

1. *IN VIVO* AND *IN VITRO* KETAMINE EXPOSURE EXHIBITS A DOSE-DEPENDENT INDUCTION OF ADNP IN RAT CORTICAL NEURONS

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Ketamine is used as an anesthetic agent when surgical procedures are required for young children. Repeated exposure to ketamine may cause learning disabilities in children (<4 years), likely due to alterations in calcium homeostasis when ketamine binds to N-methyl-D-aspartate (NMDA) receptors. Several studies implicate the activity-dependent neuroprotective protein (ADNP) gene, a putative homeodomain transcription factor, in cell survival following ketamine administration. Additionally, low doses of ketamine administered prior to sedative doses purportedly prevent cell damage. Thus, a possible mechanism for this prophylactic dosage of ketamine may be induction of ADNP. In this study we investigated the use of a protective dose of ketamine *in vitro* and *in vivo* to induce ADNP expression and ameliorate neuronal damage resulting from ketamine exposure. We found that primary cultures of cortical neurons treated with ketamine (10 μ M – 10 mM) at 3 days-in-vitro (3DIV) displayed a dose-dependent decrease in expanded growth cones. Furthermore, neuronal expression of ADNP varied as a function of both ketamine dose and length of exposure. Cells expressing the highest levels of ADNP did not display a significant decrease in expanded growth cones. Immunohistochemistry demonstrated an increase in ADNP expression following a sub-anesthetic dose of ketamine in brain regions previously found to be damaged by repeated exposure to anesthetic doses of ketamine. Administration of low-dose ketamine prior to full sedation prevented caspase-3 activation in certain brain regions. Taken together, these data suggest ADNP induction may be partially responsible for the efficacy of a low-dose ketamine pre-treatment in preventing ketamine-induced cell damage.

2. SPEED VS. EFFICIENCY: THE EFFECTS OF NITRIC OXIDE ADMINISTRATION ON MALE RAT COPULATION

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The medial preoptic area (MPOA), a region located in the hypothalamus, is vital for male sexual behavior. Dopamine, a neurotransmitter whose receptors are located in the MPOA, is released when males are exposed to females and is essential to copulation. Nitric oxide is thought to have neuromodulating effects on dopamine receptors in the MPOA, increasing male rats' sexual performance and efficiency. Upon olfactory exposure to a female rat, male rats experience a

rise in glutamate in the MPOA, which is then thought to increase the amount of nitric oxide production in the MPOA by way of NMDA receptors. We hypothesized that the direct insertion of a nitric oxide promoter, sodium-nitroprusside (SNP), into the MPOA would increase male rat sexual performance similarly to male rats exposed to female odors. We divided rats into the following groups: saline infusion into the MPOA; olfactory exposure to female rats; intraperitoneal (IP) SNP injection; and SNP infusion into the MPOA. Results showed that rats with SNP infusions and rats with olfactory exposure had more intromissions per ejaculation and more ejaculations achieved per session compared to saline infusion rats and IP injection rats. In addition, the average post-ejaculatory interval was highest in saline infused rats as compared to all other groups. These results lead us to believe that nitric oxide in the MPOA does not necessarily aid in all aspects of sexual behavior, but may aid in sexual efficiency.

3. NOVEL ANECHOIC CHAMBER DESIGNED FOR DYNAMIC UNDERGRADUATE RESEARCH IN INTEGRATED NEUROSCIENCE

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Experimental audiology is a developing branch of neuroscience research that integrates physiological and behavioral approaches to study complex neurological problems that manifest auditory disturbances, encompassing disorders such as autism and schizophrenia. Designed for dynamic audio research in the rodent-based valproic acid (VPA) model of autism, this novel and portable anechoic chamber was made for use in testing the behavioral effects of the cortical malformations recently evidenced in VPA-exposed rats. This self-contained anechoic chamber was fabricated with the capability to present auditory stimuli from six different equidistant locations while the organism is performing under a schedule of negative reinforcement. Ease-of-use coupled with the low costs of producing this anechoic operant conditioning chamber provides an accessible way for students to conduct audio-based experiments.

4. THE USE OF SECONDARY ACOUSTIC CUES TO PROSODIC STRESS IN VOCODED SPEECH

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Cochlear implants (CIs) are surgically implanted devices that provide auditory information to individuals with severe hearing impairment. While CIs allow these populations to perceive sound, the information that they provide is severely degraded. One aspect that is specifically affected is fundamental frequency (f_0), the primary cue for prosodic stress in speech. Prosodic stress, or emphasis, is used for a number of communicative functions, one of which is the

introduction of new information in speech. Speakers will typically emphasize new information, while de-emphasizing previously stated information. The current study investigated how well participants detected prosodic stress in vocoded, or CI simulated speech, where f_0 is not available. Adults and five-year-old children were presented with two instructions to move items while their eye movements were measured. Two of the items began with the same syllable, creating a period of ambiguity during the second instruction. If participants used cues to prosodic stress, and the item in the second instruction was emphasized, participants looked to the new, unmentioned item during the ambiguous period. We hypothesized that because f_0 is not available in vocoded speech, listeners would have difficulty recognizing prosodic stress. We found that while adults are better at understanding vocoded speech in general, both children and adults were able to perceive prosodic stress in vocoded speech. These data suggest that the ability to switch to alternative cues to prosody emerges early in development, and advanced cognitive resources may not be necessary.

1. CONSCIOUS NATURE

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I investigated the effects of educational background (i.e., academic major and number of classes in scientific and non-scientific fields) on beliefs regarding consciousness. I hypothesized that students with scientific backgrounds would have more materialistic and restrictive views about consciousness than those with nonscientific backgrounds. Forty nine undergraduates from a small Midwestern university participated in a 27-item survey designed to assess beliefs about consciousness in a variety of dimensions including the relation of consciousness to the brain; what mental states (sleeping, dreaming, or coma) constitute consciousness; and who or what can be conscious. 19 participants were science majors and 34 were non-science majors. Consistent with hypotheses, students with educational backgrounds in the sciences were more likely to believe consciousness is all or nothing, $r = .41, p = .004$. Specifically, as the amount of science classes increased, participants were more likely to disagree that infants under the age of one year are conscious, $r = -.33, p = .023$, and that toddlers between the ages of one and three are conscious $r = -.41, p = .004$. However, educational background did not predict belief in other areas assessed, such as being conscious while in a coma or while anesthetized, all $rs < -.25, ns$. Implications, limitations, and directions for future research will be discussed.

2. THE EFFECTS OF TACTILE STIMULATION ON REACTION TIME TO AN AUDITORY STIMULUS AND BRAINWAVE ACTIVITY

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Experiments consisting of two or more stimuli have recorded longer reaction times than those without, as the brain must decipher more information and make the correct motor response (Abrams and Balota, 1991). When multiple stimuli are presented to a participant, the brain cannot register the stimuli until the prefrontal cortex integrates them through selective-attention mechanisms (Töllner, et al., 2012). In cases where the stimuli affect different senses, such as sight and audition, response selection occurs (Abrams and Balota, 1991). This study sought to find the differences in gender regarding reactions to tactile distractions. Twenty-five university students, 14 males and 11 females, were asked to respond to stochastic auditory stimuli. A baseline without any tactile stimulation was set, followed by three trials, in random order, of a varying isochronic water drip rate on the dominant forearm of the participants, proximal to the wrist. Reaction times and EEG data were recorded using Biopac

software and statistical analyses were conducted with Minitab. Significant decreases in reaction time were found when looking at the intermediate ($t=-2.23$, $p=0.036$) and fast ($t=-2.32$, $p=0.30$) drip rates compared to the set baseline. No correlations were found between reaction times and the amplitude of alpha, theta, or delta brain waves ($p>0.05$). There were no significant differences in reaction time or EEG brainwaves based on gender during experimental conditions ($p>0.05$). The presence of the intermediate or fast drip rate decreased reaction times of both men and women, but did not affect brainwave amplitude.

3. ATTENUATION OF SECONDARY SPINAL CORD INJURY BY METHYLPREDNISOLONE AND 6-CL TRYPTOPHAN

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Spinal cord injury is a prevalent problem in the US, affecting over one million people. In addition to the primary trauma, a process known as secondary injury further contributes to tissue damage. Immune response plays an important role in this process, specifically lipid peroxidation and quinolinic acid (QUIN) production. Both of these processes lead to death of neurons and myelin surrounding the injury. Previous research has shown effective drug interventions using 6Cl-Tryptophan and Methylprednisolone (MP), albeit separately. 6Cl-Tryptophan decreases the production of QUIN by interrupting its synthesis pathway; while MP acts as an antioxidant. Due to these drugs working on different mechanisms, our goal was to explore the possibility that they have additive effects on behavioral and structural deficits. A dorsal laminectomy at thoracic level 12 and lateral compression for 15 seconds was performed on female Hartley guinea pigs. Behavioral evaluations of both sensory (*Cutaneous Trunci* muscle reflex) and motor function (toe spread; proprioceptive placing) were used to assess injury over a twelve-day period post-injury. Results were inconclusive and more trials will be needed to determine if there is an additive effect between these drugs.

4. FACILITATION OF HABIT-LEARNING BY POST-TRAINING INFUSION OF COCAINE INTO THE INFRA LIMBIC CORTEX

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Many addictive drugs facilitate release of dopamine in the basal ganglia, and drug addiction may involve the recruitment of brain systems that support habitual behaviors. Work with operant tasks has shown that relative to natural rewards, rats develop habits for actions rewarded with drugs such as cocaine and alcohol. Using post-training injections of cocaine, our lab has shown that cocaine can act directly to facilitate habit learning, and that the infralimbic

cortex is required for habit facilitation by cocaine. The present study addressed if cocaine infusion directly into the infralimbic cortex was sufficient for the facilitation of habit learning. Twenty seven Sprague-Dawley rats were implanted with bilateral cannula targeting the infralimbic cortex. Rats were trained after surgery to perform two actions (lever pressing) which were rewarded with either grain or sucrose flavored pellets. After acquiring both lever presses, rats received three training sessions on each lever, rewarded on a random interval 30 second schedule (RI-30s). After each RI-30s training session, rats received infusions of cocaine (200 mg/mL) or vehicle. Using sensory-specific satiety, extinction tests revealed that for the lever paired with cocaine infusions, lever pressing was not sensitive to devaluation of the reward while the lever paired with saline injections were sensitive to devaluation. These data suggest that drugs such as cocaine can act directly during memory consolidation in brain areas required for habitual behavior in order to facilitate habit learning.

5. A LUTENIZING HORMONE INHIBITOR AMELIORATES OBJECT RECOGNITION DEFICITS IN A RODENT MODEL OF SCHIZOPHRENIA

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Schizophrenia is a debilitating disease. Although a good functional outcome for a schizophrenic patient is best predicted by his or her degree of cognitive impairment, existing treatments fail to adequately reverse cognitive symptoms. Therefore new treatments are needed. Recent research has shown that estradiol may help alleviate cognitive symptoms in both human female schizophrenics and in animal models of schizophrenia. Thus, the purpose of this experiment was twofold: First, to replicate an experiment showing that estradiol treatment attenuates cognitive impairment in a rat model of schizophrenia. Second, as estradiol is known to have negative feedback effects on the release of luteinizing hormone (LH), we sought to determine if inhibiting LH levels would also alleviate the cognitive impairment. Female rats were ovariectomized to control hormone levels. The animals were then implanted with either a blank or estradiol-filled silastic capsule. Rats were subsequently injected with either vehicle or the N-Methyl-D-Aspartate receptor antagonist Phencyclidine (PCP: 2mg/mL/kg bidaily, 7d), which produces an animal model of schizophrenia. Cognitive functioning was assessed with the Novel Object Recognition Task, which measures recognition memory in the rat. Consistent with previous studies, estradiol reversed object recognition deficits induced by PCP. Moreover, a single, acute dose of the LH-inhibiting drug Antide given six hours before testing achieved the same effect. These results suggest that the beneficial effects of estradiol treatment may be due to LH inhibition, and that

LH inhibition may offer a viable and fast-acting treatment for at least a subset of the cognitive symptoms associated with schizophrenia.

6. THE RELATIONSHIP BETWEEN SELF-DEFEATING PERSONALITY DISORDER AND AMYGDALA VOLUME IN WOMEN

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Self-defeating personality disorder is characterized by consistently refusing help, pleasure, and knowingly engaging in activities that will invoke some degree of suffering, but without previous diagnosis of depression or awareness that the behavior is self-destructive. Studies have shown decreased amygdala volume in psychiatric disorders including bipolar disorder, schizophrenia, and severe depression. Self-defeating personality disorder shares symptoms with these, yet has not been investigated for a relationship with any discrete brain areas. MRIs of 35 right-handed women ages 19-40 were selected from a larger database. The women were divided into two groups: 15 had scores on the MCMI consistent with self-defeating personality disorder and 20 were normal controls. By design, there were no significant differences in age, intelligence, and alcohol or tobacco use ($p > .05$). Using the MIPAV program, the left amygdala of each woman was traced twice from MRI images, averaged, and the total volume calculated. An univariate analysis of variance revealed a significant difference between groups for self-defeating personality disorder ($F(1,34)=3558; p < .001$), but not in left amygdala volume ($p > .05$). The data showed no significant relationship between self-defeating personality disorder and left amygdala volume. These results suggest that self-defeating personality disorder does not manifest with the same neurological markers as other more definitive disorders do, such as bipolar disorder, despite sharing symptoms.

7. IN VIVO AND IN VITRO ANALYSIS OF THE AMINO ACID LYSINE AS A POSSIBLE INHIBITOR OF HSV-1 INFECTION

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HSV-1 is one of the most commonly encountered of all human pathogens and it has also been associated with neurological diseases such as Alzheimers and idiopathic Parkinson's syndrome. HSV-1 Infections can be treated with the prescription acyclovir, but a common homeopathic treatment for an HSV-1 infection is the over the counter supplement lysine. Using Vero cells and Zebrafish (*Danio rerio*) the effect of lysine on HSV-1 infections was analyzed. Licorice root extract (*Glycyrrhiza glabra*) is also being analyzed *in vivo* and *in vitro* because of its known antiviral activity against SARs virus and hepatitis C. Although the modes of action of these molecules are unknown, *in vitro* analysis of the amino acid lysine showed nearly a log reduction of typical viral plaques

and licorice root extract (*Glycyrrhiza glabra*) showed a log reduction in plaques. Zebrafish are now being analyzed as a organism model for infection and treatment with lysine and *Glycyrrhiza glabra*.

8. THE EFFECTS OF AGE ON CEREBELLUM VOLUME IN WOMEN AGES 20-39

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The aim of this study was to investigate the effects of age on the volume of the cerebellum in a relatively young sample of women. Longitudinal studies show decreased volume of the cerebellum with age. This study selected 24 participants out of a database of 80 women and divided into two groups based on age. There was a significant difference in age between groups in which participants were between the ages of 20 and 21(n=12) and between the ages of 30-39 (n=12; $F(1, 23) = 231.1$; $p < .001$). By design, there was no significant difference between groups in the number of alcoholic drinks per year, pack years smoking, total joints of marijuana smoked, average abuse, or intelligence as judged by Wonderlic Personnel Test ($p > .005$). MIPAV software was used to trace and measure the volume of each participant's cerebellum in horizontal section. The younger group had significantly smaller cerebellar volume than the older groups ($F(1,22) = 6.801$; $p = 0.016$), which is contradictory to our hypothesis and to previous research. The significance of this result in our small study is unknown. The main limitations were a small gap of years between the two ages, as well as only having 24 participants in the study. Further studies with more participants and a gap of at least 20 years between the two groups would be suggested to strengthen the reliability of the results.

9. THE EFFECTS TRAUMA AND POST TRAUMATIC STRESS DISORDER ON PONS VOLUME IN A COMMUNITY BASED SAMPLE OF WOMEN

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The purpose of this study was to observe the effects of trauma and Posttraumatic Stress Disorder (PTSD) on the volume of the pons. Parallel studies have shown a significant decrease in serotonin levels from the raphe nucleus of the pons after trauma which may indicate a decrease in pons volume. Forty-five female participants were divided into three groups: 16 participants developed PTSD secondary to childhood abuse, 14 participants suffered significant trauma without developing PTSD, and 15 participants were controls with no history of trauma or PTSD. No significant differences were found between groups in the number of alcoholic drinks per year, packs years smoking, intelligence by the Wonderlic Personnel Test, or age ($p > .05$). MIPAV software was used to trace and measure the volume of the each participant's pons in sagittal section. Univariate analysis of variance revealed no significant

difference in volume of the pons between the three groups ($p>0.05$), indicating that abuse and PTSD may not affect pons volume and that the results were contradictory to the hypothesis. Perhaps the changes in serotonin levels from the raphe nucleus do not indicate overall volumetric change of the pons in women with PTSD compared with controls.

10. RACIAL DIFFERENCES IN VISUAL FUNCTION AND OCULAR BLOOD FLOW IN PEOPLE WITH HEALTHY EYES

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People of African descent (AD) are disproportionately affected by primary open-angle glaucoma (POAG), a progressive age-related visual disease that causes irreversible visual loss. We sought to determine whether differences in visual function (VF) and ocular blood flow (OBF) exist between people of AD and European decent (ED) with healthy eyes. One eye of each of 68 subjects (25 AD, 43 ED) with healthy eyes based on a complete ocular examination was included. VF was measured using Standard Automated Perimetry (SAP), Short-Wavelength Automated Perimetry (SWAP) and Frequency-Doubling Technology (FDT) perimetry. Each test targets a sub-population of retinal ganglion cells. OBF was measured using the Color Doppler Imaging (CDI) in the ophthalmic artery (OA), central retinal artery (CRA), nasal (NPCA) and temporal posterior ciliary arteries (TPCA). Racial differences in OBF were assessed using peak systolic velocity (PSV), end diastolic velocity (EDV) and resistive index (RI). While no racial differences were found in VF (all $p>0.05$), trends indicated worse sensitivity in people of AD for each test. Significantly lower PSV was observed in the OA ($p=0.02$) in people of AD and lower EDV was observed in the OA ($p=0.01$), NPCA ($p=0.03$), and TPCA ($p=0.02$) in people of AD. Significantly higher RI was observed in people of AD in the CRA ($p=0.01$) and NPCA ($p=0.01$). The results of this study show a trend towards worse performance in VF and worse OBF in people of AD compared to people of ED, suggesting a possible association between OBF and VF.

11. SOCIAL INFLUENCES ON ANXIETY-LIKE BEHAVIOR IN ZEBRA FINCHES

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Zebra finches are sexually-dimorphic songbirds. One of the most prominent sexual dimorphisms exhibited in these birds is in singing – males sing and females don't. Females use male songs to select mates. These behavioral characteristics have lead to a vast number of studies in these birds, and have made them an excellent model for investigating many different psychobiological processes. These include vocal learning, memory, auditory

perception, and mate-choice. These studies have greatly enhanced our understanding of neuroendocrinology, developmental neurobiology, functional neuroanatomy, sensory processing etc. Zebra finches have recently been proposed as a new model for studying anxiety (Kingsbury & Goodson, 2013; *Hormones & Behavior*). In this experimental paradigm, zebra finches' natural tendency to be phobic to novel stimuli is exploited to elicit novelty-induced feeding suppression (NIFS). This NIFS is used as an indicator of anxiety. In the present study, we individually housed male zebra finches in visual and acoustic isolation from other birds, and calculated their base-line latency to eat after lights turn on in the morning. After calculating baseline latency for several days, we induced NIFS by introducing a foreign object in their food-bowl after lights in their booths turned off. An increase in latency to eat, after the introduction of the foreign object was used as a measure of anxiety. We will present data that supports this new model of anxiety, and examine social influences on anxiety in male zebra finches.

12. SONG DISCRIMINATION LEARNING IN ZEBRA FINCHES

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Zebra finches are sexually-dimorphic songbirds. One of the most prominent sexual dimorphisms exhibited in these birds is in singing – males sing and females don't. Males sing to attract mates, and females use male songs to select mates. Although females don't sing they learn the song, as indicated by their preferences for males that sing songs similar to their fathers/tutors. One of the issues we are interested in investigating is whether this sexual dimorphism in singing, and song function is reflected in sexual dimorphism in song perception. Using an operant conditioning paradigm, we first trained zebra finches to discriminate between songs of several different males. We found that there was no sex difference in song discrimination learning. Each male sings just one song with minimum variability between different renditions. We next tested their ability to discriminate between highly similar renditions of the same song. All males and females successfully learned to discriminate between these highly similar renditions of the same song, and there were no sex differences in this ability. In both these tasks, there was more variation within males and within females than between males and females. Several studies have indicated that males' success in attracting mates is correlated with their ability to learn their tutors' song. Interestingly, we found that males' ability to learn song discrimination is related to their ability to learn their fathers/tutors songs.

13. CHANGES IN SODIUM CHANNEL EXPRESSION DURING SPINAL CORD REGENERATION IN LAMPREY

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There are ~259,000 cases of spinal cord injury (SCI) per year in the U.S. Decreased quality of life, low chances of full recovery, and healthcare costs of \$1 million per person per year, make SCI a devastating ailment. Finding better treatments for SCI is essential. Lampreys are vertebrates that exhibit spinal cord regeneration, allowing them to swim almost normally 10-12 weeks after complete spinal transection. New knowledge on how lamprey spinal neurons regenerate and reconnect could help identify targets and mechanisms for improved recovery from SCI in humans.

Voltage-gated sodium channels (NaV) are ion channels that allow neurons to create and propagate action potentials, the basic units of information coded and communicated in the nervous system. Although NaV are required for neuronal function, excessive NaV activity after injury could cause hyperexcitability and excitotoxicity that can kill neurons. Lampreys that are recovering from SCI are resistant to NaV blockers, suggesting that the expression of NaV is changed. Hence, changes in NaV expression may be a part of the mechanism by which lamprey spinal neurons survive and regenerate after SCI.

The goal of this study was to determine NaV expression in uninjured and transected lamprey spinal cords. We used immunofluorescence microscopy to visualize NaV in spinal cord sections. We observed specific labeling of axons in control sections and lower overall labeling with no specific axonal labeling in sections from transected spinal cords. Although not conclusive, these data provide evidence of decreased expression of voltage-gated sodium channels in regenerating lamprey axons.

14. EXAMINING BEHAVIORAL EFFECTS OF KETAMINE AND MATERNAL SEPARATION IN RATS: A PILOT STUDY

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I tested the efficacy of a novel two-stressor schizophrenia model which aimed to produce a broad array of negative symptoms in hopes of furthering understanding of both their causes and possible treatments. This two stressor model combined maternal separation (P 6-18) and neonatal ketamine exposure (P 7, 9, and 11). Independently, these treatments have been known to produce abnormal social interactions, various learning and memory deficits, hyperlocomotion and neophobia (Becker et al., 2003; Chen & Wang 2010; De Hoz, Moer, & Morris 2005; Garner et al., 2007). Once weaned, rats were raised

in and enriched environment and tested on their social interaction behavior with a standard social interaction test. Rats were then tested on spatial learning in a Morris water maze, where they were trained to find a platform in less than a minute over a series of 16 trials. Finally, discriminative odor pair learning abilities were assessed using scented sand, one of which was consistently baited with a food reward. Of the tests, only the social interaction behaviors yielded significant differences between the groups, indicating some degree of model efficacy. The similarities between experimental and control group's performance on the water maze may be indicative of the modulatory effects of environmental enrichment on the treatment, which will be further investigated in the full study. Similarly, odor pair learning abilities in both groups indicate that further tests on transitive inference in the rats will be a result of a deeper cognitive abnormality and not merely a learning deficit.

15. ANXIOLYTIC DRUGS AND ALTERED HIPPOCAMPAL THETA RHYTHMS: THE QUANTITATIVE SYSTEMS PHARMACOLOGICAL APPROACH

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A common effect of various types of drugs that reduce behaviors characteristic of anxiety is the reduced frequency of a slow oscillatory activity called hippocampal theta rhythm. The frequency of hippocampal theta rhythm increases linearly with the intensity of electrical stimulation to a region of the brainstem. The reduction of mean frequency and the slope of this linear relationship between stimulation intensity and theta frequency predicts the clinical efficacy of anxiolytic drugs.

The purpose of this research was to investigate the mechanisms by which anxiolytics produce this characteristic effect on the slope and intercept of the stimulus-frequency relationship of hippocampal theta. A network of neuron populations that generates theta rhythm called the septo-hippocampal system was modeled by approximating patches of neural membrane and synapses as resistor-capacitor circuits with biophysically realistic dynamics using the neural simulator software GENESIS. The capability of synaptic and cellular parameters to control the frequency of theta rhythm in this complex network of interconnected circuits was investigated to model the membrane-level effects of potential anxiolytics.

Results suggest that anxiolytics can act on the ratio of excitatory to inhibitory synaptic decay time constants in the septo-hippocampal system to reduce mean theta frequency and the slope of the stimulus-frequency relationship. Preliminary results also suggest that blocking hyperpolarization-activated channels in pyramidal neurons can reduce theta frequency. This knowledge can be used to advance the discovery of drugs that target the septo-

hippocampal substrate specific to anxiety disorders and thus involve fewer side effects such as sedation and depression.

16. DEVELOPMENT OF AN IMMUNOHISTOCHEMICAL ASSAY TO DETECT CELL PROLIFERATION DEFICITS IN THE DENTATE GYRUS OF RATS AFTER SUBCHRONIC PCP TREATMENT

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Schizophrenia affected roughly 24 million people in 2011, yet treatments for neurological symptoms are often inadequate and poorly understood. One hypothesis is that the hindered capacity of the adult brain to undergo neurogenesis may play a role in producing schizophrenic symptoms. The present studies used the subchronic Phencyclidine (PCP) animal model of schizophrenia, a model that accurately produces long-term schizophrenia-like symptoms. First, an assay was developed to detect Ki67, a nuclear protein that is a marker for cell proliferation due to its presence throughout the cell cycle. Second, we examined whether the effect of subchronic PCP on cell proliferation can still be measured after PCP has been cleared from the body.

To validate the assay, four Ki67 antibodies were tested. Three antibodies from AbCam were unsuccessful, while Novocastra Ki67p-CE rabbit polyclonal yielded results consistent with previous literature. A dilution curve with Novocastra Ki67p-CE was performed at concentrations of 1:500, 1:1000, 1:5000, and 1:7000 - the most effective result was obtained with 1:7000 and antigen retrieval. To investigate the duration of PCP action on cell proliferation, adult rats were ovariectomized, injected with either vehicle or the N-Methyl-D-Aspartate receptor antagonist PCP (2mg/mL/kg bidaily, 7d), and allowed to recover for 2, 4, or 7 days before sacrifice. When allowed 2 days recovery, PCP-treated animals showed deficits in hippocampal cell proliferation compared to controls. Cell proliferation deficits in animals allowed further recovery were less marked. Treatments specifically targeted to address cell proliferation deficits in this schizophrenic model are currently being tested.

17. INHIBITION OF PEPTIDYL CITRULLINE EXPRESSION IN *DANIO RERIO* BY 2-CHLOROACETAMIDINE

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Myelination is the acquisition, development, and formation of a myelin sheath around an axon or nerve fiber. It has been proposed that myelin damage in the white matter of individuals with multiple sclerosis results from a failure to maintain compact adult myelin, resulting from abnormally enhanced citrullination of myelin basic protein. Peptidyl arginine deiminases (PAD) catalyze a post-translational protein modification known as citrullination. The focus is on the distribution of PAD throughout the central nervous system

(CNS). During citrullination, an arginine is converted to citrulline, and one positive charge is lost between the charged arginine side chain to the neutral citrulline side chain. This modification has been linked to the pathogenesis of autoimmune diseases including multiple sclerosis, Alzheimer's disease, and rheumatoid arthritis. 2-Chloroacetamide (2CA) is a small-molecule, PAD active-site inhibitor. 2-CA was used to determine the amount of citrullination in the CNS of larval zebrafish. Zebrafish were exposed to various concentrations of 2-Chloroacetamide in order to produce a dose-response curve and compare effects of the different concentrations. Zebrafish embryos were exposed to 2-CA (5.3 μ M, 3.0 μ M, and 0.05 μ M) for 24 hours following spawning. The results with antibody are variable. The citrullination appeared to be important due to defects in the embryos. 5.3 μ M were non-viable and the 0.05 μ M were viable. However, 3.0 μ M embryos were viable but distorted, forming a consistent phenotype. It is possible that 2-CA is toxic independent of its ability to inhibit the PAD enzyme. Further analysis is being completed to test various concentrations of inhibitor and its effect.

18. GABAB RECEPTOR AGONISTS AND ANTAGONISTS IN MEDIAL PREFRONTAL CORTEX DO NOT AFFECT ATTENTION OR DECISION MAKING

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Introduction: Schizophrenia is a debilitating mental disorder that affects about 1% of individuals worldwide; symptoms typically appear during early adulthood. The first category of symptoms to emerge are cognitive symptoms, which include deficits in attention, decision-making, and other executive functions, known to be controlled, at least in part, by the dorsolateral prefrontal cortex (DLPFC). Postmortem studies suggest that γ -aminobutyric acid (GABA) transmission is reduced within the DLPFC. Previously, we have tried to determine whether reducing GABA transmission in the rodent PFC is sufficient to cause cognitive deficits. Curiously, we have found that acutely blocking GABA_A receptors, but not GABA synthesis, causes deficits in attention and decision-making. It is hypothesized that the discrepancy in these results may be due to the regulatory role of metabotropic GABA_B receptors.

Methods: Rats were trained on the 5-choice serial reaction time test (5CSRTT), which measures sustained attention, or the rodent gambling task (rGT), which measures decision-making. Rats were tested following intra-PFC infusions of either GABA_B receptor agonist baclofen or one of the GABA_B receptor antagonists CGP55845 or CGP35348. It was hypothesized that baclofen would impair cognition, while the GABA_B antagonists would enhance cognition.

Results: Measures of attention or decision-making were not affected by the GABA_B receptor ligands.

Conclusions: Although GABA_B receptors do not appear to affect either attention or impulse control, it is possible that insufficient drug doses were used. Nevertheless, it appears that GABA_B receptor signaling does not explain the discrepancy in our previous findings following reductions in GABA transmission.

19. NEONATAL EXPOSURE TO KETAMINE PRODUCES BEHAVIORAL DEFICITS IN PREPULSE INHIBITION

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The NIH currently recognizes that young children exposed to general anesthetics during surgery are at risk for brain injury leading to cognitive and behavioral efficiencies later in life (Wilder et al., 2009). Specifically, neuronal injuries induced by exposure to general anesthetics may produce deficits in auditory processing. Therefore, pre-pulse inhibition (PPI) was employed to further explore the associated cognitive and behavioral effects of post-natal exposure to partial NMDA receptor antagonists, MK801 and ketamine. MK801-induced apoptosis was found in the inferior colliculus, which is necessary for acoustic processing. In addition, a delayed response to prepulses in PPI was identified on post-natal day 56 (P56) (Lyll et al., 2009). In order to determine if ketamine, a NMDA receptor antagonist similar to MK801, induced similar injury to the inferior colliculus, rat pups were injected with ketamine (50 mg/kg; N=2), MK801 (1 mg/kg; N=3), or saline (N=3) on P7. Neonatal rats were tested every day from P1 until P21 on behavioral milestones designed to track their neurological development. In addition, PPI testing was conducted once per week from P8 through P28 to determine the effect on their acoustic startle reflex. PPI testing revealed ketamine-treated neonates demonstrated a 45.8% decrease in peak amplitude in response to pulses compared to controls on P21. Also, ketamine and MK801-treated neonates demonstrated a 34.2% (ketamine) and 28.8% (MK801) decrease in average amplitude compared to controls on P21. Therefore, there is evidence to support acoustic startle reflex deficiencies due to ketamine exposure.