SYNAPSE 2013 Abstracts (Listed in the order that they were received)
Last update: 01-March-2013, 2359 hrs

Hinton, EA & Gourley, SL
Neuroscience Institute, Georgia State University; Yerkes National Primate Research Center, Emory
Adolescent Social Isolation Impairs Decision-making and Increases Orbitofrontal Cortical Dendritic Spine Density in Adulthood
ehinton2@student.gsu.edu / 404.861.6409

Adolescence is a vulnerability period for the development of multiple psychiatric disorders, which are commonly characterized by a failure to engage in goal-directed decision-making strategies. Complex decision-making involves prefrontal cortical structures such as the orbitofrontal cortex (OFC), which is also among the last of the prefrontal sub-regions to mature in adolescence. Adolescent neural development involves a marked elimination of synapses and dendritic spines, culminating in structural stabilization in adulthood. To better understand how known predictors of adolescent-onset psychiatric disease and adolescent dendritic spine maturation interact, we socially isolated female mice during adolescence in an etiologically- and ethologically-relevant animal model of early-life adversity. In our model, mice are re-housed in large social groups in adulthood; nonetheless, a history of adolescent social isolation impairs response-outcome decision-making, concurrent with an 18% increase in dendritic spine density in the OFC. Because dendritic spine proliferation suggests that adolescent isolation impairs dendritic spine maturation, we utilize a Rho kinase inhibitor—administered in concert with adolescent social isolation—as a novel therapeutic approach to normalizing adverse outcomes associated with early-life adversity. Given that Rho kinase inhibition facilitates cytoskeletal reorganization, our findings provide novel direct evidence that structural plasticity during adolescence determines long-term behavioral outcomes in adulthood.

Ruffle A, Savage M, & Neelon M
Department of Psychology, University of North Carolina at Asheville
The Effects of Aging on Creativity, Cognition, and Event Related Potentials in a Visual Working Memory Task
aeruffle@unca.edu / 704.307.8119

There are currently two leading hypotheses that attempt to explain the cognitive decline associated with old age. The first is the "processing speed hypothesis", which attributes cognitive impairment to slower processing speeds. The second is the "inhibitory deficit hypothesis", which suggests that the inability to suppress irrelevant stimuli leads to poorer performance on tests of cognitive function. These models further suggest different impacts of age on diverse cognitive functions such as executive attention, convergent thinking, and divergent (i.e., creative) thinking. The present study investigates these questions using a paradigm from Gazzeley et al. (2008) in which EEG is used to compare the performance of younger and older adults in a visual working memory task. The task consists of three conditions in which subjects are asked to: (1) remember faces and ignore

scenes, (2) remember scenes and ignore faces, and (3) passively view scenes and faces without trying to remember them. Following previous results, EEG responses of older adults are expected to show 1) delayed suppression of irrelevant information due to a decline in processing speed; and 2) reduced suppression to distracting stimuli due to failed attentional control. EEG results will also be compared with performance on a series of neuropsychological tests to assess the relationship between creativity and executive functioning.

Hernandez NA, Galloway CR, Lebois EP & Manns JR
Neuroscience Institute, Georgia State University
Selective allosteric activation of M_4 receptors for memory enhancement
nhernandez7@student.gsu.edu / 770.865.5138

Acetylcholine (ACh) is a neurotransmitter known to modulate cognitive functions, including learning and memory. Many cholinergic drugs bind to highly conserved orthosteric binding sites of muscarinic receptors (mAChRs) and are therefore likely to activate all mAChR subtypes (M_1-M_5) to some degree, including M_3, which is primarily thought to mediate most of the adverse peripheral side effects associated with cholinergic agonists. Drugs that bind to allosteric sites, however, have shown promise for targeting specific muscarinic receptor subtypes. There are two broad classes of allosteric activators: allosteric agonists, which can act to enhance memory in the absence of ACh, and positive allosteric modulators (PAMs), which enhance the ability of ACh to activate mAChRs and thus depend on ACh to produce a similar effect. In the present study, we sought to identify the contribution of M_1 and M_4 receptor subtypes to hippocampal memory, since these receptors are profusely found in memory related structures such as the hippocampus and believed to be crucial for memory. We therefore hypothesized that selective M1 or M4 activators would act to enhance memory in an object recognition task. To this end we utilized low, medium and high doses of the novel M_1 allosteric agonist, VU0364572, M_1 PAM, BQCA, or the novel M_4 PAM, VU0152100. Importantly, experimenters were blind to drug condition and drug order was randomized for subcutaneous injection to rats 30 minutes before they performed an object recognition memory task. Interestingly, the results suggested that the efficacy of the drugs might depend on a rat's baseline level of memory performance. In particular, when drug effects in low baseline performers (discrimination indices < 0.60) and high baseline performers (discrimination indices > 0.60) were analyzed separately, simple comparisons indicated that a low dose of VU0152100 increased memory performance in rats with low baseline performance. To our knowledge, this is the first demonstration that potentiating the M_4 mAChR subtype can increase memory performance. Fully understanding the behavioral effects of activating mAChR subtypes in the brain will be essential for developing drugs for memory deficits associated with disorders such as Alzheimer's disease and schizophrenia.

Smith GR, Lakhmani P, De Niear MA & Ramirez, JJ
Department of Psychology, Davidson College
Heterosynaptic Interaction of the Crossed-Temporodentate and Sprouted Septodentate Projections in Rats

gasmith@davidson.edu / 704.692.3824

The dentate gyrus (DG) is a region of the mammalian brain crucial for normal spatial memory and receives the majority of its innervation from the perforant path (PP) arising from the ipsilateral entorhinal cortex (EC). Also projecting to the DG are the septodentate pathway, arising largely from the medial septal nuclei, and the crossed temporodentate (CTD) pathway, arising from the contralateral EC. Following unilateral lesion of the EC (UECx), the terminal fields of the septodentate and CTD projections have been observed to sprout within the DG and facilitate electrophysiological responses in the DG similar to those produced by the PP. This project explores how the paired-pulse activation of the septodentate and CTD projections to the DG influences electrophysiological activity of the DG four days after UECx, a time point at which only the septodentate input shows a significant degree of axonal sprouting. Septodentate stimulation occurring 30-60 ms before CTD stimulation was found to depress the amplitudes of CTD-elicited field excitatory postsynaptic potentials in the DG relative to fEPSPs elicited from unpaired CTD stimulation. This may suggest a net inhibitory effect from the septodentate sprouting to the dentate at four days after the entorhinal lesion.

Strickland JC, Witte MA, & Smith MA
Department of Psychology, Davidson College
The Effects of Exercise on Cocaine Self-Administration: Role of Strength and Resistance Training
justrickland@davidson.edu / 703.919.7715

Previous studies have reported that voluntary wheel running decreases drug self-administration in laboratory rats, suggesting that aerobic exercise might be an effective intervention in substance abuse treatment programs. The purpose of the present study was to examine the effects of resistance exercise (i.e., strength training) on cocaine self-administration in rats responding on progressive ratio (PR) and fixed ratio (FR1) schedules of reinforcement. Male, Long-Evans rats were obtained as young adults (age = 7-8 weeks) and assigned to exercising and sedentary conditions. Rats in the exercise condition climbed a 0.5-m ladder suspended 1.0 m about the floor while wearing a weighted harness, whereas rats in the sedentary condition were placed at the top of the ladder without the weighted harness. In experiment 1, exercising rats performed one "superset" three days per week including 4-9 repetitions (i.e., climbs) carrying up to 150 g above their body weight. In experiment 2, exercising rats performed a three-set "pyramid" six day per week, performing 8, 6, and 4 repetitions carrying up to their body weight. No differences were observed between exercising and sedentary rats on the PR schedule of reinforcement in either experiment. On the FR1 schedule, exercising rats self-administered less cocaine than sedentary rats when responding was maintained by a low dose of cocaine, and this effect was apparent in both experiments. These data suggest that resistance exercise may be less effective than other forms of exercise at decreasing cocaine self-administration with effects apparent only for responding maintained at a threshold dose of cocaine.

Hannah H[1], Generous, R[2], & Riegel A[3]
[1]Department of Chemistry and Biochemistry, [2]Department of Biology, College of Charleston; [3]Department of Neurosciences, Medical University of South Carolina
Structural Plasticity in the Prefrontal Cortex During Neuropathic Pain
hahughes@g.cofc.edu / 864.884.9933

Chronic pain is a public health problem and often intractable to known therapies. This study investigated how and why neuropathic pain 'rewires' cortical function and identifies new cellular targets for better treatments. The prefrontal cortex (PFC) regulates pain perception and the affective (emotional) component of pain. We hypothesized that neuropathic pain induces 'growth' of a population of dendritic spines in the PFC pyramidal neurons, which may underlie the development of the negative affect associated with chronic pain. Rats were subjected to a spared nerve injury (SNI) model of neuropathic pain, where a portion of the sciatic nerve was removed to produce tactile allodynia (hypersensitivity) in the hind paw. Sensory pain thresholds were determined with calibrated von Frey filaments (VF) applied to the hind paw. SNI rats displayed lower VF thresholds compared to sham surgery rats. To quantify the affective component of pain, spontaneous aversive ultrasonic vocalizations (22 KHz) were evaluated in SNI and sham animals. SNI rats vocalized more than sham surgery animals. After 7 or 30 days post-SNI, subjects were perfused with paraformaldehyde and ballistic labeling was performed with a custom built gene gun to infuse lipophilic diI into the basal dendrites of PFC pyramidal cells. Spine density and morphology was quantified with a confocal microscope and analyzed using Imaris software. Results indicated SNI caused a robust and enduring increase in the long thin and filopodia spines classically associated with new synapses in the PFC pyramidal cells. These data suggest structural plasticity may underlie the development of pain-related affect.

Zipperly, M[1] & Knackstedt, L[2]
[1]Department of Psychology, Program in Neuroscience, Honors College, College of Charleston; [2]Department of Neurosciences, Medical University of South Carolina
Behavioral and Molecular Consequences of Concurrent Cocaine and Ethanol Use
mezipper@g.cofc.edu / 251.599.2001

Concurrent cocaine and ethanol use is more common than any other drug combination, and such polydrug use often results in increased consumption of both substances. We developed an animal model of cocaine and alcohol co-abuse in which rats self-administered intravenous cocaine for 2 hours, followed by alcohol taken orally for 6 hours. We hypothesized that subjects permitted access to both drugs would consume more ethanol and cocaine compared to groups permitted access to only one drug. In addition, we predicted that self-administration of both drugs would reduce expression of mGluR5, GLT-1, and xCT proteins, which are involved in glutamate homeostasis. We also expected elevated levels of the post-synaptic scaffolding complex protein Homer, which is associated with biochemical sensitivity to both drugs. Cocaine and ethanol consumption were measured over a 12-day self-administration period. Immediately following the self-administration period, subjects completed two weeks of extinction training, followed by reinstatement. Homer, mGluR5, GLT-1, and xCT protein

concentrations were measured via microdialysis during reinstatement. No significant difference in substance consumption was found between drug-consuming groups. There was a significant interaction between cocaine and ethanol on Homer protein expression. No other significant effects were found, although mGluR5 and GLT-1 levels were decreased for all drug-consuming groups. These results indicate that there are molecular and behavioral interactions between cocaine and ethanol when consumed concomitantly. The fact that cocaine and alcohol-consuming subjects chose to consume both substances indicates that this polydrug use results in a pleasurable experience, possibly reducing the negative side-effects of both substances.

Hilbert MLT[1] & Griffin WC[2]
1Department of Biology, Honors College, Neuroscience Program, College of Charleston, Charleston, SC; [2]Department of Neurosciences, Medical University of South Carolina
The Effects of Caffeine on Ethanol-induced Locomotor Stimulation and Reinforcement
mlhilber@g.cofc.edu / 919.244.9391
Alcohol (ethanol) mixed with caffeinated energy drinks is an alarming trend in today's society. Previous studies have found that ethanol and caffeine mixtures significantly increase locomotor activity in C57BL/6J mice compared to either drug alone. These experiments hoped to further elucidate the effects of caffeine on ethanol-induced locomotion and ethanol reinforcement. The first experiment examined whether locomotor activity after ethanol (2.5g/kg and 3.25g/kg) could be altered with low (3mg/kg) and high (15mg/kg) doses of caffeine. Consistent with earlier experiments, results indicated that caffeine increases activity of mice co-treated with ethanol. The second experiment examined the ability of caffeine to influence ethanol-induced conditioned place preference (16 total conditioning days, with test 1 occurring after day 8 and test 2 after day 16). Four treatment groups consisted of a vehicle group (normal saline), 1.75g/kg ethanol (a stimulatory dose), 3mg/kg caffeine, and both 1.75g/kg ethanol and 3mg/kg caffeine. As expected, ethanol administered alone produced significant place preference; that is, this dose of ethanol increased time spent on the ethanol-paired side. Given alone, caffeine proved to be a weak reinforcer because there were only slight increases in time spent on the caffeine paired side that only reached significance at Test 1. The ethanol-caffeine combination group demonstrated similar preference as ethanol given alone. Thus, caffeine did not alter ethanol reinforcement in this behavioral test. In summary, our findings indicate that caffeine modulates ethanol-induced changes in locomotor activity, but it does not alter ethanol reinforcement in the place preference procedure.

Bigelow MG, Taylor G, Underwood M & Neelon, M
Department of Psychology, University of North Carolina at Asheville
Context-Moderated Effect of Color on Physiological and Self-Report Measures of Emotional Response
mmunderw@unca.edu / 919.357.0726

Color psychology refers to the study of color and its effect on emotion and behavior. Elliot & colleagues (Meier et al, 2012; Elliot et al, 2012) have proposed a "color- in-context theory," arguing that the effect of color on psychological functioning is

modulated by the situational context. Specifically, it is claimed that red facilitates sexual attraction in romantic or sexual contexts, but can have a negative impact on mental and physical performance by increasing the perception of threat in achievement contexts. Past research has focused on behavioral and self-report measures. The present study will add to this work by further collecting participants' physiological data in response to color. As a measure of arousal and valence, facial EMG and skin conductance will be recorded as both male and female participants view pictures of either attractive individuals of the opposite sex or threatening images presented on a background of either blue or red. Self-reported ratings of arousal, valence, attraction and threat of the images (arousing/unarousing, happy/unhappy, attractive/unattractive, threatening/nonthreatening) will also be collected. We hypothesize that images on a red background will evoke higher physiological and self-reported arousal in all conditions (including threat and romantic), and that physiological and self-report measures of valence will be dependent on the context of the images.

Bumgarner S. & Spatta B.
Department of Psychology, Presbyterian College
Links between Parenting Style and Internalizing and Externalizing Problems in Adolescents
spbumgarn@presby.edu / 919.259.4934

The links between parenting style and internalizing and externalizing problems in adolescents was examined in 153 academically promising 7th through 10th grade students (96 females, 57 males) involved in the CHAMPS program (Communities Helping Assisting and Motivating Promising Students) a local support program. Measures assessing three different styles of parenting, harassment, fear induction, and overprotectiveness, were collected along with measures of total externalizing and internalizing problems in order to explore correlations among the constructs. It was hypothesized that more abrasive forms of parenting (harassment and fear induction) would be associated with more externalizing and internalizing problems. Significant correlations existed between harassment and total internalizing problems along with overprotectiveness and total internalizing problems. A significant correlation did not exist among any of the parenting styles and total externalizing problems. The goal of this research is to improve the effectiveness of the CHAMPS program by better understanding its students and their relationships with their parents.

Kun Xie, Hui Kuang, & Joe Z. Tsien
Brain and Behavior Discovery Institute
Warzone Mild Exposure to Blast Experiences Alter Anxiety, Memory, and the Prefrontal Cortex Neural Activity Patterns
kxie@gru.edu / 706.721.3760

Mild exposure to blast and shock during war time has been reported to produce neurological complications loosely described as "shell shock". This constellation of symptoms includes amnesia, compromised executive function, difficulty concentrating, and anxiety. Here we have developed a novel laboratory-version of mild blast exposure

comprised of high decibel sound and sudden strong air blow to the animals. This mimics the emotionally charged fearful events, yet without causing any bodily or brain injury to mice. We demonstrated that this mild blast event is capable of impairing object recognition memory, increasing anxiety and contextual generalization. Our in vivo neural ensemble recording in the mouse prefrontal cortex, a region processing attention, emotional control, and memory, revealed diverse firing changes in substantial numbers of neurons in ACC upon such fearful events. Moreover, these real-time neural ensemble patterns underwent post-event reverberations on the time-scale of seconds, indicating rapid consolidation of those experiences. Successful identification of mild blast event-induced dynamic neural signatures in the prefrontal cortex may provide a new avenue for understanding of how post-traumatic stress disorder is produced in the brain.

Quattlebaum AF[1], Wynn WD[2], Gregory RA[3], Helke KL[3], Granholm AC[2], Boger HA[2]
[1]Department of Chemistry and Biochemistry, Program in Neuroscience, College of Charlston; [2]Department of Neuroscience & the Center on Aging, Medical University of South Carolina (MUSC); [3]Department of Comparative Medicine, MUSC
Glutamate Kinetics in Middle-Aged Mice with a Partial GDNF Reduction
afquattl@g.cofc.edu / 864.710.9147

GDNF, a known growth factor, is important for maintaining the health of dopamine (DA) neurons. Parkinson's (PD) patients have a greatly decreased number of DA neurons in the substantia nigra (SN) while existing nigral neurons have a down regulation of GDNF and show signs of oxidative stress. Animal models with partial GDNF reduction show an accelerated decline in the SN DA system and motor function similar to PD patients. Increased glutamate release in the subthalamic nucleus, an indirect result of the upregulation of the DA D2 receptor in the basal ganglia, also occurs in PD patients. The purpose of the current study is to help determine the role of GDNF in glutamate release and regulation of oxidative stress. Following motor activity assessment using the open field locomotor test, KCl-stimulated glutamate release and uptake in the SN was assessed in anesthetized 12-month-old wild type (WT) and $Gdnf^{+/-}$ mice (partial gene knockouts with decreased GDNF levels) by electrochemical detection. After this procedure, tissue staining was performed to determine levels of cytokine expression (over-expression is a proven disease biomarker), COX-2 (produces cytokines), and SOD-1 (endogenous antioxidant expression). Initial results indicate the Gdnf+/- mice have greater glutamate release into the SN compared to WT mice as well as greater cytokine expression, COX-2, and SOD-1. These data support the idea that increased glutamate release promotes nigral oxidative stress and DAergic cell loss. The data also support the role and importance of GDNF in the nigrostriatal pathway and its use as a potential therapeutic.

Kassab AS[1] & Gass JT[2]
[1]Department of Psychology, College of Charleston; Program in Neuroscience, College of Charleston; [2]Department of Neurosciences, Medical University of South Carolina
Pharmacological Manipulation of Glutamate Transmission Enhances the Extinction of Alcohol Cues and is Associated with Plasticity Changes in the Prefrontal Cortex
askassab@g.cofc.edu / 843.496.3074

Drug addiction theories incorporate learning and memory principles and indicate that repeated drug use leads to compulsive drug-seeking behavior through classical and operant conditioning. Overlearning the associations between the drug effects and cues that predict drug availability occurs. Addicts are given cue-exposure therapy, the repeated exposure to drug-related cues to extinguish learned associations, but it is often unsuccessful. Exploring neural mechanisms involved in extinction training would be helpful as recent evidence indicates extinction to be an active learning process involving glutamatergic mechanisms. Enhancing glutamatergic transmission of NMDA receptors with the partial agonist D-cycloserine facilitates extinction of cocaine-seeking. Positive allosteric modulator (PAM) CDPPB has been shown to extinguish cocaine cues through modulation of glutamate at the mGluR5 receptor. This study aims to determine the efficacy of CDPPB in potentiating the extinction of alcohol-seeking behavior. Wistar rats were trained to self-administer 10% alcohol solution. Active lever presses were paired with the activation of a light and tone complex stimulus. Rats underwent extinction training receiving an injection of either CDPPB (30mg/kg s.c.) or vehicle (20% cyclodextrin s.c.) 20 minutes prior to each session. Active and inactive lever presses were recorded until extinction criteria were met. CDPPB significantly reduced active lever pressing during days 2-7 of extinction training and the number of sessions required. These data provide that mGluR5 PAMs facilitate extinction of alcohol-seeking and could act as novel, pharmacological treatment to increase success rates of cue-exposure therapy. Current studies are examining changes in PFC structural plasticity associated with these behavioral effects.

Oliver EM, Butler RK, Fadel JR and Wilson MA
USC; SOM; Department of Pharmacology, Physiology and Neuroscience
Phenotypic Differences in the Left and Right Rat Amygdala
elisabeth.m.oliver@gmail.com / 803.606.8628

The amygdala is a centrally-located brain region and is important in emotional regulation such as the management of fear and stress. Clinical and preclinical studies have shown the right-hemisphere amygdala is more sensitive to pain and emotional stress than the left. There are two primary types of neurons in the amygdala basolateral complex (BLC): glutamatergic pyramidal projection neurons and several populations of inhibitory interneurons that regulate the pyramidal neurons. Parvalbumin (PV) is a phenotypic marker for one of the interneuronal populations; Ca2+/calmodulin-dependant protein kinase II (CAMKII) is a phenotypic marker for pyramidal neurons. This study investigated differences in the density of PV+, CAMKII+ and NISSL-stained cells between left and right BLC using stereological techniques. Serial sections were collected from rat brains and stained for PV, CAMKII, and NISSL to obtain total cell counts. The optical fractionator method obtained an unbiased estimate of the number of PV+, CAMKII+, and total cells in subdivisions in the BLC as well as volume estimates for the subdivisions. The BLC was divided into lateral and basolateral, and within these groups were smaller subdivisions. The results indicate that there are no density differences between left and right amygdala for CAMKII+ neurons and total number of NISSL-stained cells. The density of PV+ neurons in the left basolateral posterior amygdala is significantly higher than the right. This indicates a greater inhibitory control of the left

basolateral amygdala over the right. Future directions include investigating differences in calretinin-, calbindin- and somatostatin-positive neurons in the left and right amygdala. SUPPORT: MH 063344 to MAW and JRF

Joudeh N & Triblehorn JD
Department of Psychology, Program in Neuroscience, College of Charleston
Evoked escape motor neuron responses in Periplaneta americana by different wind puff velocities
najoudeh@g.cofc.edu / 864.905.0266

Nervous systems transform sensory information from the environment into neural signals that underlie behavior. The wind-mediated turn-and-run escape response of the cockroach (i.e. *Periplaneta americana*) is a good model for studying this sensorimotor transformation since cockroaches have a reasonably complex neural circuitry that is easily accessible for neurophysiological experiments. We presented 300 ms wind puffs of different velocities (0-270 cm/s) to cockroaches and recorded responses extracellularly from metathoracic nerves 5 and 6 simultaneously. Nerve 5 contains the coxal slow and fast depressor motor neurons (MNs) while nerve 6 contains the coxal levator MNs. Both nerves contain the axonal branches of the common inhibitor neuron. For different wind velocities, we measured the change in spike counts elicited by wind (3 s pre- and post-wind onset). In nerve 6, wind always increased the spike count, but either increased or decreased the number of spikes in nerve 5, depending on animal. Using spike sorting analysis, we determined three units comprise the response in nerve 6 and two units in nerve 5. We hypothesize one unit is shared between the two nerves and is the common inhibitor neuron. The spike sorting analysis will allow us to determine how the responses of these identified units also vary with wind puff velocity. Future work will compare the motor neuron responses in *P. americana* to those of *Blaberus craniifer* and the hissing cockroach *Gromphadorhina portentosa*, two cockroach species that have the same escape circuitry, but do not exhibit the wind-evoked turn-and-run escape behavior.

Petz J & Sweitzer S
Department of Biology, Presbyterian College
Using Herpes Simplex Virus Mediated Gene Therapy to Decrease Neuronal Activation in Neuropathic Pain
joanne.petz@gmail.com / 864.979.1669

Over 75 million Americans suffer from chronic neuropathic pain, costing over 150 billion US dollars per year. Half of the patients with neuropathic pain are unresponsive to analgesic treatments or suffer from central nervous system (CNS) related side effects. The goal of this project is to use herpes simplex virus type 1 (HSV-1) to target peripheral neurons to produce analgesia without CNS side effects by over-expressing or knocking down expression of the delta opioid receptor (DOR). Our laboratory has previously shown an increase in nociceptive behaviors with HSV-mediated over-expression of DOR, and a decrease in nociceptive behaviors with HSV-mediated knock-down of DOR. My hypothesis is that downregulation of the DOR will decrease c-fos expression in the spinal cord, and over-expression of DOR will increase c-fos expression. C-fos is a marker of neuronal activation that is measured by immunohistochemistry. My results showed that c-

fos significantly decreased after knock down of DOR expression. This signifies that DORs interfere with peripheral analgesia, and that the knock down of DOR expression increases peripheral analgesia. This supports a growing theory of pronociceptive MOR-DOR heterodimer formation in chronic neuropathic pain states.

Vinton J, & Birgbauer E
Department of Biology, Winthrop University
Ibuprofen induces growth cone collapse in embryonic retinal neurons
vintonj2@winthrop.edu / 704.724.3559

During embryological development of vertebrates, retinal ganglion cell (RGC) axons grow out of the optic fissure and innervate the tectum in birds or the superior colliculus in mammals. A variety of chemical cues are thought to govern this nerve growth in what is known as axon guidance. These extracellular signaling molecules potentially hold the key to advancements in nerve regeneration therapy. Fu et al and Wang et al found that treatment with ibuprofen promoted nerve regeneration after spinal cord injury in mice (2007, 2009). Ibuprofen is a non-steroidal anti-inflammatory drug used to treat pain and inflammation through its inhibition of the COX 2 pathway. However, Fu et al suggested that ibuprofen promoted nerve regeneration through a novel pathway by reducing the active intracellular RhoA (2007). RhoA is a GTPase whose activation has been shown to induce growth cone collapse, an *in vitro* response to inhibitory axon guidance molecules. Lysophosphatidic acid (LPA) is a bioactive lipid that is known to induce growth cone collapse *in vitro* through a RhoA mediated pathway. Therefore, we wanted to investigate if ibuprofen would prevent LPA induced growth cone collapse in our model. A growth cone collapse assay was performed using RGC's from E6 chick embryos. Treatment with 500µM or 50µM ibuprofen did not inhibit LPA induced growth cone collapse. In fact, the 500µM ibuprofen treatment induced growth cone collapse independently of LPA and increased growth cone collapse in the presence of LPA. Time-lapse microscopy was performed to determine that LPA caused a typical growth cone collapse in the presence of ibuprofen. Furthermore, preliminary biochemical analysis of active RhoA revealed that ibuprofen treatment does reduce active RhoA in chick retinal cultures despite not blocking growth cone collapse. In conclusion, although ibuprofen does reduce intracellular active RhoA, it does not inhibit LPA induced growth cone collapse in chick retinal neurons.

Herrington S, Musolf B
Department of Natural Sciences, Clayton State University
The Effects of Male Bean Beetle (*Callosobruchus maculatus*) Antennal Length on Female Egg-Laying and Viability of Offspring
sherrington@student.clayton.edu / 404.408.7431

Part of the male bean beetle's (*Callosobruchus maculatus*) mating ritual involves antennation, stroking the female's back with his antennae. Antennation helps the male in copulation, thus fathering offspring. In male beetles with ablated antennae, the number of fathered offspring decreases. As more of the male's antennae are cut, the number of viable offspring decreases. In reducing the length of male antennae, the male is impaired

in antennation. The question being explored is whether the male's ejaculate is being rejected due to his inability to properly antennate or if copulation is shortened due to the possible removal of receptors necessary to antennate successfully. This question is answered by weighing the males and females before and after the mating period to explore this hypothesis. The effect of male antennation on the number and viability of offspring is also explored. The hatching and adult emergence rates of the offspring are being analyzed in answer to the differences of offspring viability in the control males and males with fewer segments. A scanning electron microscopy study of the male and females' antennae show a difference in number of the small sensilla basiconica, in favor of the males. These sensilla may function in mechanoreception and gustation.

Anderson RM & Sweitzer SM
Department of Pharmaceutical and Administrative Science, Presbyterian College School of Pharmacy
Do Water Fleas Feel Cold? Evidence for TRPM8 Expression In *Daphnia Magna*
rmanderso@presby.edu / 803.983.9123

The menthol or cold receptor belongs to the transient receptor potential cation channel subfamily M (TRPM). TRPM8 is expressed in mammals and fruit flies on sensory neurons and is activated by cold temperatures and cooling agents. The using of cooling agents to relieve pain is widespread and TRPM8 is thought to be a key signal transducing receptor. TRPM8 is currently a drug target for development of new drugs for the treatment of neuropathic pain. The intent of this study was to determine if Daphnia magna have functional menthol (TRPM8) receptors. A genome wide analysis identified potential gene sequences that may code for TRPM8 in Daphnia. Once these putative regions were identified, a behavioral analysis was used to determine whether Daphnia altered behavior in response to menthol. Activity plate measures were conducted to compare the activity levels of the Daphnia after being exposed to menthol. Daphnia were exposed to different concentrations of menthol for one minute and then transferred to an activity chamber. Activity was measured by counting the number of times the Daphnia changed quadrants over the course of one minute. From these studies, Daphnia activity was lower ($p<0.05$) in those exposed to the menthol as compared to vehicle control. A size-dependent change in activity after menthol exposure was also observed. As the size of the Daphnia decreased, so did their level of activity upon exposure to menthol. These findings suggest that Daphnia may possess functional menthol (TRPM8) receptors but that the behavioral response pattern is age (size)-dependent. Further studies are required to determine whether the age difference is a result of changes in gene expression or a function of the development of the hard carapace of the Daphnia. We propose that this model may provide a rapid high throughput assay for identification of TRPM8 agonists and antagonists.

Hammett J & Sweitzer S
Dept of Biology, Presbyterian College
Sickle cell pain: Protein kinase C gamma expression in the periaquaductal gray following peripheral endothelin-1 administration

jthammett@presby.edu / 864.923.9474

Sickle cell disease (SCD) is a genetic condition that produces sickle shaped red blood cells resulting in repeated painful vaso-occlusive episodes (VOE) in children with the disease. Currently, patients with SCD report inadequate pain control despite the use of current pain medications. Endothelin-1 (ET-1) is used to model VOEs and identify novel analgesic therapeutic targets. Prior research shows the greatest ET-1 induced nociception in younger male animals. The mechanisms for these age and sex differences are under investigation in our lab. Protein Kinase C gamma (PKCgamma) has been previously shown to play a role in central nociception with expression in the spinal cord, thalamus and periaquaductal gray (PAG). The purpose of this study is to look at expression of PKCgamma in the PAG in a model of VOE- associated nociception. We postulate an age- and sex- dependent increase in PKCgamma expression following administration of ET-1. Immunohistochemistry was performed on PAG tissue obtained from postnatal rats of ages 7, 21, and 60 days. Direct cell counting was used to determine the number of PKCgamma expressing neurons. Results from the P21 age group suggest a greater level of activation in rats treated with ET-1 as opposed to those treated with saline. ET-1 treated females show a higher level of PKCgamma expression in the dorsal PAG than do males. ET-1 treated males show a higher level of PKCgamma expression in the ventral and lateral PAG than do females. Overall, this suggests males have higher levels of PAG PKCgamma expression following ET-1 administration.

Patel J, Sweitzer S.
Department of Pharmaceutical and Administrative Sciences, Presbyterian College School of Pharmacy

Heating Up Water Fleas: Do *Daphnia* Magna Express the Capsaicin Receptor (TRPV1)?

jrpatel@presby.edu / 864.680.2451

Transient receptor potential (TRP) channels are an active area in therapeutic drug development. Of the TRP channels, the TRPV1 channel has been aggressively studied for new therapeutic options to treat chronic neuropathic pain. According to recent reports, chronic pain affects at least 116 million Americans each year, over half of whom still suffer from pain with inadequate treatment from the health-care system. The TRPV1 channel also known as the capsaicin receptor functions in response to temperature and chemical stimuli. The aim of the study is to determine if the *Daphnia magna* genome expresses a TRPV1 homolog and to quantify their behavioral responses to capsaicin. In genome studies, Daphnia have a high sequence similarity with putative drosophila TRPV1 homologs. At a behavioral level a T-shaped 3 well model was used to determine the chemosensation to capsaicin in three different size *Daphnia* (small, medium, large). *Daphnia magna* showed size-dependent responses to the capsaicin, where the small and medium sized water fleas spent more time in the well with capsaicin but the larger water fleas spent less time. These findings suggest that *Daphnia* may have age-dependent expression of TRPV1 receptors. Future directions are to determine where TRPV1 receptors are expressed in *Daphnia magna* and how that expression changes with development. *Daphnia magna* may provide a rapid screening for identifying putative

TRPV1 agonists and antagonists.

Claro C[1], Waters P[2], and Ruscio M[1]
[1]Department of Psychology, Program in Neuroscience, College of Charleston;
[2]Department of Neurosciences, Medical University of South Carolina
Effects of Cocaine Administration on Vasopressin and Oxytocin in Limbic Areas
cmclaro@g.cofc.edu / 864.517.6691

Cocaine is a powerfully addictive stimulant drug. Addiction to this stimulant drug can occur at a very rapid speed due to an overwhelming craving that follows. One of the most common traits of cocaine addiction is relapse after withdrawal. Increased anxiety during early withdrawal is a major instigator of relapse in cocaine addicts. This research studied how cocaine addiction affects vasopressin and oxytocin levels in the limbic system after two days of cocaine withdrawal. Specific limbic areas examined included the central nucleus of the amygdala (CeA), the bed nuclei of the stria terminalis (BNST), and the paraventricular nucleus (PVN). Together, these areas regulate anxiety and influence the hypothalamic-pituitary-adrenal axis and affects brain stress responses, including responses during cocaine addiction and withdrawal that may lead to relapse. This study used a rodent model of cocaine addiction to investigate the reinstatement of cocaine-seeking behavior during withdrawal and the impact of this manipulation on central expression of vasopressin and oxytocin. Two groups were tested: a control group, which self-administered saline, and an experimental group, which self-administered cocaine, in six hour sessions for fourteen days. Following two days of abstinence, the rats were sacrificed to obtain brain tissue. Using the ELISA (Enzyme-linked immunosorbent assay) method, we quantified levels of oxytocin and vasopressin in the CeA, BNST, and PVN. We observed no significant changes in levels of vasopressin and oxytocin in these regions. Nevertheless, these brain structures are believed to impact the underlying reinstatement for cocaine- seeking behavior.

Thomas, A & Sweitzer, SM
Department of Chemistry, Presbyterian College & Department of Pharmaceutical and Administrative Sciences
pH sensitivity in Water Fleas: Evidence for ASIC 3 Expression in *Daphnia magna*
akthomas@presby.edu / 803.727.9807

Currently, chronic pain is the third greatest health issue behind cancer and heart disease. Despite taking prescribed medication for pain, patients with neuropathic pain continue to have pain of moderate severity. Acid sensing ion channels (ASICs) are an active area of drug development. ASICs are found in tissues and cells throughout the body and nervous system with particularly high expression in the peripheral nervous system and nociceptors. The purpose of this experiment is to develop a high throughput behavioral screening method to identify potential acid-sensitive ion channel (ASIC) channel inhibitors for the treatment of pain. For this experiment, the behavior and reaction of daphnia magna in varying levels of pH was examined. A 3-chamber model behavioral system was used to examine *Daphnia* responses to changes in pH level. This behavioral characterization of *Daphnia* responses to pH is being paralleled by a genetic screening of

the *Daphnia* genome to identify putative ASIC genes. Preliminary data shows that *Daphnia* responses to acid are dependent upon the size of the organism. Lowering the pH of the test chamber causes the smaller sized *Daphnia* to avoid the acid chamber, spend less time in the test chamber, and slows down their motility. In contrast, a drop in pH does not change the behavior in the larger *Daphnia*. This could possibly suggest that the ASIC3 expression varies with development. If proven to express functioning ASIC channels then *Daphnia* can be used to screen marine extracts for potential ASIC channel inhibitors for the treatment of pain.

Stocksdale BR, Moses-Hampton M, Bleda M, Sullivan A, & Ramirez JJ
Department of Psychology, Davidson College
A Disconnection Analysis of the Hippocampal System's Role in Working Memory
brstocksdale@davidson.edu / 443. 841.5825

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 a system essential 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 system 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 four 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) sham craniotomy. Post-operative behavioral testing began after a 5-12 day recovery period and continued until 64 daily trials were completed. All three 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 evaluated the extent of the lesions and damage to surrounding tissue. Naik staining indicated lesion-induced cholinergic septodentate sprouting in BECx group dentate gyri, suggesting a possible cellular correlate to the recovery of working memory function.

Parrilla Carrero J, Butler R, Sharko A, Kaigler K, Fadel J, & Wilson MA
Department of Pharmacology, Physiology & Neuroscience, University of South Carolina School of Medicine
Amygdala mu-opioid receptor regulation of glutamatergic and anxiety responses
jcarrero@uscmed.sc.edu

The amygdala complex plays a key role in emotional behavioral responses, including the formation and storage of fear memories. Mu-opioid receptors (MOR) in the amygdala have been shown to modulate anxiety-like responses in rodents, although the specific mechanisms mediating such effects are unclear. Previously we have observed that conditioned and unconditioned anxiogenic stimuli activate glutamatergic CAMKII-positive pyramidal neurons in the basolateral amygdala (BLA). Since there is dense

mRNA expression of MOR in the BLA, and electrophysiological studies suggest MOR activation attenuates glutamate release from BLA projections to the central amygdala, we hypothesized that selectively increasing or decreasing MOR expression in glutamatergic CAMKII-positive neurons of the BLA would alter conditioned and un-conditioned fear responses. Lentiviral vectors with the CAMKII promoter driving expression of MOR sense, MOR antisense, and EGFP (control) were used to selectively change the expression of MOR in glutamatergic CAMK-positive neurons of the BLA. MOR immunofluorescence and 3H-DAMGO binding were used to assess changes in amygdala MOR expression following viral injections in the BLA. Anxiety responses were assessed using the elevated plus maze, defensive burying with exposure to predator (ferret) odor, and contextual and cue-conditioned freezing responses. We found that increasing or decreasing MOR expression in glutamatergic CAMKII-positive neurons of the BLA did not significantly alter either conditioned or unconditioned anxiety responses in these tests. In addition, using in vivo microdialysis we found that MOR activation using the agonist DAMGO increases glutamate efflux in the central amygdala, but this response was not blocked by tetrodotoxin (TTX) suggesting this is not due to MOR- induced changes in presynaptic release. Our results suggest that other neuronal populations of MOR in the amygdala, or perhaps non-neuronal MOR, mediate the effects of opioid peptides in modifying anxiety-like behaviors.
Support: MH063344 to MAW and JRF plus the Sloan Foundation to JPC.

Brahmbhatt Y, Colver R, Momin N, & Musolf B
Biology Department, Clayton State University
'Callosobruchus maculatus' and the differing roles of chemoreception between male and female beetles
rcolver@student.clayton.edu / 678.596.1507

Studying the role of chemoreception for both male and female Callosobruchus maculatus may lead to a better understanding of how this beetle identifies and decimates the bean crops in Asia and Africa. We examined separately behavior of the different sexes in maze scenarios in an effort to ascertain the role of chemoreception in mate choice for male and ovipositing for female. Data indicate that female C. maculatus relied on their antennae to find a preferred substrate for ovipositing; however, the male beetles do not seem to use their antennae in preferentially finding females over the beans from which females may emerge. Comparison of sensilla on the antennae of the male and female beetle corroborates the conclusion that chemoreception is different between the sexes. Scanning electron microscopy (SEM) revealed a number of sensilla that have mechanosensory functions and perhaps gustatory functions. Since male antennation is an important component of the mating process, it is possible that the male may have fewer sensilla that engage in distant chemoreceptors. Knowing that chemical signals received by female C. maculatus can direct their behavior may spur development of a compound that could act as a deterrent chemical signal to prevent ruination of bean crops.

Hibble JP, McQuail JA, & Nicolle, MM
Program in Neuroscience and Departments of Internal Medicine, Section on Gerontology, and Physiology, Wake Forest University

Synaptic Protein Levels in the Dorsal Hippocampus: Relationship to Age-Dependent Cognitive Decline

hibbjp9@wfu.edu / 904.537.2482

Age-related memory decline is associated with compromised integrity of hippocampal synapses, although these changes are unaccompanied by cell loss as seen the Alzheimer's brain. However, subtle changes in synaptic integrity may predispose the aged brain to more severe neurodegenerative processes. Although various transmitter systems are implicated to change with age, few studies have investigated the integrity of specific, neurochemically-defined synapses. The current study used immunofluorescence (IF) to measure changes to vesicular proteins that package acetylcholine (VAChT), GABA (VGAT) and glutamate (VGluT1) into vesicles for synaptic release in tissue sections prepared from young (6 mo; n=9) and aged (24-25 mo; n=25) FBNF1 rats that were previously characterized for spatial learning. Behavioral analysis revealed that aged rats exhibited a broad range of individual differences, including subjects with obvious impairment, but also a subset of aged rats that were behaviorally similar to young. Histological sections triple-labeled for VAChT, VGAT and VGluT1 proteins were scanned on a Typhoon FLA 9500 imaging system at a final resolution of 10 μm and analyzed using Image J software. Regions of interest were the dentate gyrus (DG), CA3 and CA1 subregions of the dorsal hippcampus. Although expression of vesicular transporter proteins was numerically lower in all 3 subregions, an age×subregion RMANOVA revealed no main effect of age or interaction with subregion. Subsequent correlations between protein expression and water maze performance revealed no reliable associations. Future studies will focus on particular synaptic zones to enhance the sensitivity of detecting changes that are associated with circuit-specific synaptic alterations.

Funded by NIA grants F31-AG038266 (JAM) and R01-AG020572 (MMN).

Maier, M [1,2], Cory W[1] & Vance J[3]

[1]Department of Chemistry and Biochemistry, [2]Program in Neuroscience, [3]Department of Biology, College of Charleston, Charleston, SC, 29424

Laboratory-induced changes of hemolymph octopamine levels in the honey bee, *Apis Mellifera*.

mmmaier@g.cofc.edu / 980.333.3341

The European honey bee, *Apis Mellifera*, adapts quickly to environmentally unpredictable situations, often by means of neuromodulation that targets flight behavior. Octopamine, the invertebrate analog to vertebrate norepinephrine, is involved in multiple aspects of flight including initiating flight motor patterns and modulating sensory proprioception during flight. Although octopamine's effects on flight motor outputs in honey bees are well-described, less is known about how octopamine affects sensory receptors. We wish to investigate octopaminergic neuromodulation of the honey bee hind wing stretch receptor during wing flight movements using extracellular recordings. The honey bee is of particular interest since, unlike other insects, the honey bee controls flight using sensory input from the hind wing instead of the fore wing. However, experimental procedures leading up to the electrophysiological recordings could cause octopamine

release, resulting in unknown elevations of octopamine prior to experimental manipulation of octopamine levels in our recordings. To address this issue, we investigated octopamine concentrations present in bees at four stages of our experimental procedures leading up to our extracellular recordings: naturally exiting the hive (baseline hormone levels), after transport from the hive to the experimental setup, post-anesthesia (CO2), and post-surgery. Freezing bees in liquid nitrogen prevented hormonal degradation and further release of hormones. Octopamine concentrations were measured from extracted bee hemolymph using High Performance Liquid Chromatography (HPLC). With these data, we can account for the average increase in octopamine levels and the individual variation of hormonal levels in subsequent electrophysiological measurements of afferent wing nerve activity following octopaminergic neuromodulation.

Peay C, Mohanty S, & Bhat, N
Department of Neuroscience, Furman University; Department of Neurosciences, MUSC
Comparing the Effects of Specific vs. Nonspecific p38 MAP Kinase Inhibitors on MBP Expression in Oligodendrocyte Differentiation
celeste.peay@furman.edu / 864.607.2563

The differentiation process from oligodendrocyte precursor (OPC) to mature, myelinating oligodendrocyte is particularly salient for MS research as the nervous system's capacity for self-repair through remyelination appears to be limited due to an inhibiting factor of the differentiation process. One pathway that has received attention is the p38 alpha MAP kinase pathway following the consensus of several successful in vitro studies identifying p38α MAPK's integral role in OPC differentiation. However, an in vivo study with Cre-loxP conditional knock-outs had a conflicting finding showing that p38 alpha MAPK knock-outs had no obvious short-term deleterious effects. Concurrently, there was also a questioning of the specificity of the ubiquitous p38 alpha MAPK inhibitor SB203580. Substantial evidence indicated SB203580 as capable of potent inhibition of distantly related kinases, notably Casein Kinase 1 delta/epsilon. The purpose of this study was to investigate and compare the regulatory roles of p38 alpha MAPK and CK1 delat/epsilon through probing with specific inhibitors and non-specific inhibitors of each kinase. We hypothesized and demonstrated through immunoblots that highly specific p38 alpha MAPK inhibitors (PD169, SD169, BIRB, and SCIO) did not affect OPC differentiation, and thus OPCs differentiated into fully functional oligodendrocytes as measured by MBP expression levels. Further, we hypothesized and demonstrated that both highly specific CK1 delta/epsilon inhibitors (IC261 and D4476) and the non-specific inhibitors (SB203580 and SB202190) would inhibit OPC differentiation through an inhibition of the CK1 delta/epsilon activity.

Nevins C[1] & Raghavachari S[2]
[1]Department of Neuroscience, Furman University; [2]Department of Neurobiology, Duke University
Modeling the Spatial Activation Patterns of Cdc42 during Dendritic Spine Enlargement

catherine.nevins@furman.edu / 919.624.6672

Long-term potentiation (LTP), the proposed molecular basis of learning and memory processing in the mammalian brain, involves selectively enhancing the sensitivity of distinct neural synapses and circuits. Morphological changes of the bulbous, postsynaptic dendritic spine structures, which house receptor proteins on postsynaptic neurons, are thought to facilitate LTP. After LTP-like stimulation, dendritic spines undergo transient and sustained phases of volume enlargement, the latter of which lasts for over 30 minutes in correlation to the length of LTP persistence. The molecular mechanisms by which spine morphology is regulated, then, merit further investigation because of their relation to LTP facilitation. In contrast and complement to several past in vivo experimental studies that have investigated these molecular mechanisms, the present study utilizes a computer modeling approach. Here, the Virtual Cell modeling software is used to construct a simulation of the non-diffusive spatial activity patterns of Cell Division Cycle Control Protein 42 (Cdc42), a protein that is known to regulate actin cytoskeleton rearrangements to yield morphological changes in many cell types as well as in dendritic spines, particularly in the sustained phase of spine enlargement during LTP. This simulation reveals novel reaction equations that may illuminate how Cdc42 operates and interacts with other signaling proteins in vivo.

Locandro, CM & Clewley, RH
Neuroscience Institute, Department of Mathematics & Statistics, Georgia State University
The Effect of the Epilepsy-Associated R1648H Sodium Channel Mutation on Neuronal Excitability: A Model Study
clocandro1@student.gsu.edu / 770.880.1034

Hyperexcitability of individual neurons is a hallmark feature of many brain diseases. For example, neuronal hyperexcitability has been implicated as a potential mechanism of seizure generation in epilepsy. This project analyzes a previously developed biophysical model of the human R1648H sodium channel mutation, which has been implicated in forms of generalized epilepsy. Using computer simulations and dynamical systems analysis software, we elucidate the physiological mechanisms by which this mutation causes hyperexcitability when incorporated into model neurons. First, we compare steady-state properties and response to voltage changes of the wild-type (normal) versus the mutant channel. We illustrate the tendency of the mutant channel to inactivate at a slower rate than its wild-type counterpart. To understand how the mutation alters the action potential waveform, we incorporate each channel into a generic Hodgkin-Huxley model neuron with three ionic currents (sodium, potassium, and leak). We discover that the mutation induces subtle increases in spike-base width and refractory period of this simple Hodgkin-Huxley neuron. Then we implement each sodium channel model into a more complex, physiologically relevant model of a CA3 hippocampal pyramidal neuron and confirm that the mutation increases overall cellular excitability. Using a dynamical systems reduction protocol, we then explicate precisely how the mutation changes the influence of other ionic currents during the action potential. These findings not only confirm the hyperexcitability of the mutant neuron but also provide a detailed

mechanistic explanation of how a slight modification in sodium channel kinetics changes the macroscopic features of the neuronal action potential.

Shugoll, BD, McQuail JA, & Nicolle MM
Program in Neuroscience and Departments of Internal Medicine, Section on Gerontology, and Physiology, Wake Forest University
New Approaches to Examine Protein Carbonylation in a Rat Model of Cognitive Aging
shugbd9@wfu.edu / 7046046089

Cognitive deficits associated with normal aging and disease states may relate to oxidative modification of key protein substrates. Characterization of protein oxidation, specifically studying carbonylation, has historically relied on a DNPH-derivatization method that entails various technical shortcomings (low pH, precipitation, and low signal-to-noise). A newer biotin-based approach functionalizes protein carbonyls and offers advantages associated with avidin/streptavidin purification and detection. The current study made use of tissue homogenates prepared from young adult (6 mo; n=10) and aged (24 mo; n=18) FBNF1 hybrid rats that were previously characterized for spatial learning impairment. This approach distinguishes between changes associated with age, as well as those specifically associated with cognitive impairment. In the study we cross-validated the traditional DNPH assay with a biotin fluorescence assay. The fluorescent assay produced values that were within the linear range of detection while using far less sample than the DNPH method. Despite this improved approach, there was no difference between age groups, but there was a significant correlation between individual learning performance in the water maze and protein carbonyls ($p<.05$, $r=0.39$); greater carbonylation was associated with worse spatial learning. Future studies will exploit this biotinylation method to identify oxidized proteins by (1) immunoprecipitation of a priori proteins of interest and (2) streptavidin-linked pull-down of carbonylated proteins for subsequent identification using mass spectrometry and bioinformatics pathway analyses. Preliminary results from these approaches will be presented. Our initial findings suggest oxidative modification of proteins covaries with learning in a cognitive aging model, though further work is necessary and underway.

Krause EK, Upright NA, Moses-Hampton M, Lakhmani P, & Ramirez JJ
Department of Psychology, Davidson College
Electrophysiological Interaction of the Septodentate and Crossed Temporodentate Pathways 12 Days Post-Unilateral Entorhinal Cortex Lesion in Rats
emkrause@davidson.edu / 781-249-7337

The central nervous system (CNS) has been shown to undergo neuroplastic phenomena in response to neurodegeneration or traumatic brain injury. In a rat model, axonal sprouting is implicated as a significant mechanism of recovery in lesion-induced hippocampal plasticity. A unilateral entorhinal cortex lesion (UECx) results in deafferentation of the ipsilateral dentate gyrus (DG), a structure highly implicated in spatial memory, through degeneration of the perforant path (PP). This disconnection results in proliferation of the remaining afferent pathways to the DG, specifically the crossed temporodentate pathway

(CTD) and septodentate pathway (SD). Sprouting of the CTD has been shown to highly correlate with behavioral recovery, while the functional significance of the SD proliferation is not well understood. This research assesses the electrophysiological significance of SD sprouting by recording the evoked potential in the DG upon paired-pulse stimulation of the spouted CTD and SD pathways 12-days post-UECx. As rats exhibit behavioral recovery of spatial memory and the sprouted CTD acquires the ability to fire cells in the DG 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. If neuronal activity in the DG is enhanced by paired-pulse stimulation of the SD and the CTD, then we expect to see a significant difference between the slope or amplitude of the CTD waveform when stimulated alone versus when paired with prior SD stimulation.

Rogers E, Costello M G, Zhu D, Salinas E, Stanford T
Wake Forest University School of Medicine; Department of Neurobiology and Anatomy
Neural Correlates of Perceptual Decision Making in the Macaque Frontal Eye Fields and Motor Thalamus
rogeee0@wfu.edu / 336.906.1103

Perceptual decision making involves information from both motor and sensory inputs in the brain. The motor thalamus contains "oculomotor loops" that incorporate and return to frontal eye fields (FEF), which have potential contributions to saccadic target selection . Visuomotor neurons in both FEF and oculomotor thalamus (OcTh) were evaluated to determine their role in choice behavior. In order to perform a choice behavior, a subject makes a perceptual judgment and a subsequent motor action. Monkeys performed a compelled-saccade task, in which the amount of time available to discriminate between a target and distracter was experimentally controlled in order to incorporate both random and informed choices that were dependent on the time available to process the sensory information. Previous data suggested that time available to interpret perceptual information includes both accelerating (correct) and decelerating (incorrect) motor plans. It also suggests that in the FEF, this process is responsible for the differences in timing of neural differentiation for both random and informed choices. FEF and OcTh visuomotor neurons show dependence on perception time (PT) with motor selection only for trials with short PTs, but dependence on both motor choice and sensory information for trials with long PTs. Both structures interpret initial stimuli associated with choosing one of the two alternatives, and both the intensity of the stimuli and time at which it is resolved are consistent with the heterogeneity of sensory and motor processes as determined by the unique temporal demands of the compelled-saccade task.

Vanderweyen DC, Tuck D, Oprisan SA.
Department of Physics and Astronomy, College of Charleston
The Effect of the Shape of Presynaptic Stimuli on the Phase Resetting Curve of a Neuron Model
d.vanderweyen@gmail.com / 843.300.2400

Nervous systems are composed of complex networks of neurons, which are chemical and electrical signal lines. Central Pattern Generators (CPGs) are autonomous networks of

neurons that send signals within the brain and to muscles controlling bodily actions such as walking and breathing. Although each CPG is a complex system, its component neurons can be modeled as intrinsic bursters (pacemakers) that fire at regular intervals. When an intrinsic burster receives signals, or inputs, from other neurons in the CPG network, it converts these signals into measurable changes of its firing rate and passes this output to the next neuron. We investigated how the input-output relationship of individual intrinsic bursters, i.e., the phase resetting curve (PRC), and the coupling between neurons generate complex firing patterns in CPGs. The novelty of our approach resides in the realistic analysis of triangular shaped currents, which are more realistic stimulus currents for action potentials generated by neurons compared to previously studied rectangular pluses. We found that the relationship between the stimulus amplitude and the response of the neuron was linear over a realistic range of values. Since the product of the amplitude of injected current and its duration is proportional to the net electric charge injected into the neuron, we also investigated the influence of variable duration on the PRC. Our results incite that the duration of the stimulus induced a pronounced non-linear response form the neuron. This suggests that the neuron does not simply integrate the area under the curve of the stimulus, but is more sensitive to the temporal dimension of its input.

Hamilton S, Blake D, Heinzelmann M, & Ramirez J
Department of Psychology, Neuroscience Program, Davidson College, Davidson NC
Effects of inter-trial delays on the performance of rats with bilateral entorhinal cortex lesions in a radial arm maze.
sehamilton@davidson.edu / 713.502.2991

We investigated the effects of different inter-trial time delays on the performance of rats in a Radial Arm Maze (RAM), a spatial and working memory maze. We hypothesized that a longer time delay would lead to more errors, defined as reentries into previously visited arms, than a shorter time delay. Nine Sprague Dawley rats were gentled, food deprived to 80% of their body weight, and trained to run in a RAM. After training the rats received electrolytic, bilateral entorhinal cortex lesions (BECX) and were given seven days to recover. After recovery, rats began running in the RAM once a day for 5 weeks with either a 30 second inter-trial delay or a 120 second inter-trial delay in each arm of the maze. The average errors per week for each group were compared. Contrary to our hypothesis, we found there is no significant difference between the number of errors made by the 120 BECX second and 30 second BECX rats ($p>0.5$); however, for the first week the 30 second BECX rats made significantly more errors than the 120 BECX second rats ($p<0.5$).

Olsen ACK, & Triblehorn JD
Department of Biology, Department of Psychology, Program in Neuroscience, College of Charleston
Stimulus velocity encoding by primary afferents in the wind-sensitive cercal systems of three cockroach species
acolsen@g.cofc.edu / 610.761.8321

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 escape response unlike its close relatives (*Blaberus craniifer* and *Gromphodhorina portentosa*) despite possessing the same underlying neural circuit. Our lab has previously 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 WSI activity originate from the WSIs themselves or from the direct sensory receptor neuron input. To determine how afferent activity differed across these species, we extracellularly recorded the summed wind-evoked responses from the cercal nerve afferents (wind puffs varied from 0-250 cm/sec). Stimulus-Response (S-R) curves were generated for the First 100 ms and Second 150 ms of the summed response. *P. americana* consistently showed stronger afferent activity compared to *G. portentosa* for both the First 100 ms and Second 150 ms of the stimulus, which is consistent with the WSI responses. However, there was a linear relationship between stimulus velocity and afferent activity for both parts of the stimulus. This is different from the S-R relationships for the WSIs in both species. Preliminary results suggest the S-R relationship for the afferents in *B. craniifer* are also linear, but it is currently inconclusive whether *B. craniifer* resembles *P. americana* or *G. portentosa*. Future experiments will investigate the transfer of neural information between the afferents and the WSIs.

McPherson EE, Long CB, & Meyer- Bernstein EL
Department of Biology, College of Charleston
Behavioral and molecular analyses of circadian rhythms in *Nematostella vectensis*
eemcpher@g.cofc.edu / 803.622.7528
Circadian rhythms are endogenous biological oscillations that occur over a 24 hour period in many animals. Many marine organisms also exhibit circatidal rhythms of approximately 12.4 hours. The “time keepers”, or zeitgebers, such as temperature, light, tides, and the presentation of food can be used to synchronize animals to an internal biological clock. The sea anemone, Nematostella vectensis, is being developed as a model for studying both circadian and circatidal rhythms. Our research has employed both behavioral and molecular analysis in order to better understand the mechanisms behind oscillatory behavior in this species. Animals were entrained for two weeks in a simulated tidal cycle in conjunction with a 24 hour light:dark cycle. Their locomotor activity was recorded for five days in constant light using Ethovision software. Both tidal and photic cues were found to influence the rhythmic locomotor behavior of these animals. In addition, we have successfully localized known circadian genes in these animals using in-situ hybridization. In order to characterize the cells in which the circadian genes are localized and investigate their function, we have employed the use of various neuronal markers, GABA, NORPA, FMRF, and OTX for secondary immunohistochemistry staining. Preliminary analysis suggests GABA and OTX co-localize with circadian gene expression. Together, these behavioral and molecular experiments will enhance our knowledge of the marine invertebrate rhythmic behavior and the organization of the circadian system in N. vectensis.

Lench DH, den Hartog CR, Gilstrap MJ, Fedarovich H, Homanics GE, &

Woodward JJ
Department of Biology and Program in Neuroscience, College of Charleston, Charleston, SC; Department of Neurosciences, Medical University of South Carolina
Chronic Ethanol Exposure in Knock-In Mice Expressing Ethanol-Resistant NMDA Receptors
203.505.5814

Inhibition of glutamatergic N-Methyl-D-Aspartate receptors (NMDARs) is thought to play an important role in mediating the acute rewarding effects of ethanol. Previous studies with recombinant systems have identified a residue (phenylalanine) in NMDARs at position 639 within the TM3 domain of the NR1 subunit that, when mutated to alanine, reduces the ethanol sensitivity of the receptor. Heterozygous mice carrying this mutation (F639A Het) show blunted responses to the locomotor and anxiolytic effects of ethanol and consumed less alcohol than their littermates with short-access drinking paradigms. Given these results, we examined the effects of the mutation on ethanol drinking where mice were given 24-hr intermittent access to increasing concentrations of ethanol solutions with saccharin. We also examined how this mutation would affect protein expression changes seen with repeated ethanol treatment from mice that underwent drinking or were treated with a chronic injection protocol. Het mice consumed more sweetened ethanol than their littermates in a long-access paradigm although no differences in protein expression were seen between the groups. F639A Het mice expressed normal amounts of GluN1 and GluN2B protein in a variety of brain regions but showed a small reduction in levels of GluN2A in the medial prefrontal cortex. Surprisingly, no differences in protein expression were found following a chronic ethanol treatment paradigm regardless of genotype. Follow-up studies will investigate whether this lack of effect was due to the treatment or the 129Sv/C57 background strain. Overall, these data support the hypothesis that NMDA receptors are important in mediating effects following exposure to ethanol.

Collett K, Arrington P, Nesbit A, Southard M, Conner H, & Nichols D
Department of Psychology, Roanoke College
Brain Activity While Viewing Attractive and Unattractive Faces
kacollett@mail.roanoke.edu / 919.323.9958

Facial attractiveness has long been understood to be an evolutionary trait that is beneficial in mate selection and other social interactions. Society tends to prefer attractive faces to unattractive faces. The current study sought to determine how attractiveness of faces is processed neurologically. Using electroencephalography (EEG), subjects were presented with unattractive and attractive images of faces to measure for visual mismatch negativity (vMMN), a type of event related potential (ERP) signal. ERPs are tiny, time-locked electrical signals that occur in response to the presentation of a particular type of stimulus. MMN research involves the use of a standard and a deviant stimulus. One type of stimulus is presented less frequently than the other. The less frequent stimulus is the deviant, and the more frequent stimulus is the standard. If presentation of the deviant stimulus results in a significant difference than response to standard stimuli, an MMN is said to be present. The study compared processing in the occipital lobe (channel 1) to the

frontal-parietal lobe (channel 2). Processing of faces was also analyzed across time windows, from the time when one stimulus was presented to the next. No overall MMN for attractive or unattractive faces was found. However, there was some indication that whether a stimulus is standard or deviant may matter within particular time windows.

Larkin, TE, Dhanraj, DR, Hummer, DL
Department of Psychology, Morehouse College
Sustained Activation of GABA-A receptors and NMDA receptors in the SCN produce similar phase-shifting effects at dusk but opposite phase-shifting effects at dawn
telarkin2@gmail.com / 478.973.8913

Circadian rhythms are daily cycles in behavior and physiology generated in the suprachiasmatic nucleus of the anterior hypothalamus (SCN). Daily cues in the environment adjust the phase of these endogenous rhythms and allow organisms to entrain a 24-hr cyclical environment. Although light exposure at specific times of day has a powerful phase-shifting effect on circadian rhythms, much about the biological mechanism underlying circadian entrainment remains unknown. Previous studies from our lab demonstrate that sustained activation of GABA-A receptors in the SCN is critically involved in the ability of light to phase delay the circadian clock during early night (i.e., dusk). However, the sustained activation of GABA-A receptors in the SCN does not appear to be involved in the ability of light to phase advance the clock during late night (i.e. dusk). This experiment explores the hypothesis that sustained activation of GABA or glutamate receptors in the SCN mediates the ability of light to phase shift the circadian clock. Male Syrian hamsters were implanted with guide cannula aimed at the SCN. After recovery, they were introduced to running wheels and allowed to establish a stable free-running activity rhythm in constant darkness. Animals received a series of 4 intracranial injections of muscimol (GABA-A agonist), NMDA or vehicle at one-hour intervals beginning at CT13.5 (i.e. early subjective night) or CT19 (i.e. late subjective night). The magnitude of phase shifts was calculated by measuring the difference between the onsets of activity on the day of treatment, predicted from the daily onsets of activity before and after drug injections. Preliminary data show that sustained activation of both GABA-A and NMDA receptors in the SCN during the early subjective night produced a light-like phase delay in wheel-running activity. Sustained activation of NMDA receptors in the late subjective night produced a light-like phase advance in wheel running activity. However, sustained activation of GABA-A receptors in the late subjective night produced a phase delay in wheel running activity. The sustained activation of GABA receptors may mediate the phase shifting effects of light in the early night but not in the late night. Based on these data we hypothesize that the effects of sustained activation of GABA receptors in the SCN are excitatory in the early subjective night and inhibitory in the late subjective night.

Jannat Khan, Jennifer Round, & Barbara Lom
Department of Biology, Davidson College
Visualizing Slitrk 5 protein and identifying axon tracts in the developing zebrafish central nervous system.

jakhan@davidson.edu / 330.669.6768

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 Slitrk expression patterns to understand what regions of the nervous system express specific Slitrks during development. 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 Slitrk 5 expression and labeled axon tracts in the developing zebrafish central nervous system. In order to map the normal axon tracts in untreated embryos we successfully immunostained for acetylated tubulin, an axonal marker in wholemount embryos. We also immunostained tissue sections with a custom Slitrk5 antibody to visualize the Slitrk 5 protein distribution in normal embryos. Our results suggest that the Slitrk 5 antibody does stain in a specific or consistent pattern. Thus, future research will investigate alternative procedures to visualize Sliltrk protein distribution.

Stankeviciute NM[1,2], Scofield MD[3], Kalivas PW[3], & Gipson CD[3]
[1]Department of Biology, 2Program in Neuroscience, College of Charleston; [2]Department of Neurosciences, MUSC
Rapid, transient potentiation of dendritic spines in context-induced relapse to cocaine seeking
nstankev@g.cofc.edu / 843.298.2693

Addiction to cocaine produces long-lasting, stable changes in brain synaptic physiology that might contribute to the vulnerability to relapse. Specifically, the nucleus accumbens, which is part of a corticostriatal brain circuit involved in learning behavioral tasks and modulating reward-seeking behaviors, has been shown to activate during relapse behavior. In rats, cue-induced reinstatement produces temporary changes in the spine head diameter of medium spiny neurons in the nucleus accumbens core (NAcore). In humans, exposure to environmental contexts previously paired with drug use evokes relapse, but the neurobiological mechanisms mediating this relapse are unknown. This study followed the A-B-A renewal paradigm using Sprague Dawley rats. Rats learned to self-administer cocaine by pressing one of two levers during two hour sessions in an environment with distinct tactile, visual, olfactory and auditory cues. Self-administration lasted for ten day with a minimum of ten active lever presses. Drug seeking was extinguished in an environment lacking the original contextual cues. After extinction, the animals were returned to the original context for reinstatement. We quantified synaptic plasticity by measuring the spine head diameter of medium spiny neurons. Initiation of cocaine relapse via re-exposure to a drug-associated context elicited reinstatement of cocaine seeking as well as rapid, transient synaptic plasticity in the NAcore. This effect was not observed in rats that self-administered saline and followed the same A-B-A paradigm. Results showed that rapid context-evoked synaptic potentiation in the NAcore may underpin relapse to cocaine use. Further research may lead to pharmaceutical

options to prevent relapse.

James M, Galasso A, & Meyer-Bernstein EL
Department of Biology, College of Charleston
Temperature Entrainment of Rhythmic Behavior in the Starlet Sea Anemone.
meyerbernsteine@cofc.edu / 843.953.2298

Daily cycles in physiology and behavior are controlled by an organism's circadian system. We have been investigating the circadian system of the sea anemone, *Nematostella vectensis*. Thus far, we have found that the *Nematostella* express rhythms in locomotor behavior that can be synchronized to a 24-hr light:dark cycle. Their rhythms persist in the absence of any environmental cues indicating an endogenous circadian clock mechanism. In addition to the photoperiod, these intertidal marine animals are also exposed in their natural environment to oscillations in temperature. In the present study, we investigated whether a temperature rhythm could provide a temporal cue to the circadian clock similar to what we have shown for light. The animals' locomotor activity was initially synchronized to a 24 hour light:dark cycle for two weeks. Sea anemones were then exposed to a temperature rhythm (12hr:12hr; 32:22°C) for an additional two weeks. The ability of the temperature cycle to synchronize the animal's locomotor behavior was assessed for up to five days using Ethovision behavioral analysis software. We have found that temperature can be effective in synchronizing the circadian clock in *N. vectensis* and that the animals are more active in the cooler temperature (22°C). In addition to the behavioral analysis, we have recently initiated experiments to identify temperature sensitive molecules in *N. vectensis*. Eventually, we plan to identify components of the temperature entrainment pathway that provides input to the molecular clock. This will provide insight into the circadian system of Cnidarians and circadian clock evolution.

Coker A[1], Boan A[2], & Lackland D[2]
[1]Dept of Psychology, C of C; Program in Neuroscience, C of C; Department of Neurosciences, Medical University of South Carolina (MUSC)
Hemodynamic Variables in Stroke Patients with Diabetes and Hypertension
accoker@g.cofc.edu / 843.260.3199

Stroke is a leading cause of death and disability in the United States, especially in the Southeast. Hypertension and diabetes mellitus are important risk factors for stroke incidence and recurrence. Also, hyperglycemia upon admission is associated with poor stroke recovery. This project assessed admission blood pressure (BP) and hemoglobin A1c (HbA1c) levels, antihypertensive and anti-diabetic medication regimens prescribed post stroke discharge, and stroke severity (NIHSS) scores among patients ≥45 years old at MUSC between Oct 2008-Oct 2009. Patient demographics, comorbidities, hemodynamic values, and discharge medications were compared by age, race, and gender using t-tests for continuous variables and chi-square tests for categorical variables. Analysis of a preliminary cohort (n=158) found that 26.6% of the patients were diagnosed with diabetes, with significantly higher proportions among African Americans compared to Caucasians (p=0.03). A total of 20.9% of the cohort had an HbA1c ≥ 6.5%.

Among patients with diabetes, only 66.7% were discharged on anti-diabetic therapy, while 60.1% of the patients were diagnosed with hypertension (no significant difference by race). Admitting BP values ≥140/90 mmHg was found in 49.4% of the patients. Among patients with hypertension, 89.5% were discharged on anti-hypertension therapy and had an average NIHSS score of 6.2 (no significant differences in scores by race, or hypertension or diabetes status). Medication regimens to control hypertension and hyperglycemia are important in secondary stroke prevention, but a significant proportion of patients with diabetes were not prescribed anti-diabetic medications post stroke. Stroke severity was not associated with comorbidity status.

Cullum E, Hanna JM, Haugsnes E, & Askew A
Department of Psychology, Presbyterian College
Learned Avoidance in the Male Syrian Hamster
jmhanna@presby.edu / 803.429.6902

When adult male Syrian hamsters are paired, they readily engage in territorial behavior and this typically leads to one establishing the dominant role. In subsequent encounters, the subordinate hamster will show fear responses that are not typically seen prior to defeat. In a preliminary experiment, defeated male hamsters exhibited learned avoidance of dominant opponents after being defeated in our modified passive avoidance apparatus. This apparatus is a sectioned runway with seven chambers and a fight arena. It differs from the typical passive avoidance apparatus in that it uses defeat as the aversive experience. There is overwhelming evidence that glucocorticoid hormones are involved in fear learning. In a follow-up experiment, we will use the glucocorticoid antagonist mifepristone (30mg/kg, s.c.) to investigate the role of glucocorticoids in reconsolidation of learned avoidance. Adult male hamsters (7-8 weeks old) will be randomly assigned to one of four conditions: 1) Defeat + Memory Reactivation + Drug, 2) Defeat + No Reactivation + Drug, 3) Defeat + Reactivation + Vehicle, or 4) No Defeat + Reactivation + Vehicle. Subjects will be tested for memory deficits 48 hours and 1 week after the drug/vehicle is administered. It is hypothesized that 1) mifepristone administration will produce memory deficits only when the defeat memory has been reactivated, and 2) this deficit will be observed at 48 hours and 1 week after the drug administration. Prolonged deficits that are dependent upon memory reactivation would suggest that glucocorticoids play a role in reconsolidation of learned avoidance. Future experiments may target glucocorticoid receptors in the basolateral amygdala.

B Blaker, Miller C, Lea A, Wilson T, & Rives T
Department of Neurosciences, Furman University
Slc6a3 Dopamine Transporter and Tyrosine Hydroxylase Expression in the Rat Septohippocampal Pathway Following Lesioning of the Entorhinal Cortex
cole.miller2066@furman.edu / 864.978.2428

Years ago the central nervous system was thought to be beyond repair as the loss of neurons was viewed as an entirely irreversible process. However, due to the interest given to this field by researchers, recent findings have indicated that neuron regeneration is a very active process in certain areas of the human brain. The dentate gyrus of the

hippocampus is capable of this phenomenon of adult neurogenesis. By removing perforant path input to the hippocampus, the septodentate innervations to the dentate gyrus increase to maintain the excitatory input to the region. The septohippocampal pathway is subject to modulation by the neurotransmitter dopamine. The A10 cell group of the ventro-medial tegmentum has been shown to be the only form of dopaminergic innervations to the septum, and dopamine seems to have an attenuating effect on the septodentate pathway. Dopamine-related genes are specifically addressed in the current paper. Specifically, tyrosine hydroxylase, a rate-limiting enzyme in the formation of dopamine, and Slc6a3 (solute carrier family 6 member 3) of the dopamine transporter (DAT) are key targets in this study. Lesioning occurred of every rat and AChE staining was used to indicate sprouting. Of the nine rats that underwent surgery, seven had successful indications of sprouting new connections from the septum to the hippocampus. RT2qPCR gene analysis of the septum showed a 2.2 upregulation of slc6a3 and tyrosine hydroxylase was downregulated 3.01 times. These results are consistent with our hypothesis that there decrease in dopamine to prevent attenuation of the septodentate pathway thereby allowing for the generation of the cholinergic input to the dentate gyrus.

Whitmill M, Restifo L, & Conner W
Department of Biology, Wake Forest University
Effects of a Drug Treatment on the Locomotory Behavior of Drosophila with a Fragile-X Mental Retardation Gene Mutation
whitma9@wfu.edu / 704.929.6504

Autism Spectrum Disorder (ASD) represents a broad range of disorders with similar behavioral and developmental symptoms, but different causes. Fragile-X syndrome (FXS) is one such disorder, and is the most common form of ASD caused by a single gene mutation. The affected gene, Fragile-X Mental Retardation 1 (FMR1), codes for Fragile-X Mental Retardation 1 Protein (FMRP), which helps regulate postsynaptic protein synthesis in response to group 1 metabotropic glutamate receptor activation. It is believed the drug MPEP, a mGluR5 antagonist, will restore proper functioning to this pathway. Drosophila melanogaster have an orthologous gene to FMR1, dFMR1, which allows this disorder to be extensively studied in a well understood model organism. Previous studies in the Conner laboratory have shown that MPEP is able to restore the grooming behavior of dFMR1 mutant Drosophila to wildtype patterns. This experiment compares the locomotion of homozygous dFMR1 mutants and wildtype (EX16) Drosophila, and uses these measures to investigate the effectiveness of MPEP. Individual Drosophila were placed in a 50mm diameter plate, and recorded for 30 minutes. Noldus Ethovision XT software suite was used to track the animalâ€™s position and analyze its movement. The frequency of starts and stops, similar to the darting behavior observed in human autistic children, was found to be significantly greater in mutant drosophila than control groups. This behavior change was successfully rescued with MPEP treatment. Other behaviors were also investigated and found to have trends suggestive of MPEP rescue.

Tran P[1], Reissner K[2], Boger H[2], & Kalivas P[2]
[1]Department of Psychology, College of Charleston; [2]Department of Neurosciences,

Medical University of South Carolina
Effects of Cocaine Self-administration on Astrocytes in the Nucleus Accumbens
transk@g.cofc.edu / 843.467.8288

Recent discoveries have revealed important roles for glial cells in the neurobiology underlining drug addiction. For example, self-administration of drugs of abuse, especially cocaine, results in decreased levels of astroglial glutamate transporter EAAT2/GLT-1 and glutamate antiporter catalytic subunit xCT (Knackstedt et al., 2010). Given these changes in expression of astrocyte-enriched proteins, the current study seeks to examine other cocaine-dependent changes in astrocyte protein expression, and whether these changes might influence astroglial cell morphology and function. We find that following cocaine self-administration and extinction training, GLT-1 and GFAP are downregulated in the nucleus accumbens (NAc) core and shell. Chronic administration of the glial modulator propentofylline (PPF), partially restores the expression of GLT-1 and GFAP in the NAc core and shell and blocks cue-primed reinstatement to cocaine by a mechanism that is dependent upon the restored expression of GLT-1. In addition, using quantitative immunohistochemistry and densitometry, we also find a reduction in GFAP-positive astrocytes and GFAP mean density in the NAc core. All together, these findings present new evidence for the essential role of glial cells in the neuropathology of drug addiction, and provide a potential target for the treatment of addiction-related behaviors.

Pathak G, Hartman A, Harding I, & Kelly MP
Department of Pharmacology, Physiology, & Neuroscience, USC School of Medicine
Mapping mRNA and Protein Expression of Phosphodiesterase Families Across Brain Regions To Assess Conservation Between Rodent Species
pathakg@email.sc.edu / 803.707.1135

Phosphodiesterases (PDEs) are the only enzymes known to break down cyclic nucleotides. Thus, PDEs are critical to the regulation of cell signaling. Individual reports have shown that various PDE families differ in function and vary in distribution across tissues. That said, very few studies have directly compared expression of multiple PDE families within a tissue and fewer still have compared expression of a particular PDE across multiple species. It is important that we understand potential species differences in PDE expression because mice and rats have long been used as animal models of human disease. Because mouse and rat PDEs are highly homologous (91-99% protein homology), we hypothesized that PDE distribution across brain regions would be conserved between mice and rats. Here, we mapped out the mRNA distribution of all brain-expressed PDE families in brains of C57BL/6J mice and Sprague Dawley rats as well as a limited number of PDE families in brains of 129S6 and Balb/CJ mice. To map mRNA expression, brains were cryosectioned and processed by autoradiographic in situ hybridization. We also characterized the protein expression of select PDE families (e.g. PDE11) in brains of C57BL/6J mice, 129S6 mice, Balb/CJ mice, and Sprague Dawley rats. To measure protein expression, dissected brain regions were processed by Western blotting. Overall, the distribution of each PDE isoform (at both the mRNA and protein level) was highly similar across mouse strains and between mice and rats, with only a few exceptions being noted (e.g. PDE2A mRNA is enriched in anterior ventral nucleus of

thalamus in mice but not rats). Therefore, our data suggest expression patterns of PDE families are conserved across rodent species.

Smith BM[1,2], Sakuaria A[3], & Katz PS[3]
[1]Agnes Scott College, Decatur, GA 30030; [2]Atlanta NET/work, Georgia State University, Atlanta GA
Evidence for a homologue of the meteacerebral giant neuron in the nudibranch, Melibe leonina
bsmith@agnesscott.edu / 706-206-8486

Comparing the nervous systems across species provides insights into how they evolved. Nudibranch molluscs have large, identifiable neurons, which often can be recognized across species allowing their functions to be compared across species. Previously, the serotonin (5-HT) immunoreactive neurons in eleven nudibranch mollusc species were mapped. In general, the presence of 5-HT-immunoreactive neurons and neuronal clusters was conserved across species. However, one prominent serotonergic neuron which is found in nearly all gastropods, the metacerebral giant (MCG) neuron, could not be identified in the species, Melibe leonina. The MCG is the largest of all serotonergic neurons in the anterior region of the cerebral ganglion and the only serotonergic neuron to innervate the buccal ganglia,; which control feeding behaviors. Melibe has a unique method of feeding, which might be correlated with a loss of MCG. However, although there are no serotonergic neurons in the cerebral cluster that are overtly larger than surrounding 5-HT immunoreactive neurons, the presence of a 5-HT-ir axon in the cerebral-buccal connective indicates that there may be a serotonergic neuron similar to the MCG. We hypothesized that there is an MCG homologue in Melibe, which is about the same size as its surrounding serotonergic neurons. To address this, we used biocytin backfilling techniques to label neurons with axons traveling from the buccal ganglia into the cerebral ganglia. We then performed immunohistochemistry against 5-HT. We found a single cell body in each of the paired cerebral ganglia that was both labeled with biocytin and 5-HT immunoreactive. This neuron must be the MCG homologue in Melibe because it is 5-HT immunoreactive and innervates the buccal ganglia. The discovery of the MCG in Melibe suggests that despite the evolution of a novel feeding mechanism, the central neural contral has been conserved.
This work supported by funding from NET/work and by NSF-IOS-1120950

Bailey Ryan[1], Xiaowei Zou[2,4] and Colleen A. Hanlon, Ph. D[3,4],
[1]Department of Biology and Program in Neuroscience, College of Charleston, Charleston, SC
[2]Biomedical Engineering Department Columbia University, New York City, NY
[3]Center for Biomedical Imaging and [4]Departments of Psychiatry and Neurosciences Medical University of South Carolina, Charleston, SC
Neural Systems in Cocaine Addicts: an Interleaved TMS/ASL study
b.elle.ryan7@gmail.com / 518.469.7505

Addiction is a complex disorder that affects multiple frontal-striatal systems in the brain, including dorsolateral and ventromedial circuits, which, respectively, regulate

reward-seeking and executive control. While prior studies of these neural circuits have been restricted to invasive animal models, it is now possible to probe the integrity of these circuits in human cocaine users using simultaneous transcranial magnetic stimulation (TMS) and arterial spin labeling (ASL). TMS is a non-invasive procedure that when coupled with ASL, allows visualization of elevated neural activity in the cortex below the coil as well as monosynaptically connected targets such as the striatum. This study investigated the functional integrity of dorsolateral and ventromedial circuits in chronic cocaine users through interleaved TMS/ASL. Interleaved TSM/ASL imaging date was acquired for 19 healthy individuals and 7 cocaine users. All participants received TMS in 2 runs with the coil positioned over the: 1) dorsolateral prefrontal cortex (DLPFC) and 2) ventromedial prefrontal cortex (MPFC)(Magstim MR-compatible coil, 9 second interpulse interval, 100% motor threshold). Pulsed ASL data was acquired (14 slices, 3X3X5 mm resolution, 2.25 s TR) and analyzed using standard parametric techniques (SPM5, Matlab 6.5). There was a significant difference in cortical and striatal perfusion following DLPFC relative to MPFC stimulation in both groups. Relative to the controls, cocaine users had significantly less perfusion following MPFC stimulation and significantly more perfusion following MPFC stimulation. These preliminary data demonstrate that cocaine users have attenuated functional activity in executive control circuits (MPFC) and a hyperactive response in limbic circuits (DLPFC). Additionally, given that ASL has a greater test-retest reliability than blood-oxygenated-level-dependent (BOLD) imaging, these data demonstrate that interleaved TMS/ASL may be a valuable tool for longitudinal assessment of cognitive and limbic function in recovering addicts.