increases in D2 receptor sensitivity interacts with environmental enrichment differently than in normal animals and the manner in which the animal responds to nicotine, which may have implications towards smoking cessation in schizophrenia.

26 Hauver AJ, LaFevre J, Mills J, Russell C, Clasen M, Gaffney K, Pardes A, Pruett R, Uyguner H, Vassalo M, Franssen CL, Franssen RA
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Discrimination between Own and Alien Pups in the Maternal Rat
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One of the striking behavioral modifications in rats is the transition from fearful and anxious around pups as a virgin to attentive and nurturing toward pups as a mother. Previous research has demonstrated that mother rats are able to identify their own pups (OWN) versus those from another mother (ALIEN); somewhat surprisingly, mother rats eventually care for ALIEN pups once her natural pups are attended to (Beach and Jaynes, 1954). However, the underlying neural basis for the responses of mothers to pups is unclear and may aid in understanding the triggers of maternal response. In this study we attempt to elucidate the neurological underpinnings of the decision to care for both OWN and ALIEN pups. We compared three groups of female Sprague-Dawley rats (Rattus norvegicus): Mothers with OWN pups; Mothers with OWN and ALIEN pups (creating a MIXED group); and Mothers with ALIEN pups. Pup exposures were video-recorded for analysis of behaviors including latency to retrieve and grooming. Rats were then sacrificed and neural tissue examined through immunohistochemistry for differences in c-fos and oxytocin in several regions of the brain. Results indicate that mothers will care for both OWN and MIXED pup groups more quickly than a completely an ALIEN group. Data from the brain is being collected and will be discussed.

27 Novo D, Oprisan SA, Buhusi CV
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Effect of Prefrontal Cortex Pre-Allocation on Cortico-Striatal Network Response
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Time is an essential dimension of the world around us, determining the decisions we make, rate calculation, and the very precision of our slightest movements. Millisecond timing is important for speech recognition, auditory processing, playing music and dancing. Circadian timing controls sleep and wakefulness, and is critical for metabolic and reproductive fitness. Interval timing, or timing in the seconds-to-minutes range, is crucial for rate estimation, decision-making and foraging. Interval timing has been demonstrated in many species, from invertebrates to many vertebrates. In most species, interval time estimation follows a Gaussian-like response centered on the desired criterion time. Furthermore, the time estimation error increases quasi-linearly with the estimated duration, a characteristic known as scalar property. We used a biophysically realistic striatal beat-frequency model, which mimics the activity of cortico-striatal structures responsible for producing a Gaussian-distributed motor response that peaks at the learned criterion time and obeys scalar property. We investigated the effect of the number of neurons allocated to interval timing task on scalar property.

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A menthol incentive promotes nicotine self-administration at low-doses in rats.
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Mentholated cigarettes account for approximately 25% of the cigarettes sold in the United States and are disproportionately smoked by youth, female, and African American smokers. Most individuals experience menthol as a flavor additive in foods and beverages (e.g., candy canes, ice cream, etc.) that impart it with conditioned reinforcing properties prior to tobacco use. Nicotine is a psychomotor stimulant with complex reinforcing properties that can increase the salience of conditioned and unconditioned reinforcers. We hypothesized that the conditioned reinforcing properties of menthol could promote human tobacco use and nicotine self-administration. Thus, the present studies investigated the impact of adding a menthol conditioned reinforcer (CR) to the nicotine self-administration paradigm in rats. Adult male rats were rats were randomly assigned to one of two groups that received menthol (0.0005% w/v) either paired (Menthol-CR, n=8) or unpaired (Menthol-Neutral, n=8) with 20% sucrose. Following taste conditioning, rats were shaped to respond at a nose-key and were subsequently implanted with indwelling jugular catheters for intravenous (IV) nicotine self-administration. During self-administration tests, meeting the schedule of reinforcement on the active response key resulted in delivery of two stimuli: unsweetened menthol solution (0.0005% w/v) was delivered in a liquid dipper (oral) and nicotine infusions (30 ug/kg/infusion) were delivered to the intravenous catheter. After acquisition, several nicotine doses (1.5, 3.25, 7.5, 15, 30, 60 ug/kg/infusion) were tested to investigate the relationship between nicotine dose and operant behavior. At the lowest nicotine doses tested (1.5-7.5 Î¼g/kg/infusion) robust increases in operant responding were observed in the Menthol-CR group, relative to the Menthol-Neutral group. These findings suggest that menthol CRs may increase the abuse liability of tobacco products by enhancing the reinforcing effects of nicotine at low unit doses.

29 Kilroy EA, Moorman DE, & Aston-Jones, G
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The Control of Ethanol-Seeking Behavior Directed by Lateral Hypothalamic Orexin Neurons
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As a progressive brain disease, alcohol addiction causes physical abnormalities within the neurocircuitry for reward and motivation. Addicted individuals will enter a cycle encompassing consistent patterns of alcohol consumption and the inability to effectively control such behavior. The lateral hypothalamus (LH) is a targeted region in the reward circuitry that plays an important role in motivation and reward. In the rat model, the activation of localized orexin neurons in the LH following alcohol consumption triggers the subsequent release of dopamine from the ventral tegmental area. This further excites the mesolimbic dopamine system, the most prominent of the natural reward circuits. As a proposed mechanism for reducing ethanol self-administration and reinstatement of ethanol-seeking behavior, we administered an orexin-1 receptor antagonist, SB-334867 (SB). Rats were trained to self-administer ethanol on a fixed-ratio 3 schedule. Following the conditioning phase, each rat was exposed to three conditions at random over a course of one week: a 10 mg/kg dose of SB, a 20 mg/kg dose of SB, and vehicle 30 minutes prior to the self-administration session. Following extinction, this protocol was again repeated prior to cued-reinstatement; three days of extinction separated each cued-reinstatement session. Our results demonstrate that both doses of SB decreased ethanol consumption as a measure of

active lever presses (ALP) and well entries (WE), but only reached significance ($p < 0.05$) at the 10 mg/kg dose during the conditioning phase. During cued-reinstatement, both ALP and WE decreased, but only significantly for the 20 mg/kg dose. Further, a significantly greater effect of SB on reducing ALP and WE during self-administration and cued-reinstatement was found in rats with a greater preference for ethanol. These results indicate that SB administration may help limit maladaptive consummatory behavior to that of a 'social drinker' and that the orexin system may be more involved in high motivation for ethanol consumption.

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Alcoholism and the Beta Endorphin: The Effects of Stress on EtOH Self Administration
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The search for clinical and pharmacological treatments for alcohol dependency is an extensive and complex endeavor which considers systems in various brain regions and behaviors. However, one of the main areas of study involving ethanol (EtOH) abuse is the correlational relationship between stress and drinking behavior. While the clinical relationship between stress and drinking is well established, it has not yet been fully explained. Recent studies of the endogenous opioid systems have yielded very promising results which coincide with findings in other systems associated in EtOH abuse. In particular, endogenous beta-endorphin (β-E) mediates the stress response and has been implicated in reinforcing and mediating the effects of EtOH. Because stress sensitivity is also sexually dimorphic and females appear to be more sensitive to the effect of stress on EtOH sensitivity, this study asked whether the effects of stress on EtOH self-administration is influenced by levels of β-E and sex. This study utilized the drinking in the dark (DID) paradigm with running wheel access as a stressor in C57BL/6J male and female mice. The results of this study indicate that the beta-Endorphin mediates, at least in part, behavioral responses to stress in a sex dependent manner. Importantly, the relevant behavioral response was a sex-dependent increase in EtOH self-administration, further implicating sex differences within β-endorphin deficiency responses in diseases such as alcoholism and in the otherwise abuse of EtOH.

31 Stark, A. & McGovern, R.

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The Effects of Amphetamine and Acute Ethanol or Ethanol Withdrawal on a Behavioral Measure of Impulsivity
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Alcohol, a common recreational drug, can have adverse effects when combined with other drugs. This study used a rodent model to test the influence of acute ethanol (EtOH) and EtOH withdrawal with or without amphetamine (AMPH) on a behavioral test of impulsivity. The differential reinforcement of low rates (DRL) task was used to measure impulsivity. The hypothesis of this study was that there would be a difference in the response accuracy between the six different treatment groups: saline control, EtOH, AMPH, EtOH and AMPH, EtOH withdrawal, and EtOH withdrawal and AMPH. The within subject design allows for each of the six rodents to receive each treatment group in the previously stated order. After a repeated measures ANOVA the interaction of overall treatment on impulsivity was significant. Thus, this study found that when a drug is present compared to no drug at all, more impulsive choices are made.

32 Preslar J., Kalinoski A., DeRocher M., Hollis D., & Hestermann E.
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A Novel Aryl Hydrocarbon Receptor 1 (AhR1) Sequence from Rainbow Trout (Oncorhynchus mykiss) Brain.
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The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor in the bHLH-PAS family of proteins. In addition to being commonly used in toxicity studies, members of this protein family, including AhR, are known to play key roles in development and other biological functions. Activation of AhR is known to inhibit fin regeneration in fish, and we hypothesized that it may act similarly in the brain. The AhR is found in two forms: AhR1 and AhR2, with differences in their distribution patterns; AhR1 is found predominantly in the brain and AhR2 is distributed throughout the body. Two AhR2 isoforms (AhR1 and AhR2) have been sequenced in the rainbow trout (Oncorhynchus mykiss), a vertebrate model of brain regeneration. However, AhR1 has not been described, despite its potential importance in the brain. Using rapid amplification of cDNA ends (RACE), we isolated a 1345 bp fragment of a new AhR1-like gene from trout brain. Quantitative RT-PCR revealed that expression of this novel form is limited to a few tissues relative to the two AhR2 forms. Future studies will focus on obtaining a full-length sequence and investigating AhR1 expression and function during brain injury and repair.

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Cognitive Effects of Sleep Deprivation in College Students
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The function of sleep has thus far eluded physicians and academics alike. While there is no exact function of sleep, many studies have been done on the effects of sleep deprivation. Sleep deprivation has shown to have a large impact in the abilities of individuals to function physically and cognitively. College students have proven to be among the most sleep deprived individuals due to academic and social demands. The aim of this study was to compare the cognitive function of college aged students after having a full night of sleep versus a night of total sleep deprivation. Using the psychomotor vigilance task (PVT) and the Uniform Field of View (UFOV) we assessed the reaction times and field of view integration for subjects after each night of study. The reaction times of sleep-deprived individuals were much slower when compared to the times of individuals who had a full night of sleep.

34 Diner I, Rabenold L, & Seyfried N
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Prion-like activity of the U1-70k protein in Alzheimer's disease
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Alzheimer's disease is characterized by a multitude of proteinaceous aggregates including amyloid-beta and hyperphosphorylated tau. In addition, U1 small nuclear ribonucleoproteins (snRNPs) are shown to form both homotypic and heterotypic aggregates with tau. These soluble, nuclear proteins form insoluble, extranuclear aggregates in a fashion specific to AD. To understand this aggregation, a prion-like mechanism is proposed. Indeed, prion-like "seeding" occurred when control and AD brain homogenates were mixed. These results suggest that U1 snRNPs could potentially act as a novel

biomarker for the diagnosis of AD and aid in elucidating the mechanism of pathogenesis. As such, further research into the characterization and pathology of U1 snRNPs is warranted.

35 Harrell, J. R. & Wilhelm, J.C.
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Enhancement of axon regeneration by treadmill training is not dependent on estrogen signaling in mice.
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Moderate exercise in the form of treadmill training following peripheral nerve injury enhances regeneration of the damaged axons in a sex dependent manner. The mechanisms that mediate this sex difference are relatively unknown. Previous studies have shown that androgens, such as testosterone, can enhance axon regeneration to a level similar to treadmill training. However, testosterone is converted to estrogen in the body via aromatase; therefore, the enhancement found after exogenous testosterone administration may be due to an increase in estrogen signaling rather than testosterone. In this study, we investigated the effects of estrogen signaling on axon regeneration in gonadally intact wild type mice. Silastic capsules filled with estrogen or left blank were implanted subcutaneously to release the drug continuously for two weeks. Immediately after implantation, the common fibular branch of the sciatic nerve was transected and repaired. Starting on the third day post transection, a subset of mice not treated with estrogen received treadmill training for five days/week for two weeks. Fourteen days post transection, a fluorescently labeled retrograde tracer was applied 1500 microns distal to the original transection site to label all axons that regenerated at least that distance. Regeneration was quantified as the number of fluorescent labeled motoneurons present in the spinal cord. We found that treadmill exercise significantly enhanced axon regeneration; however, this enhancement is unlikely to be mediated by estrogen as estrogen treatment did not significantly alter axon regeneration.

36 Bailey Hill, Candler Paige, E. Alfonso Romero-Sandoval
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Assessment of pro-inflammatory factor expression on human THP-1 macrophages.
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After surgery macrophages play a role in surgical postoperative pain and wound healing. Interleukin-6 (IL-6) is a cytokine implicated in the incision pro-inflammatory milieu following surgery, and the levels of this cytokine parallels the development of chronic postoperative pain or the resolution of acute postoperative pain. We postulate that the induction of an anti-inflammatory phenotype in macrophages will drive the return of IL-6 to basal levels. We first conduct in vitro experiments to determine the basal expression levels of IL-6 in human macrophages in the presence of a pro-inflammatory stimulus, lipopolysaccharide (LPS). THP-1 monocytes (a human cell line) were differentiated with phorbol-12-myristate-13-acetate (PMA, 60 ng/ml, 48 h). Then, cells were incubated in the presence or absence of LPS for 0, 4, 24, and 48 hours. We quantified the expression of IL-6 through real time reverse transcription polymerase chain reaction (qRT- PCR), using CD11b, a monocyte marker, as the control house-keeping gene. We observed that IL-6 basal expression was minimal, and that LPS induced an increase of IL-6 picking at 24 hour after LPS incubation. Our house-keeping gene, CD11b remained unchanged at all times tested. These data set the basis for further experiments (currently ongoing) in which the anti-inflammatory molecule, ED2/CD163 will be evaluated under the same conditions in our

setting. We anticipate that ED2/CD163 will pick at the time in which IL-6 start to return to basal levels. These studies will be the foundation to test the role of ED2/CD163 in the resolution of postoperative pain.

37 Tran M,Desai V,Anand S, Vasudevan S, Cheng J, Keefer E., Romero-Ortega M.
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Functional Regeneration of Axons into Surrogate Muscle and Skin Targets
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Robotic prostheses controlled by innate nervous system hold promise for individuals suffering from limb loss. It has been shown that after limb amputation or peripheral nerve injury, axons of the residual stump are electrically active and retain the ability to regenerate. We have previously shown that a Regenerative Multi-electrode Interface (REMI) can be used to interface with regenerated axons of the rat sciatic nerve. However, due to mix modality regeneration into the REMI, distinguishing motor from sensory signals remains a challenge. To address this limitation, we designed Y shaped REMI interface to segregate the regenerating axons into separate motor and sensory compartments. To differentially entice the growth of motor and sensory fibers into separate arms of a Y conduit we used muscle and skin as surrogate targets. These were compared to Y conduits with non-discriminatory nerve targets. Briefly, adult Lewis rats (n=3) were implanted with Y tubes attached to the proximal end of a transected sciatic nerve, while the distal sciatic nerve was avulsed. Regeneration was assessed by immunolabeling of Î²-tubulin and NF-200 to confirm successful regeneration into arms. Functionality of the regenerated axons was ascertained by measuring Compound Nerve Action Potential (CNAP) by stimulating proximal to the regenerated Y nerve near the sciatic notch and recording the response in both arms of the Y nerve. Responses were recorded both at threshold and three times threshold to ensure activation of majority axons within the regenerated nerve. Measured CNAP response was evaluated for the presence of distinct peaks using a custom program developed in MATLAB to measure the conduction velocities and Area Under Curve (AUC) of each peak. Results confirm that both the muscle and skin targets were able to induce the regeneration of functional fibers into the surrogate targets. The measure values for conduction velocity ranged from ~50 - 3 m/s in both the groups. This study indicates that Y shaped conduits can be used to differentially guide the growth of regenerated fibers into separate recording/stimulation chambers for neural interfacing.

38 Dowdy N, Koski-Vacirca R, & Conner W
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Computational Analysis of Bat and Moth Sonar
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For 65 million years, echolocating bats and tiger moths have participated in an evolutionary arms race, developing advanced acoustic techniques for increased survival. These animals have complex and incompletely understood ultrasonic interactions demonstrating survival strategies. The vocalization characteristics of bats and moths are unique and critically important to identifying their interactions in nature. However, acoustic analysis of these vocalization characteristics has been historically tedious and manually performed. The aim of this study was to develop unique computational software automating the detection of bats and moths in controlled settings and in the field. To this end, acoustic data was recorded containing ultrasonic interactions between tiger moths and brown bats both in the lab and at field sites in Arizona. These samples were analyzed using new automatic identification paradigms in

MATLAB with in-house code. Characteristics tested included vocalization intensity by frequency, intensity by time, and frequency over time. Success of automatic identification of bat and moth calls over large (n=150,000) samples of data varied by paradigm. Using many iterations of code, we successfully automatically identified 95 percent of moth calls in an ultrasonic audio file polluted with concomitant bat calls. These moth calls were identified using a multi-characteristic analytical approach able to distinguish between the acoustic signatures of bats and moths. Our results suggest that automated, computational analysis of bat-moth ultrasonic data could provide a more conclusive, detailed insight into the nature of bat-moth evolutionary interactions and strategies.

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Stimulus velocity encoding by primary afferents in the wind-sensitive cercal system of three cockroach species.
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Extracting information from the environment is an important function of sensory systems. How this information guides behavior can vary between closely related species. In cockroaches, *Periplaneta americana* exhibits a distinct wind-mediated terrestrial escape response unlike its close relatives (*Blaberus craniifer* and *Gromphodhorina portentosa*) despite possessing the same underlying neural circuit. Previously, we discovered that wind evoked more activity in the wind-sensitive interneurons (WSIs) of *P. americana* and *B. craniifer* than of *G. portentosa*. However, it is not clear whether these differences in the WSI activity originate from the WSIs themselves or from sensory receptor neuron input. To address this question, we recorded from the cercal nerve to determine whether the afferent activity differed between these three species. We extracellularly recorded the summed wind-evoked responses from the cercal nerve afferents (wind puffs varied 0-250 cm/sec, 300 ms duration). Stimulus-Response (S-R) curves were generated for the first 100 ms and second 150 ms of summed response for all species. S-R curves were calculated for individual animals and averaged to generate a single afferent S-R curves for each species. Our results demonstrated that wind stimuli elicited greater afferent activity in both *P. americana* and *B. craniifer* than *G. portentosa*. Furthermore, *B. craniifer* and *P. americana* afferents had a greater dynamic range of encoding stimulus velocities. Response latency did not vary for stimulus velocity in all species, but *P. americana* had a shorter response latency in both afferent and WSI response latency than the other species. These results indicate the afferent input contributes to differences in the WSI responses indicating exhibited behavioral responses are likely not solely due to differences in afferent input.

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Individual Variability in Punishment Resistance Following Progressive Footshock Administration
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A hallmark feature of addiction is continued use of a substance despite awareness of negative consequences. Previous studies have shown involvement of the lateral habenula (LHb) and the rostromedial tegmental nucleus (RMTg) in behavioral responses to aversive stimuli, suggesting a potential role for these brain regions in addiction. There is a large degree of individual variation in tolerance to aversive stimuli (i.e. footshock) indicating that there may be neurobiological variation in punishment resistance. The present study tries to better understand the underlying differences that

contribute to this variation. After rats were trained to lever press for a food reward, they received daily sessions in which response to the rewarded lever was punished by footshock. The intensity of footshock increased within each session until an intolerable intensity of shock intensity was reached. We then quantified the number of activated cells within the LHb and the RMTg in response to this behavioral paradigm using cFos immunohistochemistry. Ablations to the RMTg have been shown to raise the tolerance to shock, and thus, we hypothesize that individual variation in this structure contributes to individual differences seen in resistance to punishment. Preliminary findings detected a negative trend in the correlation between cFos activity in the RMTg and shock tolerance, but not in the LHb. We expect further findings to support a negative correlation between neural activity in the RMTg and resistance to punishment furthering our understanding for why individuals continue substance abuse even given detrimental consequences enabling us to better treat related disorders.

41 Williams NR, Enabore JG, Williams EN, Korte J, Roberts D, & Edwards JC
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Feasibility of Developing a Neurophysiologic Assessment of Concussion
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It is estimated that 63,000 concussions occur every year among high school varsity athletes participating in a range of 10 sports across the US. Concussion is currently a clinically subjective diagnosis given the lack of objective measures of concussive injury (CI). An increasing concern in CI is a growing body of evidence listing repetitive concussion with risks for dementia, depression and second impact syndrome, a fatal condition associated with diffuse brain swelling and brain herniation. In this study, we determined the feasibility of developing a neurophysiological baseline assessment in an effort to establish a database of normal brain physiology for healthy teenage athletes (ages 14-18 years old). We did this through the use of paired pulse transcranial magnetic stimulation (ppTMS) and computerized gait assessment. When looked at retrospectively, previous studies have shown ppTMS abnormalities in athletes with CI. Also, athletes with a history of previous concussions adopted a more conservative gait strategy statistically different than those individuals with no concussion. We acquired pre-season TMS and gait assessments for 25 high school soccer athletes and 16 athletes returned for post-season data collection. All 25 athletes were able to tolerate the assessment with no discomfort and no adverse reactions to the stimulation. After analyzing the data, pre and post time points were found to be relatively well correlated on left-sided measurements; significant correlations were seen with left sided intracerebral inhibition ($p=0.0438$) and intracerebral facilitation ($p=0.0407$). We ultimately conclude that collecting pre-season baseline neurophysiological data is not only feasible, but appears to be safe and well-tolerated. Knowledge of these metrics can be used to both help with establishing the diagnosis of concussion as well as to help in predicting time of recovery and outcome.

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Mechanisms Underlying Reinforced Behavioral Variability
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Behaving variably sometimes is adaptive; it can increase chances of survival and solve problems. Additionally, society tends to value creative, original efforts. However, some individuals (e.g., people with autism) behave repetitively. Behaving variably can be maintained by reinforcement, but the mechanisms by which that happens are unclear, given that reinforcement typically produces repetitive behavior. Several explanations of reinforced behavioral variability have been proposed, such as remembering previous behavior and producing different behaviors, reinforcement of random responding, and even reinforcement of variability as a byproduct of other processes. Two experiments were conducted to elucidate the variables that impact reinforced behavioral variability. In each experiment, four male pigeons were trained to emit four-peck sequences across two keys (e.g., LRRL, where L and R are left- and right-keypecks, respectively). Under baseline conditions, the pigeons were required to vary among these response sequences by providing reinforcement for only those sequences that had been emitted relatively infrequently. We assessed variability as a function of inter-response interval and inter-trial interval durations and found that variability was affected only by changes in inter-response interval duration. We also compared the direct reinforcement of variability with the reinforcement of switching between keys, and found that variability was higher when directly reinforced. These results support the claim that reinforced behavioral variability is a result of reinforcing the random generation of behavior. In addition to the experimental examination of the behavioral mechanisms underlying reinforced behavioral variability, its potential neural mechanisms are explored theoretically.

43 Krause EL, Upright NA, Monuszko KA, Moses-Hampton M, Lakhmani P, & Ramirez JJ
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Electrophysiological Interaction of the Septodentate and Crossed Temporodentate Pathways 12 Days Post-Unilateral Entorhinal Cortex Lesion
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The central nervous system (CNS) has been shown to undergo neuroplastic phenomena in response to neurodegeneration and traumatic brain injury. In rat models of lesion-induced hippocampal plasticity, axonal sprouting acts as a significant mechanism of recovery. A unilateral entorhinal cortex lesion results in degeneration of the perforant path and consequent deafferentation of the ipsilateral dentate gyrus (DG), a structure highly implicated in spatial memory. This disconnection induces significant proliferation of several afferent pathways to the DG, including the crossed temporodentate pathway (CTD) and septodentate pathway (SD). While past studies have shown sprouting of the CTD to be essential for behavioral recovery, the functional significance of the SD proliferation is not well understood. This research assesses the electrophysiological significance of SD sprouting at 12-days post lesion. This time point is an essential step in linking the electrophysiological interaction of the SD and CTD to behavioral recovery because at 12-days post lesion rats recover behaviorally and the sprouted CTD acquires the ability to fire granule cells in the DG. This study measures the electrophysiological interaction of the SD and CTD pathways using a paired-pulse stimulation paradigm, in which the CTD is stimulated both alone and with prior SD stimulation at inter-pulse intervals (IPIs) of varying durations. If SD stimulation influences the synaptic efficacy of the CTD, we expect to see either inhibition or facilitation of the response evoked in the DG as a function of the IPI.

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The Capabilities of the Predictive Visual Imagery Abstract
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Visual imagery is an important cognitive function that plays an imperative role in a variety of higher order cognitive behaviors including dreaming, hallucinations, visual memory, and object recognition. A greater understanding of this ability would have profound implications in an array of fields such as hallucinogenic disease research and computerized object recognition. Previous research has shown that object recognition relies on both imagery dependent top-down and retinal stimulation dependent bottom-up visual processes. Our experiment seeks to determine which of these perceptual paradigms more heavily facilitates recognition. This is accomplished by showing participants a series of 1000 photographic images, half of which have one object removed and half of which have all but one object removed. The participants will then be asked to identify the missing or highlighted object in question for each image. The results will be measured as the percentage of objects correctly identified in each condition and will be interpreted in the context of several important variables including intra-object contrast, location, category, and size. We hypothesize that there will be significant differences between the two conditions and that the strength and direction of this difference will be dependent on the aforementioned variables.

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An Assessment of Novel Cancer Treatments on Breast Cancer and Neuronal Cell Lines
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Previous studies have shown the potential human benefits derived from berry and plant extracts. This study investigated the anticarcinogenic properties of *Rubus idaeus* (red raspberry) extracts in both natural and pill form on the MCF7 and T47D breast cancer cell lines. Additionally, extracts obtained from *Phytolacca americana* (pokeweed) and *Clusia rosea* (renaquilla) were tested for their anticarcinogenic properties using the PC12 cell line derived from the rat adrenal medulla. Cells were cultured, counted, and subsequently separated into 96 well plates where the various extracts were added in increasing ratios. An MTS assay was used to determine viability, and absorbances were read using an ELISA plate reader. High absorbances corresponded to greater viability. It was seen that raspberry extracts in both forms had an anticarcinogenic effect on MCF7 cells, whereas both extracts showed a mitogenic effect on T47D cells. Pokeweed extracts from the stem/leaf and root generally had a mitogenic effect whereas pokeweed berry extracts had a slight anticarcinogenic effect on the PC12 cells. *Renaquilla* was shown to have anticarcinogenic effects, but further trials are necessary to validate its significance. These novel extracts shed light onto the potential anticarcinogenic properties of naturally occurring substances easily found in nature that may have clinical implications in the future.

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Biological Mechanisms of Cocaine-seeking
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Drug addiction is a global issue, and many of the problems associated with addiction involve compulsively seeking and taking the drug of abuse. These behaviors stem from classical and operant conditioning wherein the stimuli that become associated with drug taking serve as salient cues to reinstate drug-seeking. Relapse behavior is one of the most difficult aspects of addiction to treat, thus making it our prime target. The dorsomedial prefrontal cortex (dmPFC) plays a critical role in the reinstatement of cocaine-seeking behavior. Following forced abstinence, brain-derived neurotrophic factor (BDNF), when infused into the dmPFC, has been shown to attenuate drug-seeking. Previous research has shown that both BDNF's receptor, TrkB, and extracellular signal-regulated kinase (ERK)

activation are required for BDNF's suppressive effect. However, the mechanisms of BDNF's ability to affect reinstatement behaviors are not fully understood. Src family kinases (SFKs) are involved in TrkB trafficking and activation, and may play a role in BDNF's ability to suppress cocaine-seeking. The goal of this study is to use a SFK inhibitor to determine if SFKs are necessary for BDNF's attenuation of cocaine-seeking and normalization of ERK deactivation following cocaine self-administration. In this experiment, a SFK inhibitor, PP2, and its inactive isomer, PP3, were infused into the dmPFC prior to BDNF in order to test whether SFK inhibition blocks BDNF's effects on cocaine-seeking as well as ERK phosphorylation. An understanding of the mechanisms underlying BDNF's ability to attenuate drug reinstatement could lead to advancements in the prevention of relapse in a drug administration paradigm.

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Effects of dopaminergic antagonists on nicotine-enhanced sign tracking in rats.
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Nicotine increases approach to a discrete conditioned stimulus (CS) that is paired with a rewarding unconditioned stimulus (US; e.g., sucrose). We have hypothesized that this increase in 'sign-tracking' reflects increased incentive motivational impact of the CS and depends on increased mesotelencephalic dopamine (DA) release. To investigate this hypothesis, 10 rats were assigned to one of two groups that received a pre-treatment injection of 0.4 mg/kg (free base) nicotine (NIC group) or placebo (SAL group) 15 min prior to behavioral testing sessions. During testing sessions, a 30 s CS (illumination in a receptacle) was presented immediately prior to delivery of the US (0.1 ml of 5% Nesquick) in an adjacent receptacle. Sign tracking and goal tracking were defined as entries into the CS and US receptacles, respectively, during presentation of the CS. Both groups displayed comparable levels of goal-tracking; however, NIC pretreatment potently increased sign tracking. After approach behavior was stable, we investigated the role of DA receptors in the incentive-promoting effects of nicotine using pre-test injections of SCH 233090 (D1), eticlopride (D2/3), and flupenthixol (non-selective) 30 min before test sessions. Placebo 'wash-out' tests were conducted between antagonist tests and activity during all tests was recorded with a behavioral tracking system. All three antagonists reduced sign-tracking, but not goal tracking, in NIC rats. However, all three antagonists also reduced goal tracking in the SAL group, suggesting that DA systems may play an important role in time-locked responses to appetitive CSs and the potentiation of their incentive properties by nicotine.

48 Jones L, Cobb D, Rossi D, Ester C, Sasser K, Russell D, Sledge R, Johnson H, Krueger H, Moore E, Hoffman D, Defelice S
A Decade of the IMPULSE: International Growth and Impact
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The journal IMPULSE was started in the spring of 2003. In the decade since, it has grown from 14 student reviewers from three countries to 100 reviewers representing 24 institutions in six countries and four continents. There are eleven Reviewer Training Sites, each with their own Faculty Advisor, one of those in South Africa and one in Spain. As the first cohort of students has now moved at least 6-8 years into their post-baccalaureate careers, the impact on editors, reviewers, and authors can begin to be assessed. In this study, there were 20 female and 25 male respondents coming from 12 universities (four international). Most reported spending up to 5 hours/month reviewing manuscripts (40.9%) and serving for two (40.9%) or three (31.8%) years. Also, most reported reviewing at least 5 manuscripts (37.2%). In response to questions on whether IMPULSE was a positive influence on writing skills,

literature research, ability to read papers, or selection of career choice the majority marked Agree to Strongly Agree (>90%). However, most were Neutral or only Agreed that it had a positive influence on their lab research skills or that it raised their awareness of career options. Similarly, responses were spread on whether IMPULSE helped with their post-baccalaureate program or on professional performance, though the largest responses were Strongly Agree + Agree (>51% and >73% respectively). Most Strongly Agreed (64.3%) that they would recommend the experience to others; they also indicated that they list it on their current resume (78.6%). In following up on their current positions, the largest single group was pursuing Ph.D.s (26%), followed by currently working (23.8%) or in medical school (19%).

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The Role of the Hippocampal Formation in Working Memory: A Disconnection Analysis
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Alzheimer's disease (AD) is a neurodegenerative central nervous system disorder that has been associated with working memory impairment. Although the hippocampal formation has been established as an essential structure for various types of memory, its contribution to working memory remains unclear. Atrophy of the perforant pathways and cholinergic septohippocampal fibers, two major extrinsic hippocampal pathways, are hallmarks of AD. Here, we aim to elucidate the role of the hippocampal formation and several of its key afferent and efferent connections in working memory using a disconnection model in rat. After reaching criterion on a Delayed-Non-Matching-to-Sample (DNMTS) task in an operant chamber, rats were randomly assigned to one of five surgical groups: (1) bilateral fimbria-fornix transection (BFFx); (2) bilateral entorhinal cortex lesion (BECx); (3) unilateral fimbria-fornix transection + contralateral entorhinal cortex lesion (UFFx/CECx); (4) unilateral dorsal psalterium and fimbria-fornix transection + contralateral entorhinal cortex lesion sham craniotomy (UDPx/CFFx); (5) sham craniotomy. Post-operative behavioral testing began after a 5-12 day recovery period and continued until 64 daily sessions were completed. All four lesion groups demonstrated working memory impairment in early post-operative testing. Both the BECx and UFFx/CECx groups showed recovery to preoperative performance levels within 4 weeks of testing. The BFFx group resulted in a permanent working memory deficit across the 12 weeks of testing. Histological analysis confirmed lesion placement, and histochemical staining indicated lesion-induced acetylcholinesterase-containing sprouting, a measure of cholinergic septodentate sprouting, in BECx group dentate gyri. Along with the pattern of behavioral recovery, this suggests a possible cellular correlate to the recovery of working memory function in entorhinectomized rats.

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Electrophysiological Interaction of the Crossed Temporodentate and Septodentate Pathways 8 Days Following Unilateral Entorhinal Cortex Lesion in Rats
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Alzheimer's disease (AD), the most common form of dementia, continues to affect a wide range of individuals around the globe. Characterized by a variety of symptoms including memory loss, confusion, depression, and changes in personality, the disease triggers a distinct degeneration of the entorhinal cortex (EC). This structure provides afferents to multiple regions in the brain, notably the dentate gyrus (DG), a region of the hippocampus that plays a crucial role in spatial memory. Axonal sprouting, an example of neuroplasticity, has been investigated following damage to the brain from AD, stroke,

traumatic brain injury (TBI), and other forms of acute brain damage. This investigation seeks to explore the sprouting response that occurs in two major projections eight days following a unilateral lesion of the EC: the crossed temporodentate pathway (CTD), which projects from the EC to the contralateral DG; and the septodentate pathway (SD), which arises from the medial septal nucleus and projects bilaterally to the dentate gyrus. Sprouting of the CTD, in particular, has been shown to correlate with recovery of spatial memory tasks. The eight day time point after an EC lesion is a significant period for the sprouting response as previous research has shown that both CTD sprouting and moderate behavioral recovery have begun at this time. Rats in the experimental group (n=12) were given unilateral lesions to the EC, while those in the control group (n=9) were given craniotomies alone. Eight days post-lesion, the electrophysiological activity of the DG was assessed in all rats by paired-pulse stimulation of the medial septal nucleus and the intact EC in the contralateral hemisphere. This paired-pulse activation of the SD and CTD consisted of first stimulating the medial septal nucleus and subsequently the intact EC at multiple inter-pulse intervals (IPIs) ranging from 10-500 ms. Our preliminary data illustrate a lesion effect by an increase in amplitude of the CTD field excitatory postsynaptic potentials (fEPSPs) across all IPIs at the eight day time point. At this time, there is no difference in amplitude or slope between unpaired and paired-pulse stimulation of the SD and CTD. One case has displayed evidence of a population spike, a downward point in the waveform that represents the discharge of cells in the granule cell layer. The eight day time point characterizes an important period in the timeline of axonal sprouting, reflecting the beginning of behavioral recovery and modest CTD sprouting. These data, specifically the increase in amplitude of the CTD-fEPSPs, demonstrate that there is some sprouting response occurring in these pathways at the eight day time point and we find this increased neurophysiological response may correlate with the increase in behavioral recovery shown in previous research.

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Activation of spinal cord neurons in a rodent model of sickle cell vaso-occlusive crisis
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Sickle cell disease is one of the most common chronic diseases that occur in children. This disease is characterized by vaso-occlusion and rigidity of the erythrocytes in the blood. These children have recurrent episodes of inflammation in their cells which will eventually progress to the organs. There is more research to be done in order help develop effective treatments that target pathphysiological changes and clinical obstacles. Our model of sickle cell disease focuses on a certain chemical mediator, Endothelin-1 (ET-1). Endothelin-1 is released in the body in response to vaso-occlusive crisis. This study tests the hypothesis that vaso-occlusive crisis lead to activation of spinal cord neurons associated with pain processing. Postnatal day 7, 21, or adult rats were administered intraplantar saline, Endothelin-1 or control naive. Spinal cords were collected at 2 hours an changes in protein kinase C gamma was assessed by immunohistochemistry. Both sex and age-related changes in protein kinase C gamma were observed supporting activation of spinal cord neurons in a vaso-occlusive crisis. This study suggests that inhibitors of protein kinase C gamma could be useful therapeutics in the treatment of painful vaso-occlusive crisis associated with sickle cell disease.

52 Burns M, Pavlinchak B, Peters J, Stefanik M, Thomas C, Ruscio M, & Riegel A
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The Effect of Retigabine in the Prefrontal Cortex on the Pain and Fear Response
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abstract_: Though pain and fear have been established as two separate processes, they can sometimes be inextricably intertwined and have malignant, lasting damage on the body and the mind as well as the pocketbook. Treatment of chronic neuropathic pain has been estimated to cost $150 billion in the United States. In conditions of neuropathic pain as well as mental distress, such as Post Traumatic Stress Disorder, the amygdala displays hyperexcitability which is responsible the fear response. A cohort of 32 (16 control and 16 experimental) Long-Evans rats were given a Spared Nerve Injury (SNI) in order to mimic the effects of peripheral neuropathic pain and then immediately cannulated in the prelimbic cortex (PL) in order to receive an infusion of the drug, Retigabine. Retigabine activates potassium channels and has been shown to decrease hyperexcitability in the amygdala which should cause a reduction of fear response. Rats were then put in a fear conditioning paradigm with a tone and footshock pairing, where fear was measured by freezing behavior. After conditioning, rats were infused with Retigabine then put on an extinction phase where a tone was emitted sans footshock in order to assess recall. Later that day, rats were exposed to two non contingent shocks in the absence of tones to determine if a fear response is exhibited. We hypothesize that rats with a SNI that were infused with Retigabine would exhibit less of a fear response and a slower reinstatement than those without Retigabine.

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Peroxiredoxin Gene Expression in *Nematostella vectensis*
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An organism's biological clock controls daily cycles in physiology and behavior. We have been investigating the circadian clock of the starlet sea anemone, *Nematostella vectensis*. *N. vectensis* serves as an excellent model organism because of its basal evolutionary position and its sequenced genome. Specifically, we have been studying the role of peroxiredoxin (PRX) in temperature dependent biological rhythms. Environmental temperature oscillates throughout the 24-hour photoperiod, and can serve as a temporal cue for many invertebrates. In *N. vectensis* we have demonstrated that a 24hr temperature cycle (32°C: 22°C) can synchronize locomotor behavior with more activity occurring during the cooler temperature. Peroxiredoxins are a highly conserved family of anti-oxidant proteins involved in the control of intracellular peroxide levels and may serve as a universal marker for circadian rhythms. By assessing the levels of PRX in response to a temperature cycle, we aim to further establish temperature as an input to the circadian clock mechanism in *N. vectensis*. Animals were exposed to a 12 hr 32°C: 12hr 22°C temperature cycle for two weeks. Temperature-entrained animals were collected at 8 time points across the 24-hour day and protein levels of PRX were quantified by Western blotting. Results indicate that similar to behavior, PRX rhythms are also synchronized by temperature in *N. vectensis*. Moreover, PRX is more highly expressed during the lower temperature time points as has also been shown in human red blood cells. Our data will provide a foundation for additional investigations into temperature regulation of circadian clocks.

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A Behavioral Rat Model of the Affective Component of Neuropathic Pain
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Neuropathic pain has a large economical and emotional cost to public health; not only does it disrupt the lives of those who suffer from it, but it also exacerbates other physiological and psychological problems. While acute pain has many effective clinical treatments, chronic (neuropathic) pain however

is persistently refractory to clinical treatments, likely because the factors that underlie the basic mechanisms of chronic pain are not well understood. Neuropathic pain is known to be associated with an affective component that influences cognitive and emotional processing. The purpose of this study was to determine if the affective component of the behavioral output in response to fear conditioning is altered in a rat model of chronic pain. In this study 16 rats underwent a spared nerve injury surgery to model neuropathic pain, and 16 rats underwent a sham surgery. The measured allodynia (pain threshold) was determined using Von Frey Filaments every four days up to a month post-surgery. The rats then underwent a fear conditioning paradigm. We predict that the rats experiencing neuropathic pain will have a higher rate of fear response on the reinstatement day then that of the sham rats, which indicates an increased ability to recall the extinct fear response. This result would be indicative of the affective component of neuropathic pain and suggests that rats experiencing neuropathic pain have a harder time suppressing inappropriate fear then do non-neuropathic pain rats. This provides further evidence that there are cellular/structural changes that may be occurring in the underlying pathways associated with neuropathic pain.

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Nonlinear Dynamics of Postural Stability
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abstract_: Falls are the leading cause of hip fractures and injury-related hospitalization among older adults. Upright postural stability relies on three sensory inputs: vision, vestibular, and proprioception. Proprioception integrates muscle spindles, joint and skin afferent fiber inputs. By using a combination of self-report (Activities-specific Balance Confidence Scale), Joint Position Sense (JPS), Kinesthesia, and dynamic balance (Mini BESTest), results from our lab have demonstrated significant proprioception declines suggesting a global versus distal-to-proximal proprioceptive decline across lifespans. Our static balance (force plate) measures (RMS displacement or RMS velocity) did not show significant differences between age groups, so the primary purpose of this study is to explore the use of nonlinear time series measures of Applied Entropy (AppEn) and Hurst Rescaled Range (R/S) to assess fall risk and postural stability across the lifespan. Our current results show that older (versus young and middle age) participants demonstrate more random sway in the mediolateral direction, putting them at higher risk for hip fractures.

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Effects of Early Adolescent and Adult Methamphetamine Exposure on Behavior and Corticosterone Levels in Mice
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Methamphetamine (MA) is a highly addictive psychomotor stimulant drug that affects the central nervous system. While much research has examined the long-term effects of adult MA use, relatively little research has been done on the effects of adolescent MA use. Adolescents in treatment for MA use show increased anxiety and depression levels compared to adolescents in treatment for other drugs. As the brain is actively developing during adolescence, it is imperative that we understand the effects of MA exposure during this developmental period. This research examined the effects of early adolescent MA exposure on behavior and serum corticosterone levels in early and late adolescent male and female C57BL/6J mice. Additionally, the effects of MA on depression-like behavior in adult mice, and the ability of the anti-depressant drug Selegiline to reverse these effects, were also examined. There was a trend for adolescent MA exposure to increase anxiety-like behavior in the open field test in early and late

adolescence, but no significant effects of adolescent MA exposure were found on other behaviors. Furthermore, adolescent MA exposure had no effect on serum corticosterone levels in adolescence. These data suggest that, compared to adults, adolescents may be relatively protected from the effects of MA. In the adult mice, MA increased depression-like behavior, but Selegiline did not reverse this increase. Thus Selegiline is likely not a good candidate treatment to reverse the increase in depression levels following adult MA exposure.

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Network Connectivity between Rest State and Working Memory
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Network science is the study of complex systems characterized in terms of their nodes and edges, allowing for the discovery of underlying structure. The current study explores neural functional connectivity relationship comparing participants at rest and while engaging in a working memory task. A one step analysis was run to observe the degree, or number of connections made, by the top 10 percent degree nodes in each of 90 brain regions. Top overlay maps were created to view the consistency of these connections. Based on visual differences in the overlay maps between resting and working memory, 17 areas of interest were found. Statistical analyses were then run on the connections of top 10 percent nodes in these areas to further explore connectivity patterns.

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An examination of the effects of stimulation or blockade of VTA serotonin 1A and 3 receptors on feeding in the food-deprived rat
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Obesity is a significant health concern in the United States, costing more than $150 billion annually. Several pharmacological treatments for weight loss target central serotonin (5-HT) pathways. Serotonin regulates feeding through actions in brainstem nuclei and hypothalamic circuitry involved in the homeostatic regulation of food intake. However, less is known about the role of serotonin receptors within the ventral tegmental area (VTA), a region that regulates motivation and effort directed towards food and drug rewards. In this study, we investigated the potential role of VTA serotonin 1A and 3 receptors on feeding and locomotion in food-restricted rats offered 2-hr daily access to standard rat chow. Male Sprague-Dawley rats were implanted with bilateral guide cannulas targeting the VTA. After surgical recovery and food restriction to 90% ad libitum body weight, rats were acclimated to 2-hr daily sessions within feeding chambers and to microinjection procedures over 6 days. On subsequent drug testing days, individual groups of rats were tested following VTA injections of the 5-HT1A receptor agonist 8-OHDPAT, the 5-HT1A receptor antagonist WAY 1000635, the 5-HT3 receptor agonist mCPBG, or the 5-HT3 receptor antagonist ondansetron. Each group received several doses of the same drug, randomly determined for each rat and tested at least 48 hrs apart. Dependent measures included food and water consumed across the 2-hr feeding session, as well as counts of ambulation and rearing. These experiments will help to further our understanding of the serotonin 1A and 3 receptors in the VTA, specifically regarding their involvement in the regulation of feeding in response to caloric need.

59 Lyons S, Riegel A, Ferland C
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Potential Differences in Cortisol Levels between Physical and Psychological Stress Sources
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The interaction between chronic pain and the stress that it can potentially cause is a topic of great interest particularly for a population such as ours with increased number of soldiers and veterans who experience chronic pain and are under already stressful conditions. This study evaluated the impact of different stress sources on cortisol levels in male Long Evans rats. There were three subject groups included: Sham surgery, Spared nerve injury (SNI) surgery, and fox urine exposed. The sham surgery rats act as the control group. The SNI rats are in a state of chronic neuropathic pain, it is understood that pain is stressful and this is a physiological source of stress. The fox urine rats are experiencing purely psychological stress as a result of their instinctual fear when faced with a signal of nearby foxes. After SNI rats have reached chronic pain (21+ days) and fox urine rats have undergone 5 exposures, each group will undergo rapid decapitation followed by cortisol serum extraction. Although both physiological and psychological stress have been described as impacting cortisol levels, the mechanism of these two types of stress work in different pathways. Our hypothesis is that chronic-pain rats will have lower than normal cortisol levels compared to the fox urine rats which will show increased serum level of cortisol. This is based hypothalamic pituitary adrenal axis is suppressed when pain goes unabated for an extended period of time, leading to lower rather than increased serum levels. This experiment will provide insight into the differences in stress response when faced with psychological and/or physiological stressors.

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Event-Related Brain Potentials for Emotional Words versus Pictures
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Some of the most common place methods advertisers use to entice consumers to try or buy their products are pictures and words. Entire divisions of companies conduct market advertising research in order to determine the most effective way to market their product (using pictures or words). Along with self-reported emotional and physical reactions to emotionally charged images, changes in brain activity also occur when someone is exposed to certain visual stimuli. Previous studies have shown that event related potentials (ERPs) are enhanced for emotional pictures and words, but none have yet to consider related words and pictures in the same study. This study examined the effects that type of stimulus and level of emotional valence had on brain activity. Electroencephalography (EEG) was used to record P300 and LPP activity of 21 undergraduate students. Two methods of stimuli presentation were used; pictures and words, and three levels of emotionality were used, positive (happy, excitement), neutral, and negative (fear, sadness). Analysis using repeated measures ANOVA showed that pictures generated a higher magnitude P300 peak and LPP peak when compared to words for all emotion levels. Also positive and negative stimuli generated higher magnitude P300 peaks and LPP peaks compared to neutral stimuli in a parietal electrode. Overall, a consistent increase in P300 and LPP amplitudes in relation to type of stimuli showed that pictures produce more brain activity than words, information that could have a beneficial impact on advertising approaches and educational techniques.

61 Mitchell B, Heitsch S, Gaita R, & Cleland CL
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Stimulus and Postural Determinants of the Escape Response of Crickets to Localized Heat Stimuli
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Animals respond to aversive stimuli with escape or withdrawal responses. In crickets, wind or looming stimuli, which might normally be produced by an approaching predator, evoke an escape response in which the cricket turns and then runs or jumps away. Although in mammals aversive heat stimuli have been used routinely to evoke withdrawal responses, there have been no studies on the cricket's response to localized heat stimuli. The goal of this study is describe the escape response of the cricket (*Acheta domesticus*) to heat stimuli delivered to each of its six tarsi and determine the factors that control direction and magnitude of the response. Heat was delivered to the tip of the leg in 20 crickets with an infrared laser diode, the response was quantified by high-speed video (650 fps, 1080p) and the location of features on the cricket were tracked in software. In response to heat stimuli, crickets first retract the stimulated tarsal, then turn by pivoting about a point toward the rear of the animal, and finally either walk (86%), jump (9%) or remain largely stationary (5%). As with wind or looming stimuli, the turn was always away from the location of stimulus. In contrast, however, jumping was less frequent than with the other types of stimuli. These results demonstrate that crickets escape from heat as well as from looming or wind stimuli, and offer the opportunity to identify common movement strategies by comparing the escape responses to the three different stimuli.

62 Hartmann M, Chrzan C, Kabore M, Moore K, & Cleland CL
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Rat Hind Limb Withdrawal Response to Heat Stimuli Depends on Initial Paw Posture but not Stimulus Location
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Rats rapidly withdraw their hind limb in response to a noxious heat stimulus applied to the plantar surface of their paw, which is known as the Nociceptive Withdrawal Response (NWR). Previous studies in spinalized, unanesthetized non-human mammals have shown the direction of response depends on stimulus location. The goal of this experiment is to determine if stimulus location, or other factors, determines the direction of withdrawal in the intact, unanaesthetized rat. Rats were placed on a glass plate through which an infrared laser beam was directed to heat a small (1mm) localized portion of the plantar surface of the foot. The resulting withdrawal was recorded with three conventional camcorders (60 fps @ 1080p), one on the left, one on the right, and the third underneath the rat. From the video, the initial location and angle of paw was recorded. The rat then withdrew and rapidly (~40ms) replaced its paw on the glass, at which point the final location and angle of the paw were recorded. Rats withdrew and then replaced their paw on the glass in all possible direction. To determine if the location of the stimulus influences response direction, the ratâ€™s paw was stimulated in five locations (three aligned rostral-caudal and three aligned left-right). Unexpectedly, we found no dependence on stimulus location. However, we did notice the initial position of paw varied in both location and angle. Consequently we explored if initial position (left-right and rostra-caudal) and paw angle influenced final location and angle. Correlation between initial and final locations and angles did reveal a highly significant linear relationship ($p<0.001$). These results suggest, in contrast to studies in spinalized or anesthetized animals, that initial posture plays a greater role in the programming of the NWR than stimulus location.

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Dominant and Subordinate Aspect of Play Fighting in Juvenile Male and Female Rats
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Reports that male rats demonstrate play fighting more frequently than female rats have been criticized as being too simplistic, that gender differences in play fighting are more complex (Pellis, et al., 1997). An exploratory study compared “hard” dominance behaviors involving confrontation and attack, 2) “soft” dominance behaviors which claim physical space and 3) subordinate behaviors, by gender. The study found that males showed more soft dominance and subordinate behaviors than females. We interpret our findings as indicating that dominant rats contribute to preventing play interaction from escalating to serious fighting, especially among males. Due to our small sample size, we conducted non-parametric comparison of the means of soft dominance, hard dominance and subordinate dominance between male and females. We found differences in soft dominance, $U = 65.00$, $df = 1$, $p = .04$ and subordinate behaviors $U = 39.50$, $df = 1$, $p = .002$, indicating that males showed more soft dominance behaviors and more subordinate behaviors than females. There were no significant gender differences for hard dominant behaviors.

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Septal facilitation of long-term-potentiation in the perforant path in rats
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One neurobiological mechanism that is thought to contribute to memory formation is long-term potential (LTP). LTP is the increase in synaptic efficacy over time and is exhibited extensively within the perforant pathway (PP) of the hippocampus. This pathway is the largest afferent to the hippocampus and arises in the entorhinal cortex and synapses onto the dentate gyrus (DG). Though the PP is extensive and important, it is not sufficient for complete hippocampal functioning. The septodentate pathway (SD), arising in the septum, helps contribute to the functioning of the hippocampus though its full influence in this structure is inconclusive. Many studies suggest the SD cannot even produce a response within the DG while others conclude that it can significantly augment the response of the PP when stimulated prior to PP stimulation This study examines the role of the SD in hippocampal functioning and PP LTP. Using a paired-pulse electrophysiological paradigm, the response of the PP is measured both alone and with a conditioning SD stimulation. The responses are also measured pre-and post-tetany to determine whether the SD can effect the LTP response exhibited by the PP. This study is continuing; however, preliminary results show a clear SD influence over PP response within the hippocampus. Conditioning SD stimulations augment not only the pre-tetany PP response but also the post-tetany PP response.

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Understanding Post Conflict Behavior in the Male Syrian Hamster
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Syrian hamsters are a suitable species to study social conflict since they are solitary animals that are naturally aggressive during social interactions. Male hamsters that experience social defeat exhibit post-defeat behaviors that include learned avoidance, the avoidance of their dominant opponent. We have developed a modified passive avoidance apparatus, the conflict alleyway, which allows for the study of post-defeat behavior. The apparatus yields an automated measurement of a hamsterâ€™s position relative to a caged opponent. We have named this variable the mean position. The manipulation of frequency and duration of the defeat experience can produce measurable differences in post-defeat agonistic submissive, aggressive, and fighting behaviors. The purpose of our study was to investigate the relationship between mean position and defeat experience duration. Hamsters were matched by pre-

defeat mean position and randomly assigned to either 3 minutes or 15 minutes of inescapable social defeat. Post-defeat avoidance tests were conducted 48 hours after defeat. Procedures used in the post-defeat avoidance trials were identical to those used to assess pre-defeat behavior. We report that defeat experience and duration had a significant effect on our avoidance measure; more avoidance was observed in subjects experiencing the 15-minute defeat. Our future work will assess the relationship between mean position and measures of the agonistic behaviors that occur during the defeat.

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The Effects of Stimulated Activity on Zebrafish Circadian Rhythms
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Circadian rhythms are behavioral and physiological patterns that cycle daily and can be synchronized to environmental stimuli such as light and temperature. Zebrafish have become a useful model for studying vertebrate circadian rhythms due to their daytime activity and sleep-like state at night. In constant conditions, zebrafish exhibit an endogenous circadian period between 24 and 25 hours. It was recently shown that forced exercise in the late afternoon can improve the robustness of rhythms in adult mice (Schroeder et al., 2012). We sought to test similar manipulations on circadian period in the zebrafish model. Adult animals that had been maintained on a 14:10 light:dark (LD) cycle (lights on at 0700, lights off at 2100) were transferred to either constant dark (DD) or constant light (LL) recording conditions; animals were allowed to acclimate for 24 hours prior to experimentation. Individual locomotor activity was then recorded for three days to establish a stable baseline using the EthoVision 7 video tracking system. On day 4, swimming activity was stimulated for 30 minutes at 1500 hrs with two small submersible aquarium motors. To determine rhythm robustness, locomotor activity was tracked for six full days following stimulation. Four experiments were performed in DD and 2 in LL. Dependent measures included circadian period and rhythm amplitude prior to and following the manipulation; analyses were conducted with ClockLab. Analyses indicated a significantly longer period in DD following stimulation (t=2.06, p<.04); there was no significant effect on rhythm amplitude (p=0.09). In LL, we found no significant effect on period or amplitude of the rhythm. Given that zebrafish are diurnal, a similar manipulation in the morning may also have an effect on periodicity and/or a positive impact on rhythm amplitude. Manipulations like these in humans could serve as a potential remedy for common sleep problems, such as early morning awakening in elderly populations.

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Selective Activation of Alpha-2/3/5-Containing GABA-A Receptors Increases Intake and Motivation for a Sucrose Solution, but not Taste Palatability
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The hyperphagic effects of benzodiazepines have been explored in great depth for the past several decades. The binding of benzodiazepine ligands to GABA-A receptors, primarily alpha-1/2/3-containing receptors, is believed to be of paramount importance in inducing hyperphagia. Prior research with more nonspecific benzodiazepine receptor ligands has shown that activation of alpha-1-containing GABA-A receptors induces sedative effects. L-838-417 is a novel partial GABA-A receptor agonist with a high affinity for alpha-2/3/5-containing GABAA receptors, while acting as a partial antagonist at alpha-1-containing GABAA receptors. The purpose of the current experiment was to test how central

administration of this more selective compound affected taste and the motivation to consume a sucrose solution. Male Sprague-Dawley rats were surgically implanted with a cannula into the 3rd ventricle for administration of L-838-417 (1nM, 10nM, and 100nM). Feeding and licking behaviors were monitored with an AC-108 lickometer for 90 minutes following injection, with exposure to 300 mM sucrose solutions. Results showed a significant increase in meal size at 100nM doses of L-838-417 relative to vehicle injection. This increase in meal size was associated with a modest, but non-significant, increase in meal duration and an increase in the number of lick bursts per meal. The increases in meal size, however, were not accompanied by changes in lick rate or licks per burst. Our preliminary findings indicate that the increases in meal size may not be associated with changes in taste palatability. Rather, central and forebrain stimulation of GABA-A receptors by L-838-417 appears to increase the motivation to lick, possibly through stimulation of the hypothalamus.
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An investigation of pro-social behavior in female rats
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Historically, empathy was studied solely in humans, but modern research has suggested that pro-social behaviors can be the ultimate result of empathetic reasoning in humans and rodents. In this study, we further examined pro-social behavior in rats based on the hypothesis that as conspecific distress increases, empathy-like motivation will increase thus increasing pro-social behaviors demonstrated by the rats. Once a day for forty days rats were placed into an arena that included a locked restrainer that could only be opened from the outside. One rat was placed into the locked restrainer (trapped rat), while the other rat was placed in the free-space of the arena (free rat). Several behaviors of the freed rat were observed during each experimental trial. Latency for the free rats to approach the restrainer remained consistent across the trials. There was a trend for an inverse relationship between contacts with the empty restrainer and the latency for the freed rat to open the door. As contacts with the restrainer increased, the latency to open the door decreased. There was no significant change in the number of contacts with the restrainer while the trapped rat was present; however, there was a trend for a decrease in the number of restrainer contacts over trials. Additionally, there was a trend for an increased number of contacts over trials between the rats once they were both freed. Overall, the data suggest that there is a lot of variability with regard to empathy-like behavior. These data suggest that there are interesting correlations between various aspects of empathy-like behavior in female rats.

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Cortical responses to different resolutions of sound movement
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The visual system has been shown to contain neurons particularly responsive to motion. Just as we can detect visual motion, we can determine the location of sounds in space and detect motion as sounds shift position. This study seeks evidence of neural structures within the auditory system which can differentiate true sound motion from changes in static location. If such structures exist, then a distinct cortical response should be detected when a subject is presented with a continuously moving sound versus a jumping sound that undergoes an instantaneous change in spatial position. Electroencephalography (EEG) was recorded while subjects listened over headphones to sounds which moved in steps of increasing motion resolution of 1, 3, 4, or 12 steps from midline to the periphery (Exp

1) or from the periphery to midline (Exp 2). From these recordings, event-related potentials (ERPs) for the varying sound conditions were formed, and the peak values and latencies of specific ERP components occurring after movement began, called the cN1 and cP2, were compared across conditions. For both experiments, the results showed an inverse relationship between cN1 and cP2 component magnitudes and latencies such that more discontinuous sounds had larger and earlier peaks. This suggests these components relate more to detection of and attentional recruitment toward spatial change rather than motion per se. However, a previously unrecognized ERP peak occurring after cP2 exhibited an opposite trend, possibly indicating a late cortical component of true sound motion processing.

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Visualizing morphology and axonal trajectory of neurons in the spinal cord of a developing zebrafish central nervous system
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Slitrks are a group of six structurally related transmembrane proteins thought to play roles in axon pathfinding and neurite outgrowth in the developing nervous system. Slitrk mutations have been linked to obsessive-compulsive disorder (OCD), muscular dystrophy, and Tourette's syndrome. To elucidate Slitrk function in the zebrafish (*Danio rerio*) we are characterizing the normal morphology and axonal trajectory of neurons in the spinal cord. With that knowledge, we then plan to knock down Slitrks and observe CNS axon tracts at regions where Slitrks are expressed. We hypothesize that disrupting Slitrk expression will lead to changes in neural wiring. This research project visualized primary motor neurons and labeled axon tracts in the developing zebrafish spinal cord. In order to map the normal axon tracts in untreated embryos we successfully immunostained using znp-1 antibody, which targets cytoplasmic vesicle, secretory vesicle and synaptic vesicle membrane. Thus, future research will investigate the validity of our hypothesis by knocking down Slitrk and comparing the axon tracts in the spinal cord of treated embryos with that of untreated embryos.

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The effects of caffeine and ethanol on locomotor activity in adult zebrafish.
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Zebrafish have become an important model organism for neuroscience in recent years – particularly for pharmacology. Caffeine is one of the most commonly consumed drugs in the modern world. In recent years, a growing trend of consuming this drug in conjunction with ethanol has generated concern about the effects of this drug combination on physiology and behavior. The present study aims to determine the combined effect of ethanol and caffeine on zebrafish behavior. Previous research has determined the effects of these chemicals administered alone via immersion and shown that ethanol induces a biphasic effect that is concentration dependent. Caffeine produces an overall decrease in activity. It was hypothesized that co-administration of caffeine and ethanol on swimming activity would be differentially affected by drug concentration and the duration of exposure. To investigate, adult zebrafish were exposed via immersion for either 5 minutes or 20 minutes to one of three concentrations of ethanol (1%, 0.1%, or 0.01%) in conjunction with a constant concentration of caffeine (10 mg/L). These concentrations were selected so that they would not be toxic to the fish; appropriate control

groups were also included. Following exposure, locomotor activity was digitally assessed and quantified using Noldus Ethovision (3.1). After a 5-minute exposure, results indicated a significant concentration effect [$F(5, 138) = 13.47$, $p<0.0001$, one-way ANOVA]. However, after a 20 minute exposure, there was no significant effect on behavior at any of these concentration [$F(5, 138) = 2.02$, $p=0.079$, one-way ANOVA]. However, a post-hoc test indicated that animals were less active at the 0.01% concentration ($p<0.01$; LSD test). Taken together, these data suggest exposure time may be an important variable in the observed behavioral response to combined caffeine and ethanol exposure. Additional experiments on these effects are in progress.