Depression within Drug-Resistant Epilepsy Population and Relation to Anti-Epileptic Drugs

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INTRODUCTION: Epilepsy is a neurological disease characterized by recurrent, unprovoked seizures, which are events caused by uncontrolled electrical disruptions in the brain. The lifetime prevalence of psychiatric disorders in individuals with epilepsy is 35%, 15% higher than that of non-epileptic individuals. Among these psychiatric disorders, depression has been found to have a bidirectional relationship with epilepsy. OBJECTIVE: Hawaii Pacific Neuroscience is participating in clinical trial evaluating pharmacokinetics and efficacy of an investigational product in patients with drug-resistant epilepsy. The primary objective of this project was to determine if there is correlation between drug-resistant epilepsy and depression and/or anxiety disorders along with if there are correlation between one most commonly taken AED; Levetiracetam. METHODS: A systematic chart review was performed on patients with any types of epilepsy and descriptive statistics were performed on this cohort in Microsoft Excel. Screened for intractable epilepsy which shows the drug-resistant epilepsy and psychiatric disorders to screen for depression and anxiety disorders along with types of AED taken. RESULTS: Out of 600 patients with epilepsy screened 178 patients were diagnosed with drug-resistant epilepsy. Most taken AED was levetiracetam with 47% and out of all comorbidities, depression was the highest then hypertension and followed by anxiety. Statistical analysis of p-value with depression was 0.867427, anxiety was 0.381213, and depression/anxiety with levetiracetam was 0.852837. CONCLUSION: Statistical analysis show there is no significance therefore no correlation between depression/anxiety within drug-resistant epileptic patients. Therefore levetiracetam does not have bidirectional relation with depression and/or anxiety disorder within drug-resistant epileptic patients.
Hypertension as a risk factor for Alzheimer’s disease: A bivariate logistic regression of patient demographics in Hawaii

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INTRODUCTION: Alzheimer’s disease (AD) is the most common neurodegenerative disorder, affecting over 12 million individuals worldwide. AD is thought to result from the accumulation of amyloid beta protein plaques and Tau neurofibrillary tangles, which contribute to its characteristic progressive dementia. Treatments have been focused on the prevention of possible indicators and comorbidities associated with AD, such as hypertension, but the literature has been mixed with regard to the relationship that exists between blood pressure and AD. OBJECTIVE: To determine whether hypertension and dementia of the Alzheimer’s type are comorbid with one another.

METHODS: A retrospective chart review was conducted at the Memory Disorders Center at Hawaii Pacific Neuroscience between January 2011 and August 2018. Patients diagnosed with dementia were filtered through eClinicalWorks using the trial’s inclusion and exclusion criteria. A bivariate logistic regression was used to determine which combination of variables is correlated with having AD. RESULTS: Asians (30.8%) and Whites (20.2%) contributed the greatest percentage of individuals with AD and hypertension. Hypertension and hypothyroidism were the top two comorbidities found in patients with AD. The bivariate logistic regression showed that older individuals are more likely to have both hypertension and AD, so age is a significant (p<0.001) confounding variable to age and hypertension. CONCLUSION: The results of the bivariate logistic regression showed that when age was factored in, all other variables were no longer significant because age increases the likelihood of having both AD and hypertension, confounding any previous associations.
INTRODUCTION: Drug-resistant epilepsy (DRE)—defined as the failure of two appropriate, well-tolerated anti-epileptic drug (AED) regimens to achieve seizure freedom for the patient—affects 20-40% of patients with epilepsy and largely contributes to the burden of $12.5 billion spent yearly on epilepsy care. Patients with DRE suffer increased seizure-related morbidity and mortality, and decreased quality of life reflected in lower academic achievement, inability to drive, unemployment, and social stigma. Currently, neurosurgery remains the only possible cure for patients with DRE. A better understanding of risk factors for DRE is required to facilitate treatment discovery. Multiple studies in predominantly white Scottish, Finnish, and American patients have shown the most important risk factor for DRE is failure of the first AED regimen to achieve seizure freedom. Studies in white Parisian and Finnish patients demonstrated symptomatic focal epilepsy is more difficult to treat than idiopathic generalized epilepsy. Other comorbidities associated with DRE in predominantly white Scottish and American patients include recreational drug use, depression, and obstructive sleep apnea. Although the aforementioned risk factors affect DRE in white patients, to our knowledge no studies have examined risk factors of DRE among ethnically diverse epilepsy patients. Given the growing heterogeneity of the United States, a sample investigating ethnic differences is warranted since factors studied with predominantly white patients may not be generalizable to minority ethnicities.

PURPOSE: The purpose of this study is to investigate risk factors for DRE in an ethnically diverse sample of epilepsy patients as a step toward developing preventive strategies and therapies serving minority patients. Our hypothesis asserts that the following factors—number of AEDs, type of epilepsy, drug use, depression, and sleep apnea—effect DRE in ethnically diverse epilepsy patients.

METHODS: Patients with a diagnosis of epilepsy were identified at a Hawaii-based neuroscience practice for diagnostic purpose from 2014 to 2018 using ICD-10 codes for epilepsy. A total of 475 patients referred to the Comprehensive Epilepsy Center at Hawaii Pacific Neuroscience were included in the final sample. Data were analyzed using Statistical Package for the Social Science.

RESULTS: Of 475 patients, 220 were male (46%) and 255 were female (54%). 98 were white (21%), 54 were Asian (11%), and 93 were Pacific Islander (20%). The average patient age was 47 years. 185 patients had DRE (39%), and 290 did not have DRE (61%). The number of AEDs, focal epilepsy, generalized epilepsy, smoking, COPD, age, and ethnicity were significantly associated with DRE. The logistic regression model was significant $\chi^2(8)=5.361, p=0.718$ (Hosmer and Lemeshow Test of good fit), explained 46.6% (Nagelkerke $R^2$) of variance in DRE, and correctly classified 79.6% of cases (sensitivity: 75.9%, specificity: 81.6%, positive predictive value: 69.7%, negative predictive value: 85.9%).

CONCLUSION: This study showed that a patient’s number of AEDs, type of epilepsy, age, and ethnicity affect the likelihood of having DRE in ethnically diverse patients. Patients on multiple AEDs were twice as likely to have DRE. Patients with focal epilepsy were 13 times more likely to have DRE, and patients with generalized epilepsy were 5 times more likely to have DRE. Vascular lesions, vascular malformation, and multiple temporal sclerosis in localization-related epilepsy is thought to contribute to DRE. Taken into considerations all other factors being constant, older age and Asian ethnicity were also significantly associated with increased likelihood of DRE. Combinations of these factors may help identify patients who are not likely to benefit from current medical treatment. The results of this study have important care implications for the 20-40% of epilepsy patients who experience DRE, especially Asians associated with higher likelihood of DRE.
Demographics of Patients Evaluated for Alzheimer’s Disease in Hawaii

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INTRODUCTION: With aging comes changes in brain mass and cognitive functions. Memory issues are expected with increasing age, however, once these problems impede our ability to perform daily activities and function normally must we begin to seek professional assistance. Alzheimer’s Disease (AD) is the most common form of dementia and greatly affects many of our elderly in Hawaii.

OBJECTIVES: Here, we take advantage of the information provided by the The Center for Healthy Aging, Memory and Brain Health at Hawaii Pacific Neuroscience to evaluate the demographics of those patients referred for treatment of AD to assess its impact on Hawaii residents. METHODS: Patients were selected based on a diagnosis of AD and those who are currently taking a drug used primarily to treat AD. RESULTS: Our study concludes that an increasing age corresponds to a greater risk of developing AD while people identifying as White comprised the majority of individuals suffering from the disease. The most common comorbidity associated with patients is Hypertension, while many are currently taking a combination of Sleep Aid or Agitation medication. CONCLUSION: While our study provides beneficial information about AD in Hawaii, a larger scale research project will offer a greater comprehensive evaluation, specifically concerning a connection between various races and AD.
Understanding Patients With Epilepsy that Use Unconventional Treatments: Medical Marijuana Use in Hawaii

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**INTRODUCTION:** Epilepsy is a neurological condition in which a patient has unprovoked and recurrent seizures. 1 in 26 people in America will develop epilepsy throughout their lifetime. Although, currently there is no cure for epilepsy, there are medications and surgical procedures that alleviate seizure manifestations. In the recent decade, there has been a surge in the use of cannabis-related products as potential treatments for epilepsy, particularly in children. Currently, the most common forms of cannabis are tetrahydrocannabinol (THC) and cannabidiol (CBD). Both forms of compounds are found to have anticonvulsant effects that can benefit epileptic patients. However, due to the undesired psychoactive effects and risk of abuse found in THC, researchers have shifted to focus on developing treatments of epilepsy from CBD. CBD has a better defined and superior anticonvulsant profile devoid of psychoactive and abuse liabilities. The difference in these two chemicals separates recreational and medical marijuana. Medical marijuana contains highly concentrated CBD in the form of an oil that can be ingested orally or inhaled through vapor. Currently, limited data is available to support medical marijuana as an alternative solution to AEDs. Researchers are still in search of the most beneficial ratio of CBD: THC to maximize treatment benefit and minimize adverse effects. **OBJECTIVES:** The object of this study is to analyze a sample of patients with epilepsy using cannabis/marijuana-related products and determine factors that drove these patients into their usage of marijuana, by comparing between patients with epilepsy using recreational marijuana and medical marijuana in Hawaii. **METHODS:** Data was extracted from patient charts using ICD-10 codes for epilepsy. Patients were grouped by ethno-culture and clinical history was reviewed. The following were analyzed: type of epilepsy, type of marijuana product, seizure frequency, substance use, depression, anxiety, quality of life, and use of AEDs. **RESULTS:** Of the patients included in this study (n=1131), 57 patients with epilepsy (PWE) were found to use marijuana/cannabis related products. Severity of patient’s epilepsy is compared between recreational and medical marijuana PWE through seizure frequency and types of epilepsy. Depression, anxiety, and number of AED’s used were compared between recreational marijuana and medical marijuana PWE. **CONCLUSIONS:** This study shows that PWE using medical marijuana were found to have more severe cases of epilepsy. In most cases, these patients have higher frequencies of seizure and intractable epilepsy. Patients are shown to have severe risks of alcohol abuse, higher numbers of AED’s use, and depression or anxiety. There is a paucity of scientific facts that are known about medical marijuana as a form of treatment in epilepsy. The findings of this study not only provide new knowledge in this area of research but also provide information for physicians to understand PWE that use unconventional methods and provide better care and treatment for future patients.
Effectiveness of Once a Month Novel Intravenous Investigational Immunotherapy (NIIT) in Patients with Drug-Resistant Focal Epilepsy

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INTRODUCTION: About 1 in 26 people will develop epilepsy at some point in their lives. Categorized by uncontrollable seizures that are unpredictable in frequency, epilepsy is the fourth neurological disorder after migraine, stroke, and Alzheimer’s disease. The primary treatment for patients with epilepsy is antiepileptic drugs (AEDs) and it is estimated that 70% of patients achieve good seizure control with AED therapy; however, the remainder of patients who are taking AEDs develop Intractable Epilepsy. It is rare for prior epilepsy patients to become seizure-free even with the newer AEDs available. Novel intravenous investigational immunotherapy (NIIT) is a recombinant humanized monoclonal antibody, approved by the U.S. Food and Drug Administration (FDA). NIIT targets the α-4 subunit of human integrin, which binds to the receptors of epithelial cells such as vascular adhesion molecule (VCAM-1). This interaction may facilitate the endothelial adhesion of leukocytes such as T-cells and their migration across the blood-brain barrier. Additionally, it is thought to suppress existing inflammatory activity present at the disease site, along with inhibiting further recruitment of immune cells into inflamed tissue by interaction with VCAM-1.3 This mechanism is now believed to improve seizure control. OBJECTIVES: The primary objective of this project is to determine if adjunctive therapy of NIIT 300 mg intravenous (IV) every four weeks reduces the frequency of seizures in adult subjects with drug-resistant focal epilepsy. METHODS: Patients were identified through Hawaii Pacific Neuroscience database and analyzed retrospectively based off the inclusion and exclusion criterion of the clinical trial. RESULTS: Three case study patients were described. Patient 1 was diagnosed in 2009 for focal idiopathic epilepsy, unspecified intractable epilepsy. Her medical history includes major depressive disorder, general anxiety disorder, insomnia, sleep apnea, and an unspecified sleep disorder. Her current medications include Lacosamide, Topamax, and Lamictal for seizure control. Patient 2 was diagnosed in 2014 for intractable focal epilepsy, intractable and convulsions. The patient’s medical history includes major depressive disorder, general anxiety disorder and attention deficit disorder (ADD) with hyperactivity. Currently the patient is taking Divalproex Sodium ER. Vagal Nerve Stimulation (VNS) was also implanted in October 2014 to improve seizure control. Patient 3 was diagnosed with non-intractable generalized idiopathic epilepsy and accompanying symptoms in addition to intractable localized epilepsy. She is currently prescribed three AEDs: Lamotrigine, Levetiracetam, and Topiramate. The patient has mild parasanal mucosal inflammatory and some demyelination, which have improved since the comparison study. Her seizure frequency increased at a more intense level, resulting in the change of medication to NIIT. CONCLUSION: This study has indicated that the novel intravenous investigational therapy (NIIT) reduced the number of recurring seizures in the three patients that potentially are taking NIIT. Electroencephalography (EEG) and video electroencephalography (VEEG) imaging after prescription of NIIT suggests that biological functioning and structure, and psychological symptoms have decreased in these patients.
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