



Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

MGH 241, Easel 161

11:00 AM to 1:00 PM

Acute Impact of Prototype Antiseizure Drugs on Exploratory Behavior of Inbred and Outbred Mice

Ali Memon, Senior, Neurobiology

Mentor: Melissa Barker-Haliski, Pharmacy

Epilepsy is a neurological disorder that affects over 65 million people globally. The initial identification of antiseizure efficacy and tolerability of any investigational agent is routinely defined in mouse and rat models of epilepsy. C57BL/6 mice are a commonly used inbred strain for antiseizure drug discovery, while CF-1 mice are a commonly used outbred strain. Although there is established data on the median effective anticonvulsant doses (ED₅₀) of common prototype antiseizure drugs (ASD) in mice, there is limited quantitative data pertaining to the acute impact of anticonvulsant doses of ASDs on locomotor activity in an open field, which may inform on the potential for adverse effects in a clinical setting. This study aimed to provide a quantitative evaluation of the impact of ASDs on locomotor behavior to provide an added way to compare investigational agents to ASD standards-of-care. Male C57BL/6 or CF-1 mice (n = 8/treatment group/strain) were habituated to an open field 24 hours prior to the testing day. On the day of testing, mice were administered prototype ASDs (valproic acid, carbamazepine, levetiracetam, lamotrigine, phenobarbital, diazepam, ethosuximide, phenytoin, gabapentin) or vehicle by the intraperitoneal route. Mice were then allowed to explore the open field for the 30 minute period encompassing the time of peak effect of each ASD. Endpoints of locomotor behavior in the open field included time spent in the center of the field, vertical rearing, fecal boli, and total distance traveled. In CF-1 mice, diazepam generally reduced all measures of exploratory behavior whereas gabapentin increased the total distance traveled. This study establishes a comparative pharmacological profile of the effect of prototype ASDs on exploratory locomotor behavior of male outbred CF-1 and inbred C57BL/6 mice.

POSTER SESSION 1

MGH 241, Easel 162

11:00 AM to 1:00 PM

Circadian Patterns of Spontaneous Seizures in a Rat Model of Temporal Lobe Epilepsy

Stephanie Ai Mizuno, Junior, Pre-Sciences

Mentor: Melissa Barker-Haliski, Pharmacy

Epilepsy is a neurological disorder in which abnormal brain activity causes spontaneous seizures, and behavioral comorbidities including anxiety, depression, and cognitive deficits. Epilepsy can result from many different inciting events, including infection, genetic background, or neurological damage. For example, status epilepticus (SE) is a clinical emergency defined as continuous seizures lasting longer than five minutes, which can increase susceptibility to developing epilepsy. Clinical studies in patients with epilepsy have shown that seizures of different severity can occur at discrete times of day or night, suggesting that there may be circadian patterns of seizure incidence in humans. In this study, a post-SE model of temporal lobe epilepsy (TLE) was used to first establish whether there are any notable circadian patterns of seizure activity in a preclinical rat model of epilepsy that is commonly used for antiseizure drug development. Male Sprague Dawley rats were implanted with cortical electrodes one week prior to the systemic administration of the chemoconvulsant, kainic acid, to induce SE insult. The rats recovered from the SE insult and then went on to develop spontaneous recurrent seizures days to week later. The onset and severity of spontaneous seizures were then continuously monitored for 6 weeks, with seizure segregated by time of day in which they occurred: light vs dark cycle. Preliminary data suggest that rats from this model more frequently experience seizures during the dark phase, i.e. the active period of this nocturnal animal. Results from this study will establish the circadian pattern of spontaneous seizures in the post-kainic acid SE model of temporal epilepsy in rats. Further, this study provides the basis on which to then determine if chronic administration of prototype antiseizure drugs can be optimally administered prior to periods of peak seizure incidence to more effectively reduce long-term seizure burden in this model.

POSTER SESSION 3

MGH 258, Easel 191

2:30 PM to 4:00 PM

Nutrition during Pregnancy and Lactation

Chase Kenneth Smith, Senior, Biology (General)

Mentor: Mary Hebert, Pharmacy

In order to maintain maternal, fetal and neonatal health during pregnancy and lactation, appropriate nutrition is necessary. Both excessive and inadequate intake are associated with significant complications for the mother, fetus and neonate. The objective of this study was to describe nutritional intake during pregnancy and lactation in healthy women (n=13) relative to current recommendations from the National Institute of Health's Office of Dietary Supplements during pregnancy and lactation as well as compare nutritional intake during pregnancy (25-28 weeks and 28-32 weeks gestation) to >3 months postpartum in lactating women. Individual daily dietary consumption was determined by averaging dietary intake for 3 days during each study window. Nutritional content was determined utilizing Fooducate®(Fooducate Ltd.). Statistical comparison of nutritional intake for study windows were conducted using repeated measures analysis of variance (RStudio). Results are reported as mean \pm SD. Significant differences were found in daily sugar intake (25-28 weeks: 82.1 \pm 25.1 grams, 28-32 weeks: 97.5 \pm 29.7 grams, and postpartum: 62.0 \pm 34.8 grams, p<0.03) and daily added sugar intake (25-28 weeks: 39.0 \pm 5.7 grams, 28-32 weeks: 54.0 \pm 19.7 grams, and postpartum: 32.0 \pm 18.0 grams, p<0.02). No significant differences were seen in daily total calories, calories from fat, total fat, saturated fat, trans fat, cholesterol, sodium, potassium, total carbohydrates, dietary fiber, protein, vitamin A, vitamin C, vitamin D, calcium and iron. During pregnancy and lactation, average dietary consumption exceeded recommended daily allowances for carbohydrates (lactation only), sodium, protein, iron (lactation only), vitamin A, and vitamin C (pregnancy only). In contrast, average daily consumption of calories, carbohydrates (pregnancy only), fiber, potassium, calcium, iron (lactation only), vitamin C (pregnancy only), and vitamin D were less than the recommended daily allowances. In conclusion, women consume more sugar during pregnancy than postpartum and average nutritional intake during pregnancy and lactation are inconsistent with current nutritional recommendations from the National Institute of Health's Office of Dietary Supplements.

POSTER SESSION 4

MGH 258, Easel 183

4:00 PM to 6:00 PM

Impact of Diet on Infection-Induced Seizures and Long-Term Comorbidities in a Mouse Model of Temporal Lobe Epilepsy

Hongyi Huang, Senior, Anthropology: Medical Anth & Global Hlth

Mentor: Melissa Barker-Haliski, Pharmacy

Infection of the central nervous system (CNS) greatly contributes to and increases the risk of developing epilepsy. Individuals who present with seizure during a CNS infection

are 22 times more likely to develop epilepsy in their lifetime than individuals who do not present with a seizure. Infection of mice with the Theiler's murine encephalomyelitis virus (TMEV) is a preclinical model that is useful to understand the mechanisms underlying acute seizures and the development of epilepsy following CNS infection. In the present study, we aimed to determine how diet sterilization (autoclaved versus irradiated) impacts the development of acute seizures and chronic behavioral comorbidities. We infected C57BL/6J mice with an intracerebral (i.c.) injection of TMEV or sterile saline, and then fed the mice either an autoclaved or irradiated diet. Next, we monitored the mice for the incidence of acute handling-induced seizures 3-7 days post-infection. Under both dietary conditions, mice developed handling-induced seizures in the acute infection phase. There were 8/13 (61%) irradiated diet fed mice that developed acute seizures whereas 9/13 (69%) autoclaved diet fed mice developed acute seizures during this period (p >0.05). We then assessed behavioral comorbidities associated with chronic epilepsy 4-5 weeks post-infection by evaluating anxiety-like behaviors in an open field test, working memory in a novel object recognition test, and electroconvulsive seizure thresholds. Mice fed an irradiated diet demonstrated preserved working memory function compared to mice fed the autoclaved diet, who demonstrated significant reductions in working memory and increased anxiety-like behavior, suggestive of worsened disease severity. At the conclusion of in-life testing, animals were euthanized, and tissues collected for histopathology and immunohistochemistry to assess the extent of TMEV-induced neurodegeneration and neuroinflammation. Our findings highlight the potential for the sterility of diet to modify disease severity in the TMEV model.