UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 16, 2014 Mary Gates Hall

Online Proceedings

Poster Session 1

Commons East, Easel 45

11:00 AM to 1:00 PM

Maturation of Nanodiscs to High Density Lipoprotein-Like Particles via Lecithin-Cholesterol Acyl Transferase

Chinonso C (Chinonso) Opara, Senior, Biochemistry
Amgen Scholar, McNair Scholar, UW Honors Program
Mentor: William Atkins, Medicinal Chemistry

High Density Lipoprotein (HDL) particles are spherical structures, which play a fundamental role in the reverse cholesterol transport (RCT) pathway, where cholesterol is carried to the liver for excretion. Apolipoprotien (Apo) A-1 is the primary protein component of HDL and plays a critical role in the RCT pathway. As lipid and cholesterol are transported from cells, they are encircled by Apo A-1, forming discoidal pre-ß-HDL particles, which subsequently undergo cholesterol-dependent maturation via Lecithin-Cholesterol Acyl Transferase (LCAT), forming spherical HDL. Man-made HDL or reconstituted HDL (rHDL) have many applications in nanotechnology, including cellular delivery of antigens and small interfering RNA. However, the large size distribution of HDL made from full length Apo A-1 raises difficulties in relation to drug delivery variability. Currently, I am using shorter constructs of Apo A-1 lacking the N-terminal globular domain as a membrane scaffold protein for nanodiscs – which resemble pre-ß-HDL particles, but differ in their more uniform size range (˜3%). We hypothesize that treatment of nanodiscs containing cholesterol with LCAT will result in spherical HDL-like particles with a more narrow size window. We have demonstrated that LCAT-mediated maturation of cholesterol-containing nanodiscs yields HDL-like particles. This reveals that the N-terminal region is not necessary for maturation. Next, I aim to optimize experimental conditions for generating HDL-like structures and characterize their polydispersity via analytical ultracentrifugation. The insight gleamed from this study will establish a base line for using matured nanodsics as drug delivery vehicles with a uniform size range.

Poster Session 1

Commons West, Easel 42

11:00 AM to 1:00 PM

Tbr1 in the Developing Mammalian Cortex

Kevin Neuzil, Senior, Neurobiology
Mentor: Curtis Easton, Biology
Mentor: William Moody, Biology

The mammalian cortex is composed of excitatory and inhibitory interneurons which regulate the firing of action potentials in the brain. Excitatory neurons increase the likelihood of an action potential in other cells while inhibitory neurons decrease this probability. Excitatory transmission develops first, resulting in electrical activity in the form of waves, which are important in the formation of neuronal circuit formation until the development of inhibition shuts down this spontaneous activity. While excitatory and inhibitory neurons are born in different locations in the brain, those that are born on the same day of development migrate and find each other in the same cortical layer. Excitatory neurons originate in the dorsal ventricles and migrate radially towards the plial surface. Inhibitory cells originate from the medial ganglionic eminence and migrate tangentially to the cortex where they then migrate radially to find their correct cortical layer. This project explores the idea that spontaneous electrical activity helps drive this organization. Tbr1 is a transcription factor shown to be important in neuronal layer finding. By using a Tbr1 KO (knockout) mouse, we show the disorganization of the neocortex compared to normal mice by quantifying the fraction of radially oriented interneurons versus non-radially oriented interneurons. Further, we examine the implication that waves and asynchronous electrical activity play a role in layer finding of excitatory and inhibitory neurons, as demonstrated by the differences in activity between Tbr1 knockout mice and controls.

Session 1G

Gender, Societal Expectations, and Health

Session Moderator: Judith A Howard, Sociology

242 MGH

12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Sex-related Drinking Motives as Mediators between Women's Sexual Victimization History and Both Alcohol Consumption and Sexual Risk-Taking

Madeleine (Maddy) Gauger, Senior, Psychology
UW Honors Program
Mentor: William George, Psychology
Mentor: Cynthia Stappenbeck, Psychiatry and Behavioral Sciences
Mentor: Kelly Kajumulo, Psychology

Women with a history of sexual victimization often have higher rates of alcohol consumption and sexual risk-taking than women with no history of sexual victimization. One explanation proposed for these associations is the self-medication hypothesis which says that women with sexual victimization histories engage in drinking and risky sexual behavior to cope with distress or to increase positive affect. Although popular wisdom and research studies link alcohol and sexual risk-taking, sexual assault victims often experience difficulty with sexual intimacy. Specific motives to consume alcohol in order to cope with or further enhance sexual behaviors have not been examined. Further, it is not known how a history of sexual assault would impact sex-related drinking motives and whether these motives would mediate the association between sexual assault history and both alcohol consumption and risky sexual behavior. We are currently in the process of recruiting undergraduate women through the University of Washington Psychology Department's Online Subject Participation Pool. Women are asked to complete a forty-five minute online survey about their drinking patterns, history of sexual experiences and sexual assault, and endorsements of sex-related drinking motives. Data collection will be complete at the end of winter quarter, after which we will conduct mediation analyses using bootstrapping to test our hypotheses that sex-related drinking motives will mediate the relationship between a history of sexual victimization and both alcohol consumption and sexual risk-taking. We expect that these motives will partially mediate the relationships between a history of sexual victimization and both alcohol consumption and sexual risk-taking. Results will help inform effective interventions tailored toward survivors of sexual assault.

SESSION 1M

NEURONAL PLASTICITY

Session Moderator: John Neumaier, Psychiatry
284 MGH
12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

The Role of Calcium Signaling in the Development of Cortical Interneurons

Charles William (Charlie) Dickey, Senior, Digital Arts & Experimental Media, Neurobiology
Mary Gates Scholar, UW Honors Program,
Undergraduate Research Conference Travel Awardee
Mentor: William Moody, Biology

Waves of synchronous spontaneous electrical activity propagate throughout the cerebral cortex of the brain during early stages of development. These waves consist of simultaneous action potential firing across large cell populations, with correlated increases in cellular calcium levels. Specific types of calcium signals mediate different developmental processes in the brain. While calcium signaling is known to regulate activity-dependent developmental programs that help to form essential connections between neurons, the particular function of spontaneous waves in cortical development is unclear. As many types of neurons participate in these waves in the cortex, it is possible that waves serve developmental roles that differ among neuronal subtypes. In this study we investigate the roles of spontaneous waves in the development of one neuronal subtype – inhibitory interneurons. At the time of wave expression, the last interneurons are migrating into the cortical plate and finding their appropriate layer within the cortex. To label inhibitory interneurons we use red fluorescent protein (RFP) under control of the dlx5/6 promoter region to label these cells, and a green calcium indicator to measure single cell activity of these interneurons. By imaging the red and green wavelengths and then analyzing the data, I have found two types of cortical interneurons: (1) Those that participate with other neurons in spontaneous waves; this type of activity is insensitive to blockers of L-type calcium channels, and (2) Those that do not participate in waves but do generate asynchronous activity between waves; this asynchronous activity is blocked by L-type calcium channel blockers. I am now testing the hypothesis that interneurons switch from asynchronous activity to participating in wave activity when they stop migrating and find their appropriate positions within the cortex. Such a finding would indicate a role for waves in determining the layer location of interneurons in the cortex.

POSTER SESSION 2

Balcony, Easel 108
1:00 PM to 2:30 PM

Experimental Evidence that Women's Victimization History, Alcohol Consumption, and Partner Relationship Potential Influence Perceptions of Risky Sex

Brittany Christine (Brittany) Allen, Recent Graduate,
Mentor: Cinnamon Danube, Psychiatry and Behavioral Sciences
Mentor: William George, Psychology
Mentor: Kelly Kajumulo, Psychology, Social Work
Mentor: Kelly Davis, Social Work

Research indicates that alcohol consumption and sexual victimization history, separately, are related to women's increased unprotected sex risk. An additional question is whether partner relationship potential (i.e., likelihood of having a romantic relationship) interacts with victimization history and alcohol consumption in their association with risky sexual behavior. Participants were 436 female heavy episodic drinkers, aged 21-30, at elevated risk for sexually transmitted infections. They completed background questionnaires that assessed sexual victimization and an alcohol administration protocol (control or BAC=.10). Next, they projected themselves into a hypothetical sexual scenario, which manipulated relationship potential (high or low) with the man in the story. Following the scenario, participants listed their reasons for and against having sex, knowing no condom was available, and rated the strength of these reasons on a 1 (not at all strong) to 7 (extremely strong) scale. We computed two difference scores. First, the number of reasons listed against having sex was subtracted from the number of reasons listed for sex. Second, the strength of the reasons against having sex was subtracted from the strength of the reasons for having sex. Higher scores indicated that women listed more reasons for having sex than against and perceived reasons for having sex were stronger than reasons against, respectively. We regressed both outcomes on sexual victimization severity, alcohol dose, relationship potential, and all interactions. Analyses indicated a significant 3-way interaction for reason strength, but not number of reasons listed. For women with high victimization severity who received alcohol, relationship potential was positively associated with stronger reasons for having sex, which is likely indicative of greater sexual risk. Results have implications for risk prevention programs and suggest the importance of providing risk information for women with victimization histories who consume alcohol prior to sexual encounters and perceive high relationship potential in their sexual partner.

POSTER SESSION 3

MGH 241, Easel 141

2:30 PM to 4:00 PM

Numerical Simulation and Experimental Verification of Percolation Diffusion-Limited Aggregation Clusters in Various Media

Michael (Mike) James, Sophomore, Computer Engineering, Edmonds Community College
Matthew Sarb, Recent Graduate, Physics, Edmonds Community College
Mentor: Tom Fleming, Department of Physics, Edmonds Community College
Mentor: William Hamp, Physics/Engineering, Edmonds Community College

Random fractal patterns exhibit an overwhelming distribution throughout the natural world, from the smallest scale we can see, to the most universal scales we can imagine, and appear to affect everything in between. In order to explore some small-scale examples of this, we used high voltage to burn surface tracking patterns into various media, then analyzed the fractal dimension of some of the better samples. Next, we theoretically modeled radial diffusion-limited aggregation clusters (DLA) and a linear dielectric breakdown model by computer simulations, and analyzed the Hausdorff dimensionality of those, as well. Similar to previous experiments by Kim and Roh, and Niemeyer et. al., the experimentally and physically modeled results agreed in their dimensionality. This comparative analysis model implies a method of non-destructive analysis for a broad spectrum of insulating materials. These processes could help engineers design more robust dielectric components or safer airplanes, help geologists better understand fault-fracture spreading and aid in earthquake prediction, or enable atmospheric scientists to study elusive lightning structures known as sprites.

POSTER SESSION 3

Commons West, Easel 24

2:30 PM to 4:00 PM

A Computational Model of GABAergic Neurons to Elucidate Initiation of Spontaneous Synchronous Activity in the Developing Mouse Cortex

Cara Elise Comfort, Senior, Bioengineering, Neurobiology
Levinson Emerging Scholar, Mary Gates Scholar, UW Honors Program, Undergraduate Research Conference Travel Awardee
Mentor: William Moody, Biology

During mammalian central nervous system development, waves of spontaneous synchronous activity (SSA) are a widespread developmental phenomenon, serving to regulate neuronal migration, physiological maturation, and synaptic connectivity. In the neonatal mouse cortex, these waves of electrical activity involve a vast number of neurons firing bursts of action potentials simultaneously and producing transient increases in intracellular calcium, which can be im-

aged using calcium-fluorescent dyes. The Moody lab has previously determined that waves of SSA are initiated by a pacemaker in the ventral piriform cortex and are dependent on GABAergic transmission. Since developmental problems may arise when waves fail to occur during the proper developmental time period, it is crucial to determine exactly how waves are initiated. In order to gain insight into how waves are generated, I estimated key network and cellular parameters that define developing cortical networks using past experimental data. I then built a computational model of GABAergic neurons that simulates wave initiation and propagation, implementing the previously estimated parameters. By matching the simulated wave propagation frequency to those determined by experimental data, I estimated the parameter space of cell connectivity, a free parameter of the model. Finally, I am validating the model by gathering data that estimates synaptic connectivity via patch clamp experiments. This knowledge will ultimately help elucidate the pacemaking function of GABAergic cells that generate waves of SSA by characterizing intrinsic physiological properties and synaptic connectivity.

POSTER SESSION 3

Commons West, Easel 25

2:30 PM to 4:00 PM

Differential Excitability of Cortical Regions in Response to Electrical Stimulation

Teresa Jiang, Senior, Neurobiology
Mary Gates Scholar, UW Honors Program
Mentor: William Moody, Biology

During neurological development, waves of spontaneous activity propagate through structures in the central nervous system including the hindbrain, retina, hippocampus, and midbrain. The presence of waves of activity is essential for proper maturation of these structures and aids in cell path-finding, the establishment of synaptic connections, and the expression of mature firing properties of neurons. These waves initiate at pacemaker sites and electrical stimulation of those sites can produce waves comparable to those initiated spontaneously. In our research, we compare the excitability of the hippocampus to that of a known pacemaker site in the ventral cortex and a non-pacemaker site in the dorsal cortex. To do this, we use blunt glass electrodes to electrically stimulate a mouse brain slice preparation at P3 or P4 and determine the threshold of electrical stimulation that is necessary to evoke a wave of activity at various sites in the cortex. We have found that the threshold of the dorsal cortex is higher than that of the ventral cortex—a known pacemaker region—or that of the hippocampus. The hippocampus is a common initiation site for seizure activity. So, the finding that the hippocampus and pacemaker sites are similarly excitable may aid in developing a better understanding of temporal lobe epilepsy.