Second Annual
Midwest/Great Lakes Undergraduate Research Symposium
in Neuroscience
Hosted by Ohio Wesleyan University

Generously Sponsored by:

Our Keynote Speaker this afternoon will be Dr. Dana McTigue of The Ohio State University

Dr. McTigue is an Associate Professor of Neuroscience who works in the Center for Brain and Spinal Cord Repair. Her doctoral and post-doctoral training occurred at Ohio State in the Department of Physiology.

Ongoing projects in her lab include: 1) Use models of demyelination to assess changes in oligodendrocytes and oligodendrocyte progenitor cells (OPCs). These models are used to assess treatment strategies to enhance myelin sparing and remyelination as well as axon preservation. 2) Determine the response of oligodendrocytes and OPCs to spinal cord injury in adults. New oligodendrocytes do not originate from existing oligodendrocytes (which are post-mitotic) but instead derive from OPCs found throughout the adult CNS. Thus, OPCs that survive a spinal cord injury provide a population of cells that could be induced to form new oligodendrocytes. Studies are aimed at determining the response of these cells to CNS trauma and the effectiveness of applying specific growth factors or other agents that may improve OPC survival, proliferation and/or differentiation. The long-term goal of these studies is to determine if myelination of injured CNS tissue can be improved and if this results in improved functional outcomes. 3) In vitro analysis of cells isolated from injured spinal cords. In these studies, OPCs are isolated at different times after spinal cord injury and their responsiveness to different growth factor combinations is examined. These studies will determine how OPCs are affected by exposure to trauma and can serve as an important screening mechanism to evaluate which growth factors hold the most promise for different stages of spinal cord injury, e.g., acute versus chronic times post-injury.

Platform Presentations

1. Jessica McClarren

Barko DN & McClarren JL
Departments of Neuroscience and Chemistry, Baldwin-Wallace College

Expression and Purification of Recombinant Peptidyl Arginine Deiminase from Danio rerio.
Peptidyl arginine deiminase-2 (PAD2) is an enzyme that catalyzes the conversion of arginine residues to citrulline residues in the central nervous system (CNS). The electrostatic interactions shared between positively charged arginine residues in myelin basic protein and the negatively charged lipids found in myelin are lost upon the conversion of arginine to citrulline which contributes to the degeneration of the myelin sheath. Additionally, recent studies have implicated a correlation between higher amounts of citrullination and increased concentrations of PAD2 with CNS tissue deterioration among patients with multiple sclerosis [Kim, J.K. et al. (2003) Molecular & Cellular Proteomics 2, 453-462.; Wood, D. et al. (2008) Laboratory Investigation 88, 354-364]. These findings strongly suggest that an increase in PAD2 enzyme activity is responsible for the pathogenesis of multiple sclerosis. In order to investigate this hypothesis, recombinant PAD2 was expressed and purified. An expression vector was constructed using molecular cloning techniques, and the plasmid DNA was purified and sequenced to confirm the presence of the PAD2 gene. The plasmid was linearized through multiple restriction digest procedures and purification was confirmed with agarose gel electrophoresis. The plasmid was transformed into competent BL21 Star™ E.coli cells for protein over expression. An induction study was performed to optimize the expression conditions for PAD2. The presence of PAD2 (~76 kDa) was confirmed by SDS-PAGE and Coomassie blue stain with a standard molecular weight marker.

2. William Stewart

Stewart WN, Thompson EE, Miller RLA, Bow JP, & McLaughlin PJ
Department of Psychology, Edinboro University of Pennsylvania

Alterations in response strategy explain the effects of cannabinoid drugs on attention in rats
Cannabinoid drugs (including delta-9-THC, the main psychoactive ingredient in marijuana) are believed to have deleterious effects on cognition. However, several studies have found no effects on accuracy in attentional tasks in marijuana-treated participants. In rats, attention can be modeled in an operant task by presenting brief, unpredictable visual stimuli in one of two locations, and requiring animals to report the location by pressing the lever nearest the light stimulus. In the current study, the novel cannabinoid CB1 receptor agonist AM4054 was administered to rats performing two types of operant tasks: in one version, one of two light stimuli was presented 15 seconds after the start of every trial; in the other, the onset of the stimulus was unpredictable. A deficit in accuracy was found only for the latter task. This deficit was found at all stimulus durations, suggesting that the drug did not primarily affect attention. Furthermore, rats were unaffected in their accuracy on one of the two levers (the preferred lever), even at high doses, while accuracy was dose-dependently impaired on the other (the nonpreferred lever). This pattern has been found previously in the effects of cannabinoids on memory tasks. A trial-by-trial analysis found that AM4054 selectively enhanced a win-stay strategy on the preferred lever, and a lose-shift strategy on the nonpreferred lever. Therefore, accuracy decreased because choice was increasingly (as a function of dose) influenced by the result and location of the previous choice, not because AM4054 impaired visual attention. These results suggest that the effects of CB1 agonists (including delta-9-THC) on strategy and decision-making should be investigated further.

3. Zöe Hesp

Hesp ZC, & Isaacson LG
Department of Zoology, Miami University of Ohio

Changes in Cerebrovascular Innervation Following Axotomy of the Super Cervical Ganglion.
The regeneration of peripheral nerves has been investigated in several systems. However, the reinnervation of peripheral targets that are denervated following injury is not well characterized, particularly over long-term survival periods. In the present study, we assessed the sympathetic perivascular innervation of the extracerebral blood vessels at 24 hours, 7 days, 8 weeks, and 12 weeks following transection (axotomy) of the postganglionic axons arising from the superior cervical ganglion in rats using tyrosine hydroxylase (TH) immunohistochemistry. The density of TH perivascular axons associated with the internal carotid artery (ICA) was significantly decreased at 24 hours and 7 days following axotomy, but returned to control values by 8 weeks. Likewise, the TH density of the proximal middle cerebral artery (MCA), the region adjacent to the ICA, also was similar to corresponding controls at 8 weeks. Though the innervation of the middle segment of the MCA was sparse at 8 weeks, it returned to control values by 12 weeks; however, innervation of the distal MCA remained significantly decreased at 12 weeks. The TH innervation of both the middle and rostral segments of the basilar was significantly decreased following axotomy and remained decreased at 8 weeks. By 12 weeks, the TH density associated with the middle basilar returned to control values, while innervation of the rostral basilar remained significantly decreased. Overall, these sympathetic axons do not demonstrate robust regeneration, and, in cases such as the basilar, the reinnervation seen may simply be sprouting from lower ganglia rather than regeneration.

Lindsay Boven

Boven LC, Gamo NJ, Kata A, Bryan C, Lo T, Anighoro K, Bermudez L, Peng L, Annor A, Taylor S, Patel K, Duque A, Simen A.A, Arnsten A.F.T
Department of Neuroscience, Oberlin College

Role of DISC1 in stress-induced prefrontal cognitive dysfuntion
The Disrupted in Schizophrenia 1 (DISC1) gene is a scaffold protein associated with schizophrenia, bipolar disorder, and major depression expressed in the cortex, amygdala, paraventricular hypothalamus, cerebellum, interpeduncular nucleus, STN (Austin et al. 2003). DISC1 is involved in neurodevelopment,cytoskeletal function, cAMP signaling and interacts with various other proteins (Chubb et al. 2008) Under conditions of excessive cAMP, DISC1 releases PDE4 which inactivates cAMP (Millar et al. 2005). DISC1 and PDE4 act like “molecular brakes” to restore normal levels of cAMP following stress exposure, and thus regulate PFC network connectivity. Here, we have investigated whether a loss of DISC1 increases vulnerability to stress-induced PFC dysfunction. Young, male Sprague-Dawley rats (n=27) performed a delayed alternation spatial WM task in a T-maze. The rats were trained until they performed at ~70% baseline. Rats were separated into 3 groups of n=9: Control, DISC1 KD, and DISC1 KD Scrambled. The DISC1 KD group was surgically infused an AAV2 viral construct to knockdown DISC1 expression at the prelimbic PFC (AP +3.2, ML +/-0.75, DV -4.2) The DISC1 KD Scrambled Rats went through the same procedure above but were infused with a scrambled sequence virus which did not knock down DISC1. The Control group did not have any infusion procedure. A 10 day waiting period was required for viral expression. Once rats were performing at stable baselines on the T-maze task (60-80%) they were subject to 1 hour restraint testing immediately prior to testing. One hour restraint stress had no effect on its own, where two hours was shown to impair working memory in normal rats. DISC1 expression was evaluated post-mortem on the rats. The data were analyzed using

2-way ANOVA with repeated measures. Knocking down DISC1 in rat PFC lowered the threshold for stress-induced cognitive dysfunction. DISC1 knockdown rats had impaired performance after stress in delayed alternation spatial WM task. This mechanism is immediately relevant to schizophrenia, a disorder associated with a loss-of-function translocation in DISC1 ("Disrupted In Schizophrenia"), and with profound PFC dysfunction. These findings may explain why patients with mental illness are so vulnerable to stress. We can utilize this DISC1 pathway to develop target medications for psychiatric illnesses.

Poster Presentations

4. Cahill C, Kyweriga M, & Wehr M
Neuroscience Program, College of Wooster (and University of Oregon Summer Program for Undergraduate Research)

Mechanisms of Binaural Suppression in Rat Auditory Cortex

Binaural interactions are a result of sounds entering both ears and are important in helping determine where a sound is coming from. As sound enters the ears it is transduced into electrical signals which travel up parallel neural pathways in the brainstem and midbrain before ultimately reaching the cortex. Within these pathways signals are processed, filtered and directed to different areas. One type of processing is called binaural suppression, where sound entering one ear suppresses the response to sound entering the other ear. Using electrophysiology to record binaural responses in the rat primary auditory cortex, we attempted to examine whether binaural suppression occurred at the cortical level, sub cortical level or both. To test this we applied gabazine, an agonist of GABAa receptors, to the cortex to alleviate binaural suppression. Although we could not determine whether suppression occurs at a cortical or subcortical level based on extracellular responses recorded from 4 rats, my research highlights a strategy that will be used to address whether binaural suppression occurs at the cortical or subcortical levels.

5. Kaercher L, Stone B, DeChristopher K, & Kuebler DR
Department of Biology, Franciscan University of Steubenville

Alterations in Metabolism Suppress Seizures in Seizure-Susceptible Drosophila

There is increasing evidence that alterations in metabolism can affect seizure susceptibility in a wide range of organisms. In order to investigate the link between metabolism and seizures, we took advantage of a group of Drosophila mutants, the BS paralytics, that are 3-10 times more susceptible to seizures than wild type flies. In three of the BS strains, we introduced the atsugari (atg) mutation, a mutation in the dystroglycan gene that is known to increase metabolism in flies. Following mechanical shock, all three BS;atg double mutants displayed a reduction in seizure activity and recovered quicker than the respective single mutant BS flies. To further study the correlation between increasing metabolism and seizure susceptibility, the three BS strains were fed a sulfonylurea drug (tolbutamide) that has been shown to increase metabolism in flies. Following mechanical shock, two of the three BS mutants fed tolbutamide displayed less seizure activity and recovered quicker than unfed flies. These data suggest that increasing metabolism can have a protective effect against seizure susceptibility, a result that suggests new avenues for possible drug development.

6. Ketchesin K, Ayad I, Prodan S, Rogers M, Romanchik J, Ramos L, Wilson GN, Remus J, Biesan O & Mickley GA
Department of Neuroscience, Baldwin-Wallace College

Acute, But Not Chronic, Exposure to D-Cycloserine Facilitates Extinction of a Conditioned Taste Aversion

D-cycloserine (DCS), the glutamate NMDA receptor partial agonist, has been reported to facilitate the extinction of learned fears. However, chronic exposure to the drug throughout the extinction (EXT) process does not facilitate the attenuation of a conditioned taste aversion (CTA) (Mickley et al., 2009). In the current study we evaluated the ability of acute treatments with DCS, given during different stages in the EXT process, to modulate the disappearance of behavioral indicators of a CTA. Twenty-three hour water-deprived male Sprague-Dawley rats acquired a strong CTA following 3 CS-US pairings [0.3% saccharin (SAC) and 81 mg/kg (i.p.) Lithium Chloride (LiCl)]. We then employed 2 different EXT paradigms: (1) CS-only (CSO) in which SAC was presented every-other day, or (2) Explicitly Unpaired (EU) in which both SAC and LiCl were presented, but on alternate days. Previous studies have indicated that Spontaneous Recovery (SR) of a CTA emerges following CSO EXT but the EU-EXT paradigm causes a suppression of SR (Mickley et al., 2009). In the acute drug manipulation, DCS (15 mg/kg, i.p.) or saline control injections were administered, for 4 days only, immediately after daily liquid presentations (SAC or water, alternate days). This was done during one of 3 different phases of EXT training (i.e., 2-5%, 8-16% or 20-40% SAC reacceptance). Other animals, assigned to the chronic DCS condition, received daily DCS (15 mg/kg, i.p.) throughout EXT. Changes in SAC drinking in these animals were compared to the data from rats that received no drug (saline controls). In a replication of our previous work, rats that went through the EU-EXT procedure achieved asymptotic extinction (81% of baseline SAC drinking) more quickly than did the CSO rats. However, CSO and EU-EXT rats having acute DCS treatments, extinguished their CTA more rapidly than did those animals exposed to DCS throughout EXT. CSO and EU-EXT rats in the acute DCS treatment groups also reliably extinguished their CTA more quickly than did saline-control animals. Additional control experiments confirmed that an acute injection of 15 mg/kg (i.p.) was not an effective US and did not change our animal's ability to taste SAC. Therefore, the drug effects we report here are unlikely the result of DCS-induced changes in sensation. These data agree with other findings (Vengeliene et al., 2008; Norberg et al., 2008) suggesting that DCS treatments are more effective when administered a limited number of times within a simple CSO extinction paradigm. Our data extend these findings and further suggest that acute exposure to DCS can also speed up EU-EXT. To maximize the speed of extinction animals should receive acute (4-day) exposure to DCS within the context of an explicitly unpaired EXT paradigm. The timing of the DCS treatment during EXT is less important than its duration

7. Kelley E & Cushman HN.
Neuroscience Program, Washington and Jefferson College

Lactate enhances the response of acid-sensitive C-fiber nociceptors in an in vitro electrophysiological preparation.

Ischemic pain occurs when a tissue experiences a decrease in blood supply, depriving it of oxygen and causing a build-up of lactic acid. This study used an in vitro skin-nerve preparation to test the effects of proton concentration and lactate on the activation of cutaneous C-fiber nociceptors in C57BL6 mice. Our data show a significant increase in firing rate when lactate was applied in addition to pH 6.5 acid. This suggests that lactate may play an important role in the triggering of ischemic pain.

8. Grable TL, Keller CA, Malchow RP & Kreitzer MA
Biology Department, Indiana Wesleyan University

Depolarization-dependent extracellular alkalinizations from isolated goldfish retinal horizontal cells.
Changes in extracellular [H+] have been shown to have an impact on neuronal processing including in the retina. More specifically, changes in extracellular [H^+] have been shown to impact lateral inhibition in the outer retina regulated by horizontal cells. Glutamate is the neurotransmitter released by photoreceptor cells in the absence of light resulting in the depolarization of the horizontal cell. These studies examined the nature of the regulation of glutamate on [H+] outside of horizontal cells isolated from goldfish retina. Once the horizontal cell is fixed to a dish, a microelectrode measuring [H^+] close and far from the cell is used to determine the flux of H^+ ions from the cell; this process is referred to as self-referencing. Measurement of H+ flux from the cells demonstrated extracellular application of glutamate resulted in an alkalinization outside of horizontal cells. Application of high KCl outside of the cell mimicked the glutamate-induced alkalinization suggesting the change is dependent on depolarization of the cell. Subsequent addition of voltage-gated calcium channel blockers, Co^{2+} or nifedipine, reversed the KCl-induced alkalinization. Collective results from these experiments suggest a depolarization-induced alkalization outside of retinal horizontal cells is dependent on activation of voltage-gated Ca^{2+} channels. This strongly suggests a potential role for horizontal cell-induced changes in extracellular [H+] in regulating synaptic strength in the outer retina.
This work was supported by NSF award 0924383

9. Woodrick S, Bellani R, Pariser E, Ahmed A, Nottebohm F
Department of Neuroscience, Oberlin College

Development of lateralization in the song control circuit of canaries (Serinus canaria)
Many behaviors in humans are known to be lateralized to one side of the brain or the other, but the mechanisms by which lateralization occurs remain largely unknown. Adult male canaries sing their complex learned song with the left hemisphere, reminiscent of the left-lateralization of human language. We screened begging calls, canaries' first vocalizations, to identify when lateralization occurs and then attempt to describe the mechanism underlying this change.
We show that canary vocalizations go from being controlled bilaterally to being left-lateralized between post-hatch days 16 (P16) and 17 (P17). To look for an underlying mechanism of this transition we began by mapping out the connectivity of the main song control nuclei within the avian brain as it develops. First we used Pseudorabies Virus (PRV), a transynaptic retrograde tracer, but found that signal doesn't travel more than one synapse before being innactive. We then used DiI, a passive diffusable fluorescent retrograde and anterograde neural tracer, and found that at P17 a connection is formed from the robust archistriatal nucleus (RA) to nXII, the key motor nucleus in song control (Fig 1). These data suggest a possible role for RA in the process of lateralization of vocalizations. Having confirmed connectivity between RA and nXII at day 17 of life, we wanted to test whether or not activity of these nuclei correlated with the development of connectivity between them. Using Cytochrome Oxidase staining, which correlates with levels of neural activity, we identified activity in nXII, RA, and the High Vocal Center (HVC) in adult male canaries. However, in juveniles, metabolic activity was only above background in nXII. Thus, while telencephalic song nuclei such as RA and HVC may be active and contributing to begging calls, our results suggest that during development these nuclei have low levels of activity.

10. McGuire PW, Herdman GE
Washington and Jefferson College

Behavioral Assessment of Ischemic Muscle Fatigue for use with ASIC3-null Mice

During the initial phase of exercise, an oxygen debt occurs indicating a metabolic demand for ATP and as a consequence of ATP exhaustion the muscle will become fatigued. Because creatine phosphate serves as a critical source of energy during exercise, it has been studied for its role in delaying muscular fatigue. The aim of this experiment was to design a behavioral assay to assess muscular fatigue and then to utilize the assay to determine if there is any significance between creatine monohydrate, creatine ethyl ester and creatine gluconate at delaying muscular fatigue. We constructed a 12 ft. swim lane to induce muscular fatigue during sustained exercise in C57 black-6 mice. After assessing the viability of the assay, we proceeded to analyze the previously mentioned forms of creatine in mice over a period of 8 days. Creatine groups received either creatine monohydrate (0.004mg/g), creatine ethyl ester (0.004mg/g) or creatine gluconate (0.008mg/g to account for molecular weight) via food pellets. Statistical analysis revealed that mice treated with creatine monohydrate had a significantly greater improvement from baseline than controls ($p=0.012$) and had less of an increase in swim time between trials one and fifteen than control mice ($p=0.046$). We now plan to utilize this assay to assess muscular fatigue in ASIC3 deficient mice. The acid-sensing ion channel 3 (ASIC3) is a proton-gated ion channel expressed in sensory neurons including nociceptive neurons and has been suggested to be involved in the perception of pain occurring during acidosis. The ischemic muscle pain associated with muscle fatigue might be attenuated in the mice fed creatine due to decreased lactic acid production, and since ASIC3 has been implicated in detecting ischemic pain, testing ASIC3-null mice might help to determine whether there is a sensory component involved.

11. Gross K & Kronemer SI
Neuroscience Program, Ohio Wesleyan University

Assessment of Spinal Cord Injury in a Guinea Pig Model

Secondary damage after spinal cord injury (SCI) is caused by the body's immune response. Pharmacological therapies that target specific aspects of this response may reduce damage and improve function after injury. By performing assessments of hind limb function before and after injury, the effectiveness of possible treatments can be determined in the guinea pig model. Assessments common to the rat model were tested in the guinea pig model and include contact righting, air righting, and the Photobeam Activity System (PAS) open field. A dorsal laminectomy at thoracic vertebra 12 (T12) was performed on female Hartley guinea pigs followed by compression of the spinal cord to 1.2 mm over a length of 5 mm. Before injury, baseline data was gathered using the new assessments. After injury, at 5 hours, 1, 2, 3, 7, 12, 14, 21 and 28 days, the new assessments along with measures used in previous research (cutaneus trunci muscle reflex, proprioceptive placing response, and toe spread reflex) were performed. When compared to previous assessments, preliminary evaluations show that air and contact righting scores differentiate among levels of injury severity as well as track improvement over the 28 day period. However, the PAS open field appears to be a less useful measure. Future research will include the reevaluation of these assessments, evaluation of additional assessments such as the incline plane, and the development of a scale similar to the rat Basso, Beattie, Bresnahan locomotor rating scale.

12. Midgley KJ, Ford WC, Fader JG, and McWhorter ML
Department of Biology, Wittenberg University

The Effects of Sevin™ Brand Carbaryl Insecticide on Nervous System Development in Zebrafish

Sevin™ brand insecticide is one of the most widely-used insecticides in the United States. Carbaryl is an acetylcholinesterase inhibitor. By seeping into groundwater, carbaryl (the active chemical in Sevin™) has been shown to have teratogenic effects on nontarget species, such as aquatic fish populations. In order to further study the teratogenic effect of carbaryl on nervous system development, zebrafish (Danio rerio), a commonly used vertebrate model system, was utilized. This project utilized the in situ hybridization method to determine how gene expression is affected in nervous system development in the presence of carbaryl by examining gefiltin1 (a neuronal marker) gene expression. Embryos at 24, 36, and 48 hours post fertilization (hpf) were examined for gefiltin1 expression and gefiltin-positive spinal neurons were counted. Results showed that carbaryl treated zebrafish at each embryonic stage had less gefilitin1-positive neurons in the spinal cord than the control. This is the first study to support an altered expression upon carbaryl exposure in the developing nervous system.

13. Yousuf, H
Department Of Neuroscience, The College of Wooster

Importance of Serotonin and Norepinephrine Nerves for Behavioral Effects of Vagal Nerve Stimulation.

Vagal nerve stimulation (VNS) is an FDA-approved form of therapy for treatment of refractory depression. The current treatment of depression is dominated by antidepressants such as SSRI's that target specific nerves in the brain. Although these drugs are effective, approximately one quarter to one third of patients with major depressive disorder are not treated completely. Vagus nerve stimulation (VNS) is used as a treatment for epilepsy and has recently shown promise as an antidepressant. Short-term (c-Fos) and long-term (ΔFos B) biomarkers are used for mapping brain regions where neuronal activation has taken place. Acute VNS significantly increases c-Fos staining in the locus coeruleus (LC) but not in the dorsal raphe nucleus (DRN). Chronic VNS significantly increases ΔFos B and c-Fos staining bilaterally in each region that is affected by acute VNS as well as in the DRN. The basal firing rates in the DRN and LC also significantly increases after long-term treatments with VNS. Short-term treatments of VNS increase firing rates only in the LC. Serotonin and norepinephrine are involved in the pathophysiology of depression and mechanisms of action of antidepressant treatments. The immobility levels of VNS treated animals decreases which can be tested through the forced swim test. The serotonergic pathway is stimulated through the forced swim test whereas the noradrenergic pathway is stimulated through climbing. The research project also includes lesioning of serotonin and norepinephrine producing areas in the brain in order to discover what action or brain process is affected and therefore unaffected by the damaged tissue. The behavior tests included in the project are novelty suppressed feeding and forced swim test. The brains of the Sprague-Dawley rats are collected and divided into two. One half of the brain is used for the sectioning and autoradiography and the other half of the brain is used for Track B phosphorylation. By the end of the summer, the data that I collected included the thionine stained brain slices. The stain helps in locating particular brain regions. Other data was generated from the quantitative autoradiography and the behavior tests.

14. Blake TP, Pucke ER, Kennedy, S
Department of Psychology, Denison University

Effects of Neonatal Social Isolation on Social Play and Anxiety Behaviors in Juvenile Rats Given Methylphenidate

Neonatal social isolation in the rat results in a number of behavioral, physiological, and neurochemical effects, including activation of HPA-axis, and long-lasting sensitization of the mesolimbic dopamine pathway. Behaviorally, early social stress produces less exploration in juvenile and adult periods, increased locomotion as well as heightened fear and anxiety when assessed at subsequent time points (Kosten & Kehoe, 2007; Kehoe, Shoemaker, Arons, Triano, & Suresh , 1998). Early social stress has also been found to decrease social interactions with peers and decrease social play behaviors necessary for subsequent adult social interactions. The present study examined the effects of neonatal social isolation on social play behavior and anxiety in juvenile rats challenged with methylphenidate (MPH) at three time periods throughout the juvenile period. Multiple main effects and interaction effects were observed in congruence with hypotheses showing cross-sensitization of early social stress and MPH leading to a decrease in social play. Specifically, on PN 25-26 ISOL/MPH animals were significantly less likely to socially groom. In addition, at PN 30-31, ISOL/MPH animals were significantly less likely to engage in boxing than rats in the other conditions. Finally, cross-sensitization of social condition and drug was demonstrated at PN 40-41 with ISOL/MPH animals less likely to initiate social play than animals in any other condition. This data from PN 40-41 is particularly notable demonstrates the lasting effects of early social stressors on behaviors assessed late in the juvenile period. Cross-sensitization continued into later periods of development at least for some measures of social and play behavior.

15. Solomon A, Shuss C, Pederson CL
Department of Biology, Wittenberg University

The Effect of Binge Drinking on Hippocampal Volume

Binge drinking is a dangerous habit that can have long-term consequences. The purpose of the experiment was to measure the effects of binge drinking on the volume of the hippocampus. We hypothesized that binge drinking would result in a smaller hippocampal volume due to the reaction with alcohol. Participants were right handed women ages 21 to 32 selected based on similar age, intelligence, pack years smoking and abuse history. None of the women had serious medical issues or more that 5 minutes of trauma induced unconsciousness. Participants had not used illicit drugs for the last 6 months nor had more than 2 alcoholic drinks 3 weeks prior to the MRI scans. The participants were divided into two groups based on drinking history. Binge drinkers were women who consumed 4 to 8 alcoholic beverages in one evening and the control group was composed of non-drinkers. Univariate analysis of variance in PASW program found no significant difference for Wonderlic scores, age, pack years smoking, and average abuse ($p > 0.05$, n.s.). The number of drinks per session was significantly different between binge drinkers and the control group ($F(1, 28) = 293.77$, $p < 0.001$). Univariate analysis found no significant difference ($p = 0.852$, n.s.) between the hippocampal volume of binge drinkers and non-drinkers. The data rejects our initial hypothesis that binge drinking would reduce hippocampal volume and supports the majority of current research that alcohol does not have an effect on hippocampal volume.

16. Mathis J, & Fenster C
Department of Biology, The College of Wooster

Nuclear Translocation of neuronal-interleukin-16 and the regulation of p27kip1 expression in COS-7 cells

Neuronal-Interlukin-16 (NIL-16 full) is a neuronal-specific cytokine precursor expressed only in post-mitotic neurons of the hippocampus and cerebellum, and is the larger splice variant of the NIL-16(-IL-16) gene: NIL-16(-IL-16) serves as a source of the immunoregulatory cytokine, IL-16. Although NIL-16(-IL-16) has well characterized roles in the immune system, less is known about the function of NIL-16(full). Following cleavage and release of mature IL-16, the remaining prodomain of NIL-16(-IL-16) undergoes nuclear translocation and induces cell-cycle arrest. Both NIL-16(full) and NIL-16(-IL-16) share a nuclear translocation sequence; therefore, we hypothesize that NIL-16(full) is also capable of nuclear translocation and may serve to regulate neuronal cell-cycle. Here we test the prediction that NIL-16(full) is capable of translocating to the nucleus. To test this prediction, we transfected COS-7 cells with full-length NIL-16 (NIL-16full) and with the NIL-16 prodomain (NIL-16-IL-16). Cells transfected with the pro-IL-16 prodomain (pro-16-IL-16), which localizes to the nucleus in this cell line the majority of the time (80%), served as a positive control. The localization of NIL-16(full) and the NIL-16 prodomain (NIL-16-IL-16) were visualized using immnocytochemistry and placed into categories of nuclear or cytosolic. Nuclear localization was seen at higher levels for the prodomain of NIL-16 relative to full-length NIL-16. Expression of the cell-cyclin-dependent kinase inhibitor p27kip1, was also higher in cells expressing the prodomain of NIL-16 relative to cell expressing full-length NIL-16 or control (pro-16-IL-16). Results suggest that nuclear localization depends on the cleavage and release of IL-16, as seen for Pro-IL-16. Future studies will address the role of nuclear NIL-16 in regulating cell-cycle.

17. Bowers AN, Brewer JL, and Pederson, CL
Department of Biology, Wittenberg University

Differences in Hippocampal Volumes in a Community Based Sample of Women as Predicted by WMS General Memory Test Scores

Differing hippocampal volumes have been seen as a result of depression, aging, and amnesia, but little research has been done to demonstrate how general memory affects hippocampal volumes. Our participants were right handed women, 20 to 25 years old, with no serious medical problems, no more than 5 minutes trauma induced unconsciousness, and no illicit drug use for the past 3-6 months. Our hypothesis was that women who scored in the lower range (44 – 54) on WMS general memory tests would have smaller hippocampal volumes than women who scored in the higher range (64 – 74) on the WMS general memory tests. We used the MIPAV program to trace the left hippocampi of 30 women (14 from the lower WMS range, and 16 from the higher WMS range). Hippocampi were traced twice, averaged, and summed to give the average hippocampal volume for each participant. Using PASW 18, we determined that there was no significant difference in age, alcohol use, cigarette pack years, or IQ between the two participant groups ($p > .05$, ns). While there were significant differences in WMS scores between the two groups ($F(1, 28) = 251.9$, $p < .001$), no significant differences in brain volumes were found ($p > .05$). This indicates that WMS general memory tests are not good indicators of the volume of the hippocampus in young women. We can reasonably conclude that although memory is linked to the hippocampus, other brain regions are related to memory storage and retrieval as well.

18. Amgott-Kwan A, Paine TA
Department of Neuroscience, Oberlin College

Does Desipramine Block the Effects of Cortical PKA Inhibition on Locomotor Activity?

Attention deficit hyperactivity disorder (ADHD) is characterized by inattention, impulsivity, and hyperactivity. While current treatments (e.g., methylphenidate [RitalinTM], atomoxetine [StratteraTM]) are efficacious, they are also fraught with untoward side effects that can interfere with their clinical utility. The cellular mechanism by which these drugs work is not known. It is known that treatments for ADHD block reuptake of dopamine and/or norepinephrine; both neurotransmitters can increase the activity of cAMP-dependent protein kinase (PKA). Interestingly, decreasing PKA activity in the medial prefrontal cortex (PFC) causes attentional deficits and hyperactivity in rodent models. We hypothesized the clinical efficacy of ADHD treatments lies in their ability to enhance cortical PKA activity. Here, we investigated whether desipramine (DMI, a norepinephrine reuptake inhibitor) administration attenuates the effects of cortical PKA inhibition on either locomotor activity in an open field or cortical activity. Consistent with previous research, intra-PFC infusions of the PKA inhibitor Rp-cAMPS increased locomotor activity. The ability of oral DMI administration to attenuate this effect were ambiguous: rats administered DMI prior to Rp-cAMPS administration did not exhibit significantly more activity than control rats, but also did not exhibit less activity than rats treated with Rp-cAMPS alone. Intra-PFC Rp-cAMPS administration also increased cortical activity (as measured by c-fos expression); this effect was more pronounced in rats co-administered DMI. Irrespective of condition there was a positive correlation between c-fos expression and locomotor activity. Thus, manipulations that reduce cortical activity may be effective in attenuating the hyperactivity caused by cortical PKA inhibition.

19. Shi CR, Emery SB, Lertrit P,& Lesperance MM
Kresge Hearing Research Institute, University of Michigan-Ann Arbor

Connexin 26 mutation posing as maternally inherited hearing loss in a Thai-Laotian family

Hearing loss is a common sensory disability worldwide and frequently has a genetic basis. To date, several mutations in autosomal as well as mitochondrial genes have been found to cause deafness. Here, we report the genetic cause of hearing loss in a family of Thai-Laotian descent. The pedigree of this family and transmission rate of deafness strongly suggested maternally inherited hearing loss, implying a mitochondrial DNA mutation. Following sequencing of the entire mitochondrial genomes of family samples, however, no probable disease-causing mutations were identified. Therefore, GJB2 and GJB6, the most common genes involved in autosomal recessive deafness, were investigated. We discovered a homozygous variant, V37I, in the GJB2 gene of all affected members of the family. No other variants were found in GJB2 or GJB6, suggesting that V37I is the basis for hearing loss in this family. Although the V37I mutation is prevalent among Thai populations, it is nonetheless surprising that two unrelated spouses were also carriers of this mutation, demonstrating pseudodominance. Knowledge of the specific gene mutation responsible for hearing loss in this family allows for more informed genetic counseling and a better understanding of deafness transmission.

20. Theobald SM, Matthews N
Neuroscience, Oberlin College

Visual Hemifields and Perceptual Grouping

Previous researchers have found that manipulation of attention between unilaterally presented stimuli (presented in only one hemifield) and bilaterally presented stimuli (presented in both hemifields) affects discriminability. Whether unilateral or bilateral presentation is superior is determined by the task. In this study, we wanted to further investigate how visual attention, determined by perceptual grouping requirements, affects our perception of visual stimuli presented bilaterally and unilaterally. Twenty Denison University undergraduates completed a visual attention task that required them to respond to visual stimuli consisting of black and white dots spread across four quadrants. For any given stimulus, we asked eight different numerosity-related questions: four sub-lateralities (bilateral; top vs. bottom: unilateral; left vs. right) by two grouping conditions (proximity vs. similarity). The perceptual grouping conditions of similarity (color) and proximity (quadrant) were used so that laterality and grouping anisotropies could be observed by solely manipulating attention and holding the stimulus constant. Participants were told to report whether the number of dots was same or different based on the perceptual grouping and the laterality condition they attended. Participants were measured on dPrime and a significant difference was found in the unilateral case on the similarity task whereas a significant difference was found in the proximity task for the bilateral condition. These differences suggest that the lateralized architecture of our brains imposes specific constraints on attention.

21. Smith, CA, Hood, GR, & Feder, JL
Department of Zoology , Ohio Wesleyan University and Department of Biological Sciences,The University of Notre Dame

Morphological variation between three species of parasitoid wasps attacking apple and hawthorn races of *Rhagoletis pomonella*

Natural selection can favor variation in morphological traits that allow a species to exploit a wide range of environmental conditions. Three host-specific parasitoid wasps (Hymenoptera: Braconidae) attack apple and hawthorn derived host races of the fruit fly *Rhagoletis pomonella* (Diptera: Tephritidae) in the mid-western United States. Two of the parasitoid species, *Diachasma alloeum* and *Diachasmimorpha mellea*, attack larval instars of *R. pomonella* feeding deep within the fruit while a third species, *Utetes canaliculatus,* attacks fly eggs deposited just underneath the surface of the fruit. In the present study we test the following hypotheses: (1) apple-derived parasitoids will have significantly longer ovipositors than hawthorn-derived parasitoids given differences in fruit size and (2) the egg-attacking parasitoid will have a significantly shorter ovipositor compared to larval attacking parasitoids given the life stage of the fly it exploits. Ovipositor lengths of apple- and hawthorn-derived parasitoids from central Michigan, USA, were measured to the nearest µm using a dissecting microscope fitted with an ocular micrometer. Ovipositor length varies between species. Egg-attacking parasitoid ovipositors are >5 times shorter than ovipositors of larval-attacking parasitoids. However, no significant difference was found between host association or the interaction between species and host association. These results are discussed in light of parasitoid (1) niche partitioning, (2) host shifting and race formation and (3) the potential trade-offs between ovipositor-body size and ovipositor-flight capability.

22. Getschow C, Doczy E, Durbin M, Jankord R, & Herman J
Department of Neuroscience, Oberlin College

Distinct Behavioral and Physiological Responses to Chronic Variable Stress in C57 and DBA Mice

Individuals differ in their ability to perform under chronic stress. The long-term purpose of this project is to identify genetic factors that predict an individual's susceptibility or resilience to stress. We hope to identify concrete, objective markers of adaptive and maladaptive responses to stress that will ideally translate to a human model. BXD recombinant inbred (RI) mice result from crossing C57 and DBA parent strains. In this preliminary experiment, we used these two parent strains to examine behavioral and physiological endpoints resulting from a chronic variable stress (CVS) regimen of five weeks. This study confirms the parent strains' significantly different reactions to stress. The next step is to examine the stress susceptibility of 42 genetically distinct strains of BXD RI mice to identify genetic factors that predict this susceptibility.

23. Hammack N, Nam HW, Choi DS
Department of Neuroscience, Oberlin College

PKC Mediated CREB Activity Regulates Ethanol Consumption in Mice Lacking ENT1
Type 1 equilibrative nucleoside transporter (ENT1) regulates adenosine levels and deletion of ENT1 may increase glutamate levels in the striatum. Mice lacking ENT1 exhibit increased resistance to acute ethanol intoxication and consume more alcohol compared to their wild-type littermates. We hypothesized that altered striatal adenosine-mediated glutamate signaling regulates ethanol drinking behaviors. Using proteomic and functional studies, we identified reduced protein kinase C γ (PKCγ)-driven neurogranin (Nrgn) and CREB activity in the nucleus accumbens (NAc) of ENT1 null mice. We investigated the reduced CREB activity using bi-transgenic mice expressing lacZ under the control of CRE elements in an ENT1 null background, and found that this decreased CREB activity is localized to the core region of the NAc. To study the role of PKCγ in regulating this CREB signaling pathway and ethanol consumption, we inhibited PKCγ activity in the NAc using microinjection of PKC inhibitor. Our findings suggest that inhibition of PKCγ in the NAc increases ethanol self-administration through the reduction of CaMKII and CREB activity in wild-type mice. Taken together, our study indicates that reduced PKCγ activity in ENT1 null mice appears to regulate hypo-CREB activity and increased ethanol consumption.

24. McGuire SP, Price RS, & Taheri MA
Neuroscience, Oberlin College

Drugs used to treat neuropsychiatric disorders affect a7 nicotinic acetylcholine receptors
Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels that are pentamers of a and b subunits (a1-10, b1-4)1. nAChRs are expressed throughout the central nervous system (CNS), peripheral nervous system (PNS), and at the neuromuscular junction (NMJ). Binding of ACh or other agonists causes the ion channels to open, allowing influx of cations, and causing membrane depolarization. We focused on a7 nAChRs which modulate neurotransmission in the CNS, including dopaminergic and serotonergic pathways. The goal of our research was to test the hypothesis that these drugs could modulate the activity of a7 nAChRs as part of their pharmacological action. We obtained evidence that bupropion and zimelidine are competitive inhibitors of a7 nAChRs and that fluvoxamine is a non-competitive inhibitor. The administration of gabapentin produced no significant change in channel activity. Thus, the pharmacological actions of some reuptake inhibitor anti-depressant drugs may include a7 receptor blockade.