# Hawaii Pacific Neuroscience

## Honolulu, Hawaii

# 2019

# HAWAII NEUROSCIENCE

## RESEARCH INTERNSHIP PROGRAM

## ABSTRACTS

# Association Between Smoking, Atopic Disease, and Multiple Sclerosis Severity in Hawaii Patients

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**INTRODUCTION**: Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system that affects nearly 1 million adults in the US. While the exact cause of MS remains unclear, there are numerous genetic and environmental factors that may contribute to an increased risk or severity of MS. One such established risk factor is cigarette smoking; previous research has demonstrated an increase in MS risk and progression as smoking duration and intensity increased. This study aims to verify a positive correlation between smoking and MS severity in Hawaii's unique population. In addition, MS has a higher prevalence in the developed world than in regions with higher exposure to pathogens or pollutants. Low antigen exposure may alter the immune system such that it responds inappropriately to innocuous substances, leading to atopic diseases or autoimmunity. Recent studies have focused on introducing antigen sources to humans to observe their effects on the immune system and MS activity. A 2007 longitudinal clinical trial found that relapsing remitting multiple sclerosis (RRMS) patients naturally infected with gastrointestinal helminth parasites exhibited lower levels of clinically-verified MS activity than non-infected control groups. Likewise, previous studies suggest gut microbes might be essential for the maturation of the human immune system into a non-atopic state. Given the potential common causative agent between MS and atopic disease, this study also aims to determine if a positive correlation exists between atopic diseases and MS severity. **OBJECTIVES**: Evaluate whether smoking and the presence of atopic disease is correlated with severity of MS in patients at Hawaii Pacific Neuroscience. **METHODS**: A systematic retrospective review of 103 patients seen by Hawaii Pacific Neuroscience between January 2000 and June 2019 was performed. Data was extracted from patient charts using ICD- 10 codes for Multiple Sclerosis. Smoking history and presence of atopic disease were compared against severity of MS (severity = number of symptoms / years of MS diagnosis). A two tailed T test was performed to analyze the data. **RESULTS**: Of the 103 patients analyzed, 40 (38.8%) possessed only allergies, 8 (7.77%) possessed only asthma, and 11 (10.7%) possessed both allergies and asthma. No patients reported having eczema. Average symptoms per year for patients with atopic diseases was 1.88 ± 2.62 and average symptoms per year for patients without atopic diseases was 1.66 ± 2.02 (two tailed T test, $p = 0.637$). In regards to smoking, of the 103 patients, 34 (33%) reported being a past or current smoker, and 69 (67%) reported never having smoked. The average symptoms per year in MS patients who reported smoking was 3.08 ± 3.26. In patients who reported never smoking it was 1.15 ± 1.43 (two tailed T test, $p = 6.13E-05$). **CONCLUSIONS**: Comparing MS severity in smokers (3.08 ± 3.26) vs non-smokers (1.15 ± 1.43), a significant difference was found. This data does support current research found on the continental US. However, given the large standard deviation, further studies with a larger sample size should be conducted to evaluate the validity of this possible correlation between smoking and severity of MS. In regards to the presence of atopic diseases, no significant difference was found. There may be no difference in these two populations, or our sample size may be too small to visualize a small difference. Future work can be done comparing the rates of atopic diseases in patients with MS to the general US population to see if a difference exists.

# Botox as a Treatment for Migraines: A Comprehensive Study on Hawai‘i’s Native Hawaiian Population

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**BACKGROUND**: Lifetime prevalence of migraines is 14% and females are more commonly affected than males in a 2-3:1 ratio. Migraines are recurring attacks of throbbing, unilateral headaches with symptoms including nausea, vomiting, photophobia, phonophobia, and are often functionally debilitating. As the number of non-pain symptoms associated with headaches increases, so does the probability of a migraine headache diagnosis. Migraines can be further classified into those with or without aura. Treatment of acute migraines include analgesics, triptans, and dihydroergotamines. Preventative treatment exists and examples include topiramate, beta-blockers, and amitriptyline. Interestingly, botulinum toxin (OnabotulinumtoxinA) may also be added to the repertoire of chronic migraine management. Some studies show that there is a reduction in frequency of migraine attacks through this treatment. Additionally, botulinum toxin appears to have a more tolerable side effect profile compared to traditional medications. However, current literature demonstrates conflicting and low levels of evidence on the effectiveness of botox injection. Therefore, this study was implemented to investigate the efficacy of botox injections in treating migraines in Hawai‘i’is ethnically diverse population. **OBJECTIVES**: The objective of our study is to investigate the therapeutic effect of botox injections on Hawai‘i’s Native Hawaiian population with different migraine severity levels and to analyze the differences in migraine presence among patients of different ethnicities. **METHODS**: 379 Patients with migraines that underwent botox injection treatment were identified from an initial cohort of 1,474 patients that received a migraine diagnosis at Hawai’i Pacific Neuroscience from 2010 to 2019. The patients’ demographics were recorded, and clinical aspects, such as symptoms and psychological, physical, and neurological comorbidities, age of onset, frequency of migraines, adverse effects, and triggers, as well as botox improvement percentages, were collected for analysis of the differences in migraines between ethnicities. Cross-group comparisons between patients of Native Hawaiian ethnicity and those of other ethnicities were performed using descriptive statistics and the Fisher exact test. **RESULTS**: Of the 379 patients who have completed botox treatment at Hawaii Pacific Neuroscience, 310 (81.8%) reported an improved condition after botox, 34 (9.0%) did not have a follow-up appointment, 23 (6.1%) reported an unchanged condition, and 12 (3.2%) reported a worsened condition. Native Hawaiians present with more severe migraines resulting in a higher percentage of hospitalizations (14.5%) in comparison to other ethnicities at 8.0%. All hospitalizations were pre-botox occurrences, and hospitalization percentages dropped to 0% post-botox treatment. Native Hawaiians present with comorbidities of stroke (p-value = 0.0001), PTSD (p-value = 0.05), and hypertension (p-value = 0.0382). They also present with higher incidences of risk factors for cardiovascular diseases, including modifiable risk factor tobacco use (45.5%) as compared to other ethnicities (25.3%) and non-modifiable risk factor family history of hypertension (47.3%). The most commonly identified triggers include light (8), smells (6), sleep problems (5), heat (4), and menses (4). The most common symptoms present include photophobia (89.1%), nausea (85.5%), and phonophobia (81.8%), in accordance with patients of other ethnicities. However, Native Hawaiians show significantly higher incidences of the symptoms numbness (p-value = 0.0072) and coordination issues (p-value = 0.0155). **DISCUSSIONS AND CONCLUSIONS**: Native Hawaiians present migraines similarly to other ethnicities in sex, triggers, and age on onset, but overall receive less therapeutic relief from botox injection treatment. With a migraine diagnosis, Native Hawaiians may be at higher risk of developing hypertension, stroke, and PTSD. Several lifestyle choices and medical conditions can put Native Hawaiians at a higher risk of cardiovascular diseases, including poor diet, physical inactivity, tobacco and alcohol use, overweight and obesity. Native Hawaiians have higher risk for traumatic stressors due to socioeconomic status - poor living conditions, educational attainment, employment status, access to healthcare, and discrimination/ racism. Native Hawaiians also are more likely to present with the symptoms of numbness and coordination issues, which may be related to their increased prevalence in cardiovascular diseases such as stroke, which share similar symptoms. Overall, there is no visible relationship between the severity of migraines pre-botox and percent improvement post-botox injection treatment.

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# Correlation Between Alzheimer's Disease and Education

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**BACKGROUND**: Alzheimer's Disease (AD) is a progressive neurodegenerative disease that is the sixth leading cause of death in the United States affecting more than 5.5 million Americans. The number of affected individuals is rapidly increasing and is estimated to nearly double by the year 2060. In Hawaii, there are 29,000 patients with AD and 65,000 individuals providing care. AD is characterized by a disruption in performing basic daily functions and irreversible decline in memory and cognitive skills. Two commonly used tests to measure cognitive impairment are the Mini-Mental Status Exam (MMSE) and the Montreal Cognitive Assessment (MOCA). Having a higher level of education has shown to have a protective effect on later developing dementia. Although this relationship between education and dementia has been previously well studied, the results remain inconclusive. Comparing the relationship between AD severity by MMSE score and education level has not yet been explored. It is important to understand if demographics could have a protective effect on AD in order to improve diagnosis and reduce negative side effects. **AIM**: The aim of this study seeks to strengthen a previously established relationship between education level and AD by examining the severity of AD based on the scores received on the Mini-Mental Status Exam (MMSE) or the Montreal Cognitive Assessment (MOCA). Evaluate the efficacy of the study in the context of Hawaii's unique socioeconomic and educational background. **METHODS**: Retrospective data was taken from Alzheimer's disease patients from the Center for Healthy Aging, Memory and Brain Health at Hawaii Pacific Neuroscience (HPN) from 2014-2019. ICD-10 codes for late-onset AD was used to collect all data from patient documents. Inclusion criteria included late-onset patients with an MMSE and/or MOCA converted MMSE score and documented education level. MOCA scores were converted to MMSE using Lawton et al.'s conversion table. Exclusion criteria included patients with vascular dementia and early-onset Alzheimer's. **RESULTS**: Data was collected from a total of 118 patients: 55 males (47%); 63 females (53%). The average age of the patients was 80.01 years old, the eldest being 92 and the youngest being 66. Of the total sample population, 69 had more than 12 years of education (58.5%) and 49 had less than or equal to 12 years of education. Patients with an education greater than 12 years scored 3.4 points higher on average compared to patients with an education equal to or less than 12 years. Of the patients with education levels greater than 12 years, 57% showed no cognitive impairment. Of the patients with education levels less than or equal to 12 years, only 27% showed no cognitive impairment. P-Value is less than 0.00015; there exists a significant difference between scores of patients with more than 12 years of education and scores of patients with less than or equal to 12 years of education. **CONCLUSION**: Most of the patients with more than 12 years of education were classified under no cognitive impairment (57%), which shows education's protective effect. As expected, the results portrayed in this study show that AD patients with higher education (>12 years) had a statistically significant higher cognitive function, in comparison with AD patients with lower education (< 12 years). In the future, studies should continue studying the effects of education on AD patients' cognitive functions, explore the correlation between AD and education in other states with a range in education quality, and examine other activities that may have a protective effect in developing AD. Higher education should be encouraged as a way to slow AD progression and spread awareness of the importance of education.

# Leading Risk Factors For Ischemic Stroke : A Comparative Ethnographic Study Of Patients In Hawai'i

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**INTRODUCTION**: Stroke is a leading cause of death and disability worldwide, and it affects millions of Americans every year. The established risk factors for stroke fall are mainly hypertension, diabetes, hyperlipidemia, but also behavioral risk factors such as smoking and alcohol consuming. Although there have been numerous studies on the correlation between ethnicity and certain risk factors of stroke, little is known of the stroke risk in Native Hawaiians and other Pacific Islanders (NHOPI). **OBJECTIVES**: The two main objectives of this study are to investigate the relationship between ischemic stroke incidence and risk factors of patients in Hawaii who have been referred to Hawaii Pacific Neuroscience; and to determine if there are differences in the prevalence of ischemic stroke risk factors between ethnic groups. **METHODS**: A retrospective chart review was conducted at the Stroke and Neurological Restoration Center at Hawaii Pacific Neuroscience between 2017 and 2019. Patients had to be hospitalized for a stroke on Oahu and be followed-up by a physician for the finalized diagnosis of ischemic stroke. We excluded bi-racial patients and also Hispanic and African American ethnicities, due to insufficient representation. Therefore, we gathered information about three main ethnicities: Caucasians, Asians and Native Hawaiian and Other Pacific Islanders. **RESULTS**: We collected information for 326 patients, and our main finding is that NHOPI patients significantly have more diabetes and a higher BMI than other ethnicities, and they are a decade younger at the onset of stroke. Asian people have more hypertension and are mostly represented by male, although the majority of NHOPI patients are female. Caucasian also tend to be mostly male, and they significantly drink more alcohol than the other ethnicities. **CONCLUSION**: Our analyses showed a significant difference between Caucasians, Asians and NHOPI patients regarding gender, age, hypertension, diabetes, hyperlipidemia, BMI and alcohol consuming. With a larger sample size, we could continue to add to the existing literature on stroke by analyzing further comparisons that include underrepresented populations in our study, such as African Americans, Hispanics, and Biracial or Mixed-raced people. The conclusions from this study can better inform medical recommendations for stroke prevention specific to each ethnicity.

# The Relationship Between Cigarette Smoking and Oral Levodopa Equivalent Daily Dose (LEDD) in Parkinson's Disease Patients

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**INTRODUCTION**: Parkinson's Disease (PD) is a progressive neurodegenerative movement disorder that is marked by the loss of dopaminergic neurons in the substantia nigra. Common symptoms include tremor, rigidity, bradykinesia, depression, constipation, and sleep disorders. Recent PD studies have found that smoking leads to a later onset of motor symptoms and a 50-60% reduced risk for developing PD, however, other studies have produced contradictory findings that illustrate an unsettled issue. Among the many symptomatic treatments for PD, Levodopa, a dopamine replacement drug, remains the "gold standard." Levodopa equivalent daily dose (LEDD) is a useful tool to summarize the total anti-parkinsonian medications a patient is receiving. **OBJECTIVE**: Compare the average oral LEDD of current smokers and non-smokers in our PD sample. **METHODS**: A cross-sectional chart review of Hawaii Pacific Neuroscience PD patients from 2009-2019 was conducted. Patients receiving treatment other than oral medications were excluded from the study. Patients were categorized into "non-smoker" and "current smoker," based on the respective patient's social history chart. Patient LEDD values were calculated using conversion formulas from literature studies and medications listed in each respective chart. **RESULTS**: Total sample size was 244 PD patients, with 7 current smokers (2.9%) and 237 non-smokers (97.1%). The mean LEDD for current smokers and non-smokers were 142.9 ± 134.3 mg and 402.4 ± 44.0 mg, respectively. There was a significant difference in average LEDD between current and non-smoker PD patients ($p = 0.025$). **CONCLUSION**: LEDD dosages in current smokers were significantly lower than non-smokers, with a very low overall prevalence of current smokers relative to the expected for Hawaii's elderly population. With inconsistent results among studies looking at nicotine as a PD treatment, further research needs to be done with a larger sample size.

# The Use of Systemic Anti-Inflammatory Medication in Intractable versus Not-Intractable Seizures

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**INTRODUCTION**: A seizure is defined as a sudden, uncontrolled electrical disturbance in the brain, which can cause unusual movements, sensations, behavior, and sometimes loss of consciousness. Epilepsy is the tendency for seizures to recur, and the etiology is often unknown. Intractable seizure disorder is defined as continued seizure activity at least once per month for 18 months, despite the use of two or more appropriate anti-epileptic medications. Literature states that 20-40% of seizures are intractable, which accounts for 80% of the health costs for epilepsy management. Inflammatory processes continue to be one of many areas of interest in the development of new epilepsy treatments, particularly for intractable seizure disorders. **HYPOTHESIS**: Patients with intractable seizures (ICD G40.219) will have a higher rate of anti-inflammatory drug use than those with not-intractable seizures (ICD G40.209). **METHODS**: This study was a single-centered, IRB-approved retrospective medical chart review of epilepsy patients seen at Hawaii Pacific Neuroscience over a 10 year period from 2009 to 2019. Using eClinicalWorks, data was extracted by searching for two ICD-10 codes –G40.209 and G40.219– which classify as localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, without status epilepticus, for not-intractable and intractable patients respectively. The data collected for each reviewed patient within each ICD-10 code included: ethnicity, gender, age, BMI, alcohol and tobacco use, current systemic anti-inflammatory medications, and current anti-epileptic drugs (AEDs). Excluded from this study were patients under the age of 15 and those who took neither AEDs nor anti-inflammatory medications. Data was analyzed using a two-proportion z-test and a two-sample t-test. **RESULTS**: We reviewed a total of 400 patient charts, 200 for G40.209 and 200 for G40.219. There was a total of 65 patients with not-intractable seizures taking anti-inflammatory medications compared to 60 patients in the intractable group. In reference to the amount of anti-inflammatory medications taken, there was a total of 75 patients in the not-intractable group compared to 74 in the intractable group. The use of NSAIDs, Aspirin, Steroids and colchicine was compared between groups. **DISCUSSION**: Using a significance level of 0.05, we observed no statistically significant differences in the percentage of patients taking varying quantities of systemic anti-inflammatory medications between the not-intractable and intractable patients, nor in the amount of specific types of anti-inflammatory medications taken between each group. Our data suggests that the use of known systemic anti-inflammatory medications do not influence seizure control. The limitations of this study included unknown frequency of anti-inflammatory medication use, unknown adherence to anti-inflammatory medication, and unknown reason for anti-inflammatory medication use. **CONCLUSION**: Overall, our data did not show a significant difference in the use of common systemic anti-inflammatory medications between patients with intractable and not-intractable seizures. There are still many inflammatory pathways that may influence seizures. Further studies can investigate those pathways.

# 2019 Hawaii Neuroscience Research Internship Program Students

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## Acknowledgements

Catherine Mitchell, MS, SIP Coordinator
Kore Kai Liow, MD, Neurology, Research (Program Director)
Alika Maunakea, PhD, John A. Burns School of Medicine (Keynote Speaker & Panel of Judges)
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