HAWAII PACIFIC NEUROSCIENCE

Clinical Research Center
Brain Research, Innovation & Translation Labs
2230 Liliha Street #104
Honolulu, Hawaii 96817, USA
Dedicated Research Lines: (808) 564-6141, Fax (808) 443-0774

Neuroscience Research

Center for Neuroscience Diversity

Our Commitment to
Neuroscience Diversity, Equity & Inclusions

2021-2022
Reports & Statistics

Neuroscience Clinical Trials	41 (3 NIH funded)
Neuroscience Research Projects:	21
PubMed Full Length Articles Published:	8
National or International Poster Presentations:	17

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According to NIH NIMHD (National Institute on Minority Health & Health Disparities), one of America's greatest challenges is reducing the profound disparity in health status of its racial and ethnic minority, rural, low-income, and other underserved populations.

In 2022 April, FDA released "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry" guidance *"to provide recommendations to sponsors developing medical products on the approach for developing a Race and Ethnicity Diversity Plan (henceforth referred to as the "Plan") to enroll representative numbers of participants from underrepresented racial and ethnic populations in the United States, such as Black or African American, Hispanic/Latino, Indigenous and Native American, Asian, Native Hawaiian and other Pacific Islanders, and other persons of color in clinical trials. Individuals from these populations are frequently underrepresented in biomedical research despite having a disproportionate disease burden for certain diseases relative to their proportional representation in the general population. Adequate representation of these populations in clinical trials and studies supporting regulatory submissions helps ensure that the data generated in the development program reflect the racial and ethnic diversity of the population expected to use the medical product if approved and may potentially identify effects on safety or efficacy outcomes that may be associated with or occur more frequently within these populations."*

According to 2020 US census Bureau, Asian is the 2nd fastest growing minority after Hispanics and yet, it is one of the most under-represented groups in any US clinical trials. We believe Hawaii can play an important role in reducing the disparity in minority participation & engagement in clinical trials or research especially for minority groups as defined by NIH National Institute on Minority Health & Health Disparities (NIMHD)

- Asian Americans (7% of US & over 40% of Hawaii's population)
- Native Hawaiians and Pacific islanders (10% of Hawaii's population)
- Underserved rural population (94% Hawaii's landmass)

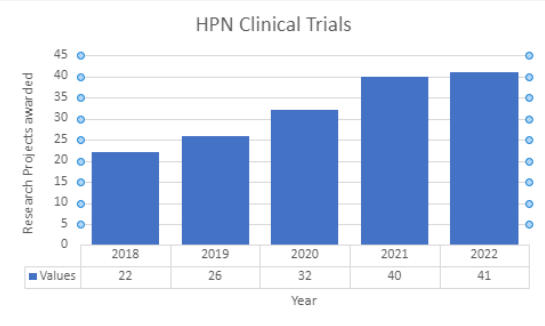
Hawaii is one of the most diverse US states and one of 6 states with majority minority population and home to several NIMHD designated US health disparity populations. Our team focus on promoting and collecting data on Hawaii's diverse population to enhance scientific knowledge and designing interventions to improve health outcomes by improving health care access, reduce health disparities especially for minorities like Asians, Native Hawaiians and other Pacific islanders and underserved and underrepresented groups.

Hawaii Pacific Neuroscience (HPN) robust clinical and academic clinical and translational research programs is on the forefront of working with NIH & biomedical organizations to fosters a culture of innovation and collaboration and is recognized nationally for our work in neuroscience research. Whether our physicians investigators & partners are in the lab exploring science to understand a disease process, working in the clinic with patients on a clinical trial, collaborating with our global partners on trial conception, design and IND application, our focus, commitment, and our hearts will always be to our serve our patients and their precious ohana (families) and to improve their quality of life

The Hawaii Center for Neuroscience Diversity working collaboratively with the Clinical Research Center (CRC) is fully staffed with full time investigators and credentialed, experienced and qualified research raters and staff.

The CRC is a highly sought after site and have a national reputation for successful completion and recruitment including rapid site start up. The CRC has successfully completed over 100 clinical trials and actively involved in investigations of:

- NIH NINDS Funded Hawaii site for NeuroCOVID Databank/Biobank
- Alzheimer's, MCI, Preclinical and other related neurodegenerative disorders
- Parkinson's, & other movement disorders including Huntington's chorea, tremors
- Epilepsy, Seizures including acute abortive therapies in overnight EMU
- MS, Neuroimmunology, Vaccine research
- Pain, Headache, Migraines research
- Neuromuscular including myasthenia gravis
- Concussion, traumatic brain injury
- Narcolepsy and other sleep disorders
- Stroke and Neurovascular research
- Neurodevice, neuromodulation studies
- Rare Neurological Diseases



Few recent examples of successfully investigated, FDA approved and launched products include Cenobamate for Epilepsy, Inbrija for Parkinson's, Kesimpta for MS, Daridorexant for Insomnia in recent years.
See list of active recruiting clinical trials.

Fully Equipped & Experienced Phase 0, I, II, III and IV Trial Capable

The Neuroscience Center with its Centers of Excellence for disease specific disorders are fully integrated so that patients have easy access to the benefits of world class groundbreaking clinical research at the Clinical Research Center specially equipped with:

- Biomarker (CSF, serum, genetic) sampling,
- Phase 0 & Phase I Normal Volunteer and Patient Subject Studies
- PK studies in overnight PK Unit
- IV Infusion studies in IV Infusion Center
- 20 Exam rooms with dedicated Monitor rooms
- Central IRB for Rapid Site Start Up
- On-site 3T MRI
- On-site Radiology Department
- Onsite Spinal Tap/Fluoroscopic LP
- Onsite Pharmacy
- Onsite IV Infusion Center
- Onsite Emergency resuscitation equipment
- Central Laboratories use & experience
- Accredited Local Laboratory
- Refrigerated, ambient temperature centrifuge
- Refrigerators -20C freezer, -70 Freezer
- Onsite ABRET accredited & CliniLab certified EEG & VEEG Labs
- Onsite AASM Accredited & CliniLab certified Sleep Laboratory
- IATA certified Lab
- Ongoing GCP training
- Onsite EMG, EEG
- Locked/secure Drug storage temperature controlled and monitored daily

HAWAII PACIFIC NEUROSCIENCE

Brain Research, Innovation & Translation Laboratory (BRITL)
2022 Student Cohort, Abstracts & Poster Presentations

The Neuroscience Center for Diversity Advancement works closely with BRITL which foster collaboration, bench to bedside translation and a culture of innovation and collaboration between departments, centers, institutions, and outside organizations.

Physicians and scientists of diverse backgrounds work closely within and across centers, institutes, and schools to collaborate whether they are basic laboratory-based scientists, bio statisticians or clinicians to encourage cross disciplinary translation bench to bedside research. Our diverse faculty also mentor aspiring diverse residents, medical students & select graduate and undergraduate students under the "Brain Research, Innovation and Translation Lab (BRITL) *Neuroscience Scholar Program"* and the Hawaii Neuroscience Summer Internship Program (SIP).

2022 BRITL Neuroscience Research Faculty & Mentors

Kore Liow, MD	Neurology, Clinical Professor of Med (Neurology)
Jason Viereck, MD, PhD	Neurology, Clinical Assistant Professor of Med (Neurology)
Enrique Carrazana, MD	Neurology, Clinical Educator, Dept. of Med (Neurology)
Vimala Vajjala, MD	Neurology, Clinical Assistant Professor of Med (Neurology)
Michael Slattery, MD	Neurology, Clinical Assistant Professor of Med (Neurology)
Eliza Hagen, MD	Neurology
Todd Uchima, PA-C	Neurology
Chris Larrinaga, APRN	Neurology
L. Nicole Little, PA-C, PhD	Neurology
Jason Chang, MD	Neurorehabilitation, Clinical Assistant Professor of Med
Kent Yamamoto, MD	Neurorehabilitation, Clinical Assistant Professor of Med
David Baskin, MD	Neurosurgery, Professor and Residency Program Director, Houston Methodist
Ricardo Burgos, MD	Neuroradiology
Qing Li, PhD	Neuroscience, Molecular Biosciences & Bioengineering, Professor, UH Manoa
Paul Smith, MD	Brain Health, Lifestyle Medicine & Wellness, Clinical Assistant Professor
Sriharsha Vajjala, MD	Sleep Medicine, Clinical Educator, Dept. of Med (Neurology)
Lawrence Burgess, MD	Surgery, Professor of Surgery & Director of Student Affairs, SOM
John Chen, PhD	Biostatistics, Professor & Chair, Dept. Quantitative Health
Chathura Siriwardhana, PhD	Biostatistics, Assistant Professor, Dept. Quantitative Health

Stroke and Neurovascular Diseases Research Lab

Lead Investigator: Jason Viereck, MD, PhD,
Neurologist & Director,
Stroke & Neurologic Restoration Center,
Clinical Assistant Professor of Medicine (Neurology)

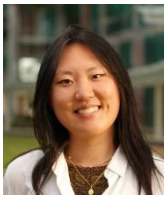
Investigating Prevalence of Carotid Artery Disease in Native Hawaiians and other Pacific Islanders

Research Assistants/Medical Students: Julia Jahansooz

Ethnicity has previously been identified as a risk factor for ischemic stroke. Native Hawaiians and other Pacific Islanders (NHOPI) were on average 11 years younger at the onset of stroke than their Caucasian and Asian counterparts. The impact of ethnicity on prevalence of carotid artery disease, a precursor to stroke, in NHOPI has not previously been documented in Hawaii. This ethnographic study aims to quantify the prevalence and extent of carotid artery disease in Hawaii to better understand the pathogenesis of carotid artery atherosclerosis in different populations.

Investigating Carotid Artery Disease in Critically Understudied Populations: Comorbidities Seen in Native Hawaiians and Pacific Islanders *Research Assistants/Medical Students: Anson Lee*

Stroke is one of the primary causes of mortality and disability in the United States, and approximately 15% to 20% of all strokes are caused by carotid artery disease (CAD). Past surveys found evidence that among Native Hawaiian and Pacific Islander (NHPI) populations, individuals were four times more likely to suffer from a stroke and 30% more likely to die from a stroke compared to non-Hispanic white adults. Comorbidities associated with CAD are especially important to assess as multimorbidity was found to be common in stroke with 94% of stroke victims having at least one other long-term condition and 10% suffering from seven or more. Yet, clear-cut information and statistics about NHPI CAD risks, outcomes, and comorbidities have been difficult to ascertain. Our project investigates the types and number of comorbidities associated with CAD and its risk factors in NHPI patients compared to other ethnicities.



Investigating Young Atypical Stroke Risk Factors, Etiologies in Native Hawaiian and Pacific Islander Population Followed up at Hawaii Stroke & Neurologic Restoration Center *Research Assistants/Medical Students: Michelle Lu,*

Strokes in younger patients (<45 years) are relatively uncommon, making up 10-15% of stroke diagnoses. However, the risk of death in younger patients is higher, can disable individuals before their most productive economic years and lower their quality of life disproportionately. Studies have not only shown that stroke risk in Native Hawaiian/Pacific Islander (NHPI) populations is 30% higher than in non-Hispanic whites, but also show that NHPI patients hospitalized for ischemic stroke were also less likely to be older and more likely to be female when compared to whites. Compared to Asians, NHPI are also less likely to be older at the time of hospitalization. This study will aim to characterize the atypical stroke patients treated at Hawaii Stroke & Neurologic Restoration Center, investigating the presence of risk factors such as the use of oral contraceptives, smoking, hypertension, diabetes mellitus, dyslipidemia, obesity, vascular risk factors, congenital cardiac disease, as well as presenting symptoms such as hemiparesis, altered mental status, abnormal movements, migraine with aura. We would also like to identify atypical causes, such as hypercoagulable states, medication-induced thrombosis, vascular conditions, drug abuse, and cardiac malformations that might have led to stroke in younger patients.

Evaluating the Role of Socioeconomic Status in Post-Stroke Disability Outcomes in Patients Cared for at Hawaii Stroke & Neurologic Restoration Center

Research Assistants/Medical Students: Amanda Chau

Hawaii's multicultural community has not been thoroughly studied, despite its significantly higher prevalence of stroke. Socioeconomic status has been shown to be a factor in post-stroke outcomes. This project will investigate the effect of socioeconomic status (SES), race, and ethnicity on post-stroke disability outcomes in Hawaii. Identifying populations in Hawaii that may be at risk for worser post-stroke disability outcomes may lead to better post-stroke care amongst these groups.

Lifestyle Research Unit

Lead Investigator, Paul Smith, MD,
Director, *Self-Care, Lifestyle & Wellness Center*
Clinical Assistant Professor of Medicine

Utilization of a Risk Acuity Scorecard for Comparison of Stroke Pre and Post Therapeutic Lifestyle Intervention Efficacy?

Research Assistants/Medical Students: Vanessa Rubel, Hannah Bulosan, Stephanie Matsuura,

Lifestyle interventions are a way to prevent, treat, and reverse diseases. The risk factors for stroke (i.e. obesity, hypertension, diabetes, smoking, etc.) are addressed by behavioral changes implemented by an individual undergoing therapeutic lifestyle intervention. By introduction of the Lifestyle Medicine Assessment (LMA) tool at the initial entry of a stroke patient into therapeutic lifestyle intervention we are able to capture subjective information and quantify that data into five objectively measurable domains- connectedness, movement, nutrition, recovery, and substance use. Our study will determine if a six month therapeutic lifestyle intervention produces any significant changes within deficient domains and across all five domains as reflected in the Lifestyle Score Total. These scores will also be assessed by grouping of patients based on their initial risk acuity scorecard categorization of: low, moderate, or high risk.

Utilization of a Risk Acuity Scorecard for Comparison of Stroke, Pre and Post Therapeutic Lifestyle Intervention

Vanessa Rubel[1,2], Stephanie Matsuura[1,2], Hannah Bulosan[1,2], Dariann Davis[1,3], Tefaiha Ashe[1,5], Jonathan Aoki[1,4], Connor Goo[1,2], Paul Smith MD[1], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]

[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]Hawaii Pacific University, Honolulu, HI, [4]University of Hawaii at Manoa, Honolulu, HI, [5]Mcmasters University, Hamilton, Ontario

Background

- The leading cause of long term adult disability and fifth leading cause of death in the United states is stroke. Incidence of stroke may be rising again due increased risk factors in the population including obesity and diabetes mellitus. Healthcare costs estimated with this rise are $34 billion per year (for medications, healthcare services, and missed days of work).[7]
- Lifestyle medicine is a rapidly expanding field that concerns a patient's lifestyle-related contributors to noncommunicable diseases, like stroke, by modifying their health behaviors. Examples of these health behavior modifications could be exercising more or quitting smoking, which should potentially lessen negative health outcomes.[2-3, 8]
- A lifestyle medicine assessment (LMA) is a tool that collects and analyzes a patient's health information in order to measure and alter modifiable risk factors. The health information provided to the clinician includes dietary habits, substance use, physical exercise, and more to examine a patient's health and health risks in order to prevent non communicable disease. [9]
- Modifiable risk factors for stroke include hypertension, diabetes mellitus, atrial fibrillation and atrial cardiopathy, dyslipidemia, sedentary behavior, obesity, diet/nutrition, substance use, inflammation, and infection. [4-6]
- Patients who have survived stroke typically experience an average of 2.38 comorbidities that are stroke-related. The 3 most common comorbidities observed are hypertension, cardiac related comorbidities such as arrhythmias or coronary artery disease, and diabetes. On average, according to Karatepe et al, patients experienced on average 3.9 complications, the most common of which was depression. [4]
- Patients with history of a prior stroke have an increased risk for future strokes as well as concomitant disability and mortality. The estimated risk for stroke recurrence is approximately 13-16% within the first year and an additional 4% for every subsequent year. Meaning that patients will have a 30% likelihood of recurrent stroke after five years and up to 43% after ten years. [1]
- Lifestyle modification can potentially lead to improvements in stroke related factors.[1]

Objectives

To determine if Hawaii Pacific Neuroscience (HPN) stroke patients who have had two or more lifestyle visits will have an improved LMA score (or improvement in one or more of the domains). Also, to investigate whether changes in LMA scores are correlated with changes in high risk factors for stroke (blood pressure, cholesterol, diabetes, smoking status, atrial fibrillation, diet/weight, exercise, and family history for stroke).

Methods

- Pre-survey data was taken from 8 patients from HPN's database who met the following criteria: had a previous stroke and had two lifestyle visits with Dr. Smith between October 2021 to July 2022.
- On initial and final visits, patients were given an LMA and PHQ-2 assessment. The stroke risk scorecard data was also taken from charts.
  - Final visits were administered in-person or over the phone.
- Stroke risk card assessment: 8 modifiable risk factors prevalent in stroke cases measured in three different categories: high risk, caution, and low risk. The three categories are assigned a score from 0-8. The higher the score in the "high risk" means a the patient was more likely at risk for stroke, the higher the score in the "low risk" category meant the patient was less likely at risk for stroke.
- LMA: consists of five different lifestyle categories: connection (time spent outdoors, socializing, mental health assessment), movement (amount of exercise the patient gets on weekly basis), substance use (control over usage of drugs, alcohol, etc), recovery (sleep patterns and how they deal with stressors), and nutrition (daily diet).
  - Total scores for the LMA and the stroke risk scorecard were calculated twice: once during the initial visit and another during the final assessment.

Results

- Of the 8 patients, 5 (62.5%) are female and 3 (37.5%) are male. Furthermore, 4 participants (50%) responded and answered survey over the phone.
- Average body mass index (BMI) is 26.89 and the average body weight is 154.22 lbs.
- There is no significance when comparing the scores of the five individual LMA domains (connection, movement, substance, recovery, and nutrition) over time.
- There is no significance in the overall LMA scores over time (p-value = 0.2072).
- There is no significance in the overall LMA scores when patients were categorized into low risk (p-value=0.125) or high risk (p-value=1) groups.
- There is no significance when comparing the individual LMA domains when patients were categorized in the low risk or high risk (connection high risk: NaN, connection low risk p-value=0.0947, movement high risk: p-value=1, movement low risk p-value=0.414, nutrition high risk p-value=1, nutrition low risk p-value=0.269, recovery high risk= NaN, recovery low risk p-value=1 substance high risk p-value=1 substance low risk p-value=0.181)
  - Although not significant, the low risk group showed an increased their individual domain scores after the initial visit.
  - The mean scores of individual LMA domains in the high risk group remained relatively unchanged after the initial visit.
- There is no statistically significant changes in LMA scores due to lifestyle interventions.

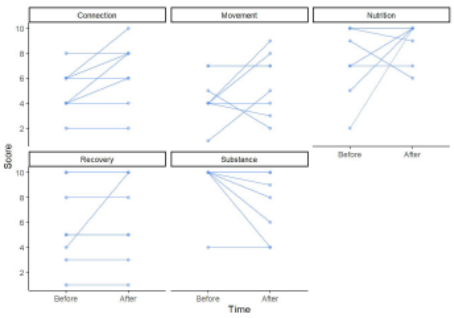


Figure 1: Comparing individual domain LMA mean scores.

Overall LMA Score

	Before, N = 8[1]	After, N = 8[1]	P-value
Overall Score	32.0 (4.8)	35.2 (6.8)	0.2072

[1]Mean (SD)

Table 1: Comparing the total LMA mean scores.

Overall LMA Score by Risk

	Low Risk		High Risk	
	Before, N = 4[1]	After, N = 4[1]	Before, N = 4[1]	After, N = 4[1]
Overall Score	32.8 (6.5)	39.5 (5.3)	31.2 (3.0)	31.0 (5.8)
P-value	0.125		1	

[1]Mean (SD)

Table 2: Comparing total LMA mean scores in low and high risk groups.

LMA Score by Domain and Risk

	Low Risk			High Risk		
Domain	Before, N = 4[1]	After, N = 4[1]	P-value	Before, N = 4[1]	After, N = 4[1]	P-value
Connection	5.00 (1.15)	8.00 (1.63)	0.0947	5.00 (2.58)	5.00 (2.58)	NaN
Movement	4.00 (2.45)	5.75 (2.22)	0.414	5.00 (1.41)	5.50 (3.11)	1
Substance	10.00 (0.00)	7.25 (2.75)	0.181	8.50 (3.00)	8.00 (2.83)	1
Recovery	8.00 (2.83)	9.50 (1.00)	1	3.50 (1.91)	3.50 (1.91)	NaN
Nutrition	5.75 (2.99)	9.00 (2.00)	0.269	9.25 (1.50)	9.00 (1.41)	1

[1]Mean (SD)

Table 3: Comparing individual domain LMA mean scores in low and high risk groups.

Conclusions/Discussion

- Lifestyle medicine can be defined by health and behavioral modifications which improve a patient's disease state, a few examples of these modifications could include implementing behaviors such as exercise, smoking cessation, and/or a healthier diet.
- The aim was to determine if certain lifestyle modifications reduced the high risk factors associated with stroke and thus, possibly reduce the chances of stroke recurrence.
- Studies such as this one are important because they raise awareness for secondary cardiovascular risk prevention as a topic needed to be explored more in a larger randomized setting.
- In contrast to our study, other small, nonrandomized studies have shown an improvement in lifestyle behaviors and risk factors.[1]
  - However, sample sizes have been too small to finalize conclusion on a reduction in stroke recurrence.
- Currently, few large-scale randomized controlled trials that examine secondary stroke reduction as their main objective have been conducted. Most have focused on primary cardiovascular stroke prevention for obvious reasons.[1]
- The present study was limited by a lack of patient data available due to the strict eligibility criteria and time needed to recruit more eligible participants.

Future Directions

- More research is needed to determine the effectiveness of the LMA and stroke risk scorecard in lowering stroke recurrence.
- More patients would be needed to be recruited overtime in future study to determine statistical significance and move this study past the pilot stage. Possibly recruit patients outside HPN community and of racial diversity (racial minorities)

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Disclosure/Correspondence

All authors reported no conflicts of interest.

Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: Paul Smith, MD, MPH, Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com

Hawaii Pacific Neuroscience Summer Internship Program
Honolulu, HI | August 13, 2022

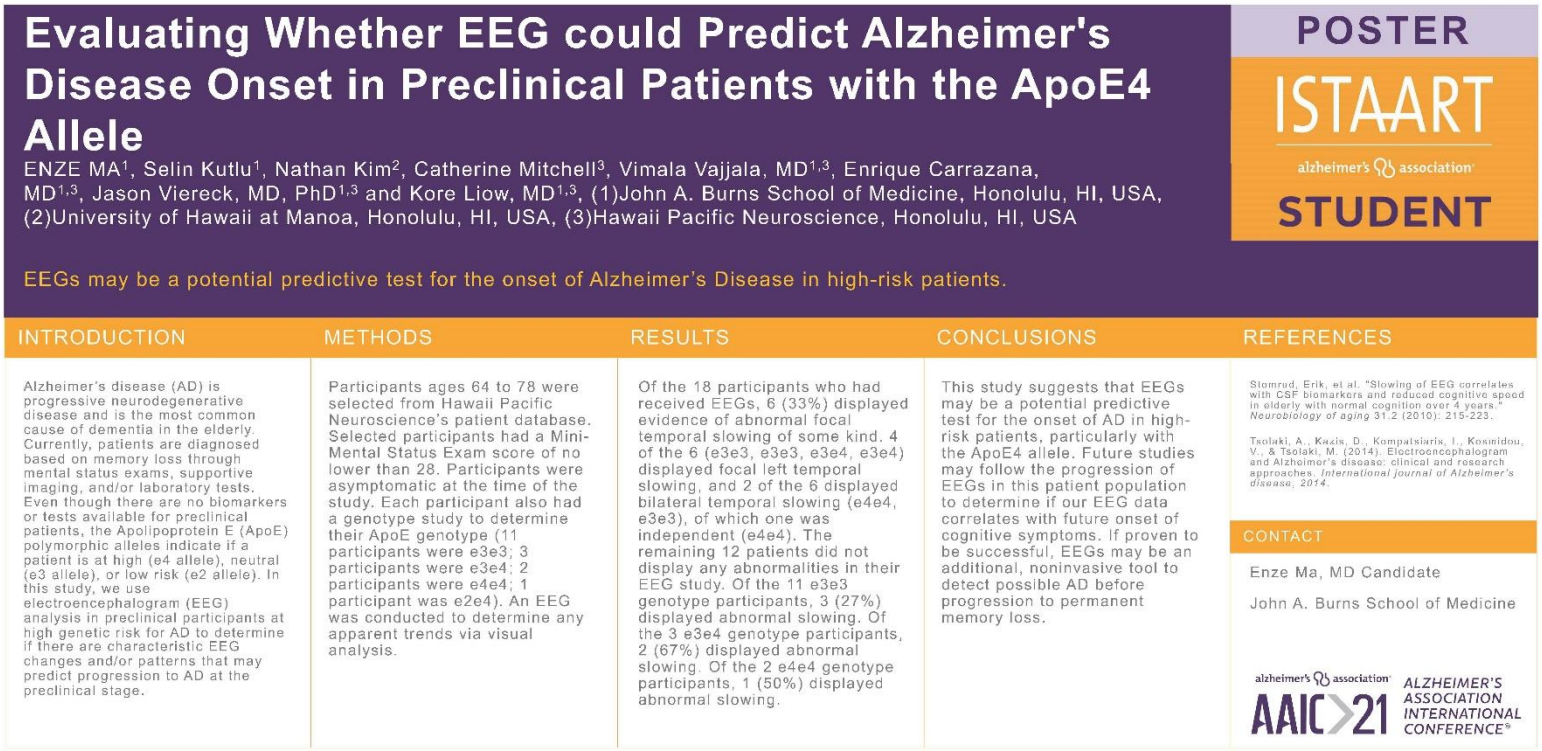
Brain Mapping Research Laboratory

Lead Investigator, Vimala Vajjala, MD, Neurologist & Director, EEG, Video-EEG & Clinical Neurophysiology Lab, Clinical Educator of Medicine (Neurology)

Can EEG Patterns Predict Onset of Preclinical Alzheimer's Disease?

Research Assistants: Medical Students Enze Ma, Charissa Tan, Nathan Kim

HPN BRITL Brain mapping research lab. is dedicated to studying how neuronal cortical networks interact with the external environment through neurophysiologic and neuroimaging modalities. The integration of behavioral neuroscience, neurophysiology and bio signal processing knowledge is translated into developing better understanding of cortical physiology and how to improve quality of life of those suffering from neurological disorders



Evaluating Whether EEG could Predict Alzheimer's Disease Onset in Preclinical Patients with the ApoE4 Allele

ENZE MA[1], Selin Kutlu[1], Nathan Kim[2], Catherine Mitchell[3], Vimala Vajjala, MD[1,3], Enrique Carrazana, MD[1,3], Jason Viereck, MD, PhD[1,3] and Kore Liow, MD[1,3], (1)John A. Burns School of Medicine, Honolulu, HI, USA, (2)University of Hawaii at Manoa, Honolulu, HI, USA, (3)Hawaii Pacific Neuroscience, Honolulu, HI, USA

POSTER

ISTAART

alzheimer's association

STUDENT

EEGs may be a potential predictive test for the onset of Alzheimer's Disease in high-risk patients.

INTRODUCTION

Alzheimer's disease (AD) is progressive neurodegenerative disease and is the most common cause of dementia in the elderly. Currently, patients are diagnosed based on memory loss through mental status exams, supportive imaging, and/or laboratory tests. Even though there are no biomarkers or tests available for preclinical patients, the Apolipoprotein E (ApoE) polymorphic alleles indicate if a patient is at high (e4 allele), neutral (e3 allele), or low risk (e2 allele). In this study, we use electroencephalogram (EEG) analysis in preclinical participants at high genetic risk for AD to determine if there are characteristic EEG changes and/or patterns that may predict progression to AD at the preclinical stage.

METHODS

Participants ages 64 to 78 were selected from Hawaii Pacific Neuroscience's patient database. Selected participants had a Mini-Mental Status Exam score of no lower than 28. Participants were asymptomatic at the time of the study. Each participant also had a genotype study to determine their ApoE genotype (11 participants were e3e3; 3 participants were e3e4; 2 participants were e4e4; 1 participant was e2e4). An EEG was conducted to determine any apparent trends via visual analysis.

RESULTS

Of the 18 participants who had received EEGs, 6 (33%) displayed evidence of abnormal focal temporal slowing of some kind. 4 of the 6 (e3e3, e3e3, e3e4, e3e4) displayed focal left temporal slowing, and 2 of the 6 displayed bilateral temporal slowing (e4e4, e3e3), of which one was independent (e4e4). The remaining 12 patients did not display any abnormalities in their EEG study. Of the 11 e3e3 genotype participants, 3 (27%) displayed abnormal slowing. Of the 3 e3e4 genotype participants, 2 (67%) displayed abnormal slowing. Of the 2 e4e4 genotype participants, 1 (50%) displayed abnormal slowing.

CONCLUSIONS

This study suggests that EEGs may be a potential predictive test for the onset of AD in high-risk patients, particularly with the ApoE4 allele. Future studies may follow the progression of EEGs in this patient population to determine if our EEG data correlates with future onset of cognitive symptoms. If proven to be successful, EEGs may be an additional, noninvasive tool to detect possible AD before progression to permanent memory loss.

REFERENCES

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CONTACT

Enze Ma, MD Candidate

John A. Burns School of Medicine

alzheimer's association AAIC 21 ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE®

Hawaii Neuro COVID Research Laboratory

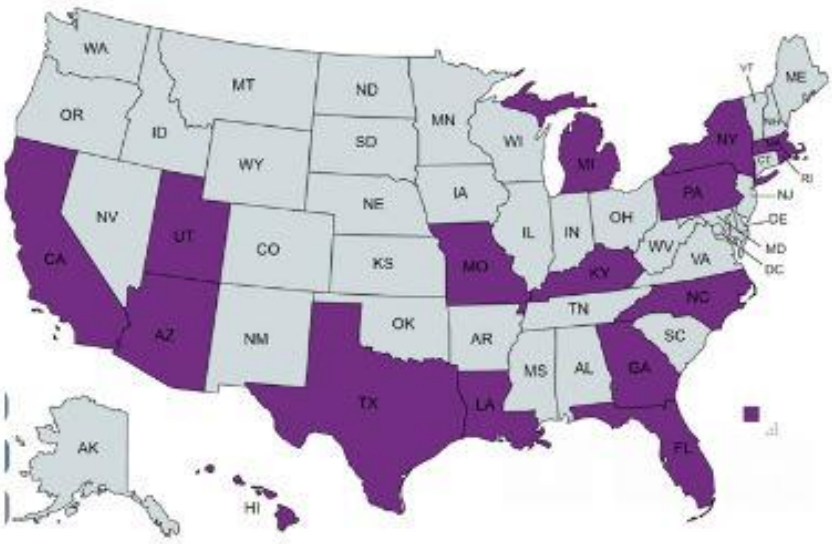
(Funded by NIH, NINDS Grant 3UL1TR002541-01S1)

Site Principal Investigator, Kore Liow, MD, Neurologist,
Director, Hawaii Neuro COVID Clinic,
Clinical Professor of Medicine (Neurology)
Research Assistants/Medical Students: Connor Goo (Lead), Hannah Bulosan, Theodore Huo, Stephanie Matsuura, Edward Weldon IV

As of April 2022, Hawaii Neuro COVID Clinic is 1 of 16 US sites selected by NIH to serve as a participating site for the NeuoCOVID Project.

The NeuroCOVID project has been initiated at New York University Langone Health to create and maintain a national resource documenting and studying neurological complications of COVID-19 funded by NINDS, NIH National Center for Advancing Translational Sciences through its Clinical and Translational Science Awards Program.

COVID-19 Neuro Databank:
The databank will collect information on adults, children with confirmed COVID-19 infection to assess neurological symptoms such as fatigue, brain fog, headache, loss of smell & taste, pain, numbness, autonomic dysfunction and others.



COVID-19 Neuro Biobank: The biobank will collect a wide variety of biosamples, including blood, plasma, cerebrospinal fluid, and tissue, from patients who have COVID-19 and experience neurological complications.

More Information: Hawaii Neuro COVID Clinic or NIH website, NYU website

Hawaii Neuro COVID Research Laboratory

Lead Investigator, Enrique Carrazana, MD,
Neurologist & Publication director,
Clinical Educator of Medicine (Neurology)

COVID-19 Olfactory Dysfunction: Differences in Prevalence Among Ethnicities & Variants in Hawaii NeuroCOVID Clinic

Research Assistants/Medical Students: Hannah Bulosan,

Olfactory dysfunction is widely known as one of the cardinal symptoms of COVID-19 infection. While earlier studies have suggested differences in anosmia between ethnic groups, the amount of available data at the time limited studies to compare primarily Asians and Caucasians. Since then, data regarding populations such as Africans and Latinos have been published and will be used to determine the prevalence of loss of smell as in a wider variety of groups. In addition to analyzing ethnic data, this study will also use epidemiological data regarding which strains of COVID-19 were prevalent in various regions throughout time in order to elucidate the impact of variants on anosmia.

Diagnostic tools for evaluating long-covid-19 syndrome (LCS): a systematic review at Hawaii NeuroCOVID Clinic

Research Assistants/Medical Students: Stephanie Matsuura

Long Covid Syndrome (LCS) is becoming more and more prevalent across the world. Symptoms of LCS such as fatigue, shortness of breath and brain fog can be very debilitating for patients. Currently, there is no universal standard for evaluating and diagnosing LCS in patients. This review will look at the different methods and scales that have been used to evaluate LCS in previous studies and compare them to each other. The Review aims to make practical suggestions as to the use of scales for evaluating LCS for the researchers and practicing clinicians.

Exercise Intolerance Following COVID-19: Comparing and Contrasting Impact of Different Viral Infections

Research Assistants/Medical Students: Edward Weldon, I

Emerging literature continues to elucidate effects of COVID-19 that contribute to lasting exercise intolerance in many recovering patients. However, what is the severity and duration of these effects compared to other viral infections such as influenza and EBV? Is COVID-related exercise intolerance different than these other infections and how do the mechanisms create intolerance compare? By answering these questions, we hope that our research will better inform how to prevent and treat exercise intolerance both regarding COVID-19 and other viral infections.

COVID-19-Related Guillain-Barré Syndrome: Comparing Differences Between Variants and Other Viral Infection-Related Guillain-Barré Syndrome

Research Assistants/Medical Students: Theodore Huo

Since the emergence of the COVID-19 global pandemic, there has been evidence showing a relationship between Guillain-Barré syndrome (GBS) and COVID-19 infection. Our project seeks to compare GBS occurrence rates and severity among COVID-19 variants and across populations in different geographic locations. In assessing severity, we will investigate the occurrence of known GBS sequelae such as chronic inflammatory demyelinating polyradiculoneuropathy (CIPD). We will also compare COVID-19 GBS to GBS seen with other viral infections such as influenza A (H1N1), avian influenza, and zika virus.

Neuromuscular Research Unit

Lead Investigator, Jason Chang, MD,
Physiatrist & Director, *Neuromuscular Rehabilitation Center*
Clinical Assistant Professor of Medicine (Neurology)

Investigating the Neuropathic Electromyography Findings in COVID-19 Patients

Research Assistants/Medical Students: Nathan Kim

COVID-19 is an acute infectious respiratory disease caused by infection with the SARS-CoV-2 virus. Although symptomatic patients with COVID-19 predominantly present with respiratory complaints, neurological manifestations have become increasingly recognized. However, the prevalence of these neurological complaints has been poorly quantified. A diagnostic procedure commonly utilized in the evaluation of patients with neuropathy is electromyography (EMG). Therefore, this study seeks to investigate the presence of neuropathic EMG findings in patients who previously contracted COVID-19.

Investigating the Neuropathic Electromyography Findings in COVID-19 Patients

Nathan Kim[1,2], Anna Fan[1,3], Matthew Calumpit[1,4], Renzelle Ponce[1,5], Connor Goo[1,2], Jason Chang, MD[1], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]

[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu, HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]University of Hawaii at Manoa, Honolulu, HI, [4]Drexel University, Philadelphia, PA, [5]Hawaii Pacific University, Honolulu, HI

Background

Coronavirus disease 2019 (COVID-19) is an acute infectious disease caused by the SARS-CoV-2 coronavirus. COVID-19 patients commonly present with symptoms including fatigue, fever, cough, headache, and symptoms of upper respiratory tract infection, but reports of neurological manifestations in the disease have become increasingly recognized, occurring in one-third of all COVID-19 patients.

Electromyography (EMG) is a diagnostic procedure commonly utilized in the evaluation of patients with neuropathy. Previous studies have found associations of myopathic EMG changes in critically ill COVID-19 patients, however there is limited research detailing the neuropathic EMG changes involved in COVID-19 patients. This study aims to evaluate the neuropathic EMG findings among previously diagnosed COVID-19 patients in Hawaii and identify possible correlations.

Objectives

To investigate the neuropathic EMG findings in patients previously infected with COVID-19.

Methods

A single-centered, retrospective chart review was performed using the eClinicalWorks electronic medical record data of patients treated at Hawaii Pacific Neuroscience from 2019-2022. Patients were identified using the ICD-10 code for COVID-19 U07.1 and U09.9. Patients were selected based on inclusion and exclusion criteria listed below. Demographics including age, sex, and ethnicity were collected for each patient. Additionally, information on chief complaint, EMG findings, past medical history, and neurological review of systems were collected for each patient.

Inclusion Criteria

- Patient has COVID-19 ICD 10 code U07.1 or U09.9
- Patient has EMG conducted following COVID-19 diagnosis

Exclusion Criteria

- Patient has EMG conducted prior to COVID-19 diagnosis
- Patient has no EMG study
- Patient has limited data in chart (i.e. did not receive full workup)

Results

Patient Information

Case	Sex	Age	Race/Ethnicity	Reason for EMG Study	Hospitalization Due to COVID-19
1	M	32	Native Hawaiian/Pacific Islander	Bilateral arm pain	No
2	F	37	Hispanic	Carpal tunnel syndrome	No
3	M	52	Native Hawaiian/Pacific Islander	Paresthesia	Yes
4	F	54	Caucasian	Pain and paresthesia	No
5	M	66	Caucasian	Numbness following COVID-19 infection	No
6	M	74	Caucasian	Weakness and Guillain-Barre Syndrome	Yes
7	M	75	Caucasian	Differentiate radiculopathy and polyneuropathy	Yes

Table 1: Patient Information

Neurological Review of Systems (ROS)

Case	Falls	Numbness	Pain	Tingling	Trouble with Balance	Dizziness	Fatigue
1	No	Yes	Yes	Yes	Yes	Yes	No
2	No	No	Yes	No	No	No	No
3	No	Yes	No	No	No	No	No
4	No	No	Yes	No	No	No	No
5	Yes	No	No	No	Yes	No	No
6	No	No	No	No	Yes	No	No
7	Yes	No	Yes	No	Yes	Yes	No

Table 2: Neurological Review of Systems (ROS)

EMG Findings

Case	Radiculopathy	Polyneuropathy	Myopathy	Plexopathy	Myelopathy	Entrapment Neuropathies	Guillain-Barre Syndrome
1	Right C6 motor radiculopathy	None	None	None	None	Carpal tunnel syndrome, left upper limb	None
2	Left C5-6 motor radiculopathy	None	None	None	None	Carpal tunnel syndrome, unspecified upper limb	None
3	Left S1 motor, Right L5-S1 motor radiculopathy	None	None	None	None	None	None
4	None	None	None	None	None	Carpal tunnel syndrome, bilateral upper limbs	None
5	Left C6-7 and L4 motor, Right S1 motor radiculopathy	None	None	None	None	Carpal tunnel syndrome, left upper limb	None
6	Multilevel bilateral lumbar motor polyradiculopathy	Acute motor and sensory axonal neuropathy	None	None	None	None	Guillain-Barre Syndrome
7	Radiculopathy, lumbar region	Mixed purely motor axonal polyneuropathy	None	None	C4-C5 cervical disc disorder with myelopathy	None	None

Table 3: EMG Findings

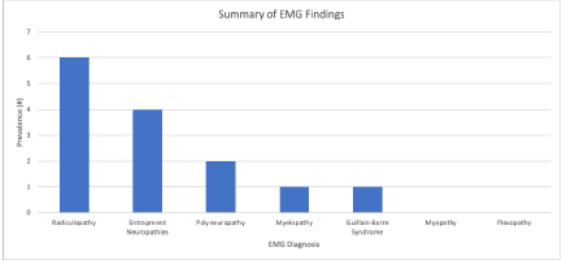


Figure 1: Summary of EMG Findings

Conclusions/Discussion

Among the seven patients, evidence of radiculopathy, polyneuropathy, and entrapment neuropathy were the most common EMG findings. Interestingly, no patients displayed evidence of myopathy, a finding that has previously been shown to occur in patients with severe cases of COVID-19. However, this could possibly be explained by the timing of when the EMG study was performed. In this study, EMG studies were performed in an outpatient setting where patients are in the subacute phase of COVID-19 and experiencing symptoms of long COVID. This is in contrast with other studies involving critically ill patients who are in the acute phase of COVID-19 and may be experiencing muscle breakdown due to inactivity as well as possibly taking exogenous steroids which could explain the presence of myopathic EMG findings.

Three patients in this study were hospitalized as a result of COVID-19. These patients likely experienced more severe cases of COVID-19 compared to patients not hospitalized. One patient with an extremely severe case of COVID-19 displayed several EMG findings including multilevel bilateral lumbar motor polyradiculopathy, acute motor and sensory axonal neuropathy, and Guillain-Barre syndrome (GBS). Other studies have also found evidence of EMG findings of GBS linked to COVID-19. Thus, GBS may be a potential EMG finding that may be linked to severe cases of COVID-19. However, further research is needed to determine the strength of this correlation.

One limitation of this study was the limited sample size. Infrequent ordering of EMG studies and the fact that EMG studies are typically not ordered for patients aside from those with severe complaints and comorbidities can likely account for this. Another limitation was the retrospective nature of this study. This study depended on the accurate record-keeping of patient charts. Finally, drug adverse effects and comorbid conditions could not be excluded. Some of the neuropathic EMG findings could potentially be attributed to pre-existing comorbidities prior to and after COVID-19 infection.

Future Directions

Future studies should focus on evaluating EMG findings in a larger population. Expanding this study to include COVID-19 patients from other hospital systems and clinics may more accurately reflect the population of Hawaii. Furthermore, thorough assessment of the severity of COVID-19 symptoms experienced by patients could provide additional context to the neuropathic EMG changes.

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Disclosure/Correspondence

All authors reported no conflicts of interest.
Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: Jason Chang, MD, Jason Viereck, MD, PhD
Correspondence or reprints: kliow@hawaiineuroscience.com

TBI Research Unit

Lead Investigator, Kent Yamamoto, MD
Physiatrist & Director, *Concussion & TBI Center*
Clinical Assistant Professor of Medicine (Neurology)

Can Mild to Moderate Exercise Modalities actually Enhance Recovery Following Traumatic Brain Injury?

Research Assistants/Medical Students: Edward Weldon, I

Long standing literature has shown that contact sports and strenuous exercise should be avoided following traumatic brain injury (TBI).. The majority of this research focuses on treadmill aerobic exercise which may be jarring to the patient's recovering brain. Furthermore, for patients with concurrent lower body injuries, treadmill exercise may not be possible. However, emerging literature indicates that some level of mild to moderate exercise may enhance patients' recovery time. We aim to analyze TBI patients' exercise modalities and patterns following TBI in order to identify effective exercises that improve symptoms and recovery time. Chart review to identify demographics, TBI severity, discharge from hospital time.

Impact of Return-to-Exercise on Traumatic Brain Injury Recovery in a Community Setting

Edward Weldon[1,2], Tracy Van[1,3], Ana Nakamura[1,4], Chancen Law[1,5], Ryan Nakamura[1,2], Meliza Roman[2], Connor Goo[1,2], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]
[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]Skaggs School of Pharmacy, University of Colorado, Aurora, CO, [4]University of Santa Barbara, Santa Barbara, CA, [5]Kamehameha Schools, Honolulu, HI

Background

Traumatic Brain Injury (TBI) is a significant cause of mortality and disability worldwide, occurring when external trauma damages the brain causing physical, cognitive, or psychological defects. Exercise recommendations following a TBI remains a highly debated topic with long-standing literature and conventional approaches to recovery suggesting that return to strenuous exercise should be avoided following a TBI. However, emerging literature indicates that some level of mild to moderate exercise may enhance a patient's recovery time. Majority of this research, however, focuses on closely monitored, sub-symptom, aerobic treadmill exercise in a laboratory setting in younger, more neuroplastic patients. Given that this is likely an unrealistic plan for the average person, this study aims to survey Hawaii's diverse population in a community setting to identify trends in exercise and recovery for TBI patients to shape recommendations on return to exercise. Furthermore, advanced age has been associated with delayed or incomplete recovery, thereby prompting a more generalizable study for ages beyond those previously researched. This study also aims to identify health inequities and factors contributing to different outcomes, which will inform efforts to address said inequities.

Objectives

- To investigate the relationship between exercise modalities, intensities, and patterns following TBI and recovery
- To identify health inequities and barriers to recovery that may negatively impact recovery

Methods

- Retrospective chart review of patients at Hawaii Pacific Neuroscience (HPN) with TBI between January 2020 and January 2022
- Data collected from patients included demographics, etiologies, ICD-10 codes, and symptoms at diagnosis
- Phone surveys were performed using a self-generated questionnaire evaluating symptom duration, recovery methods, employment, barriers to recovery, exercise patterns post-TBI, and perceptions on exercise and recovery
- Statistical analyses were performed using RStudio

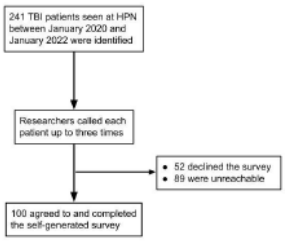

Figure 1. Patient selection and study design

Results

Characteristic	Less than 2 years (N = 37)[1]	2 or more years (N = 63)[1]	Overall (N = 100)[1]	p-value[2]
Age at diagnosis	39 (20.0)	50 (15.5)	46 (16.0)	0.003 *
History of TBI	29.7% (11)	25.4% (16)	27.0% (27)	0.64
Gender				0.20
Male	51.4% (19)	38.1% (24)	43.0% (43)	
Female	48.6% (18)	61.9% (39)	57.0% (57)	
Race				0.26
White	43.2% (16)	44.4% (28)	44.0% (44)	
Asian	32.4% (12)	17.5% (11)	23.0% (23)	
NHPI	18.9% (7)	23.8% (15)	22.0% (22)	
Other Race	5.4% (2)	14.3% (9)	11.0% (11)	
Insurance Type				0.37
Medicare	10.8% (4)	20.6% (13)	17.0% (17)	
Medicaid	32.4% (12)	31.7% (20)	32.0% (32)	
Private	54.1% (20)	39.7% (25)	45.0% (45)	
Military	2.7% (1)	7.9% (5)	6.0% (6)	

[1] Mean (SD); % (N)
[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test
* Significant p-value

Table 1. Demographics

Characteristic	Less than 2 years (N = 37)[1]	2 or more years (N = 63)[1]	Overall (N = 100)[1]	p-value[2]
Exercise Modalities				
Resistance training	32.4% (11)	21.8% (12)	25.8% (23)	0.27
Running	26.5% (9)	20.0% (11)	22.5% (20)	0.48
Swimming/ Paddling	26.5% (9)	21.8% (12)	23.6% (21)	0.62
Biking	17.6% (6)	12.7% (7)	14.6% (13)	0.55
Martial arts	5.9% (2)	5.5% (3)	5.6% (5)	>0.99
Bodyweight fitness class	29.4% (10)	18.2% (10)	22.5% (20)	0.22
Hiking/ Walking	58.8% (20)	81.8% (45)	73.0% (65)	0.018 *
Other	26.5% (9)	10.9% (6)	16.9% (15)	0.057
Exercise Intensity				0.51
Mild	50.0% (17)	60.0% (33)	56.2% (50)	
Moderate	47.1% (16)	34.5% (19)	39.3% (35)	
Intense	2.9% (1)	5.5% (3)	4.5% (4)	
Average Workout Length				0.80
0 to 59 min	50.0% (17)	50.9% (28)	50.6% (45)	
60 to 89 min	32.4% (11)	36.4% (20)	34.8% (31)	
90+ min	17.6% (6)	12.7% (7)	14.6% (13)	
Days of exercise per week	4 (1.4)	4 (1.7)	4 (1.6)	0.75

[1] Mean (SD); % (N)
[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test
* Significant p-value

Table 3. Descriptive Summary of Patients' TBI Recovery by Symptom Duration

Characteristic	Mild (N = 50)[1]	Moderate (N = 35)[1]	Intense (N = 4)[1]	p-value[2]
Symptom Change				0.920
No change / improved with exercise	72.0% (36)	68.6% (24)	75.0% (3)	
Worsened with exercise	28.0% (14)	31.4% (11)	25.0% (1)	

[1] % (N)
[2] Fisher's exact test

Table 4. Symptom Change by Patients' Exercise Intensity

Characteristic	Less than 2 years (N = 37)[1]	2 or more years (N = 63)[1]	Overall (N = 100)[1]	p-value[2]
Cause of TBI				0.93
Fall	35.1% (13)	38.1% (24)	37.0% (37)	
Motor Vehicle Accident (MVA)	27.0% (10)	31.7% (20)	30.0% (30)	
Assault	5.4% (2)	6.3% (4)	6.0% (6)	
Sports	10.8% (4)	7.9% (5)	9.0% (9)	
Other	21.6% (8)	15.9% (10)	18.0% (18)	
Migraines or headaches	75.7% (28)	74.2% (46)	74.7% (74)	0.87
Dizziness, nausea, or vomiting	40.5% (15)	44.4% (28)	43.0% (43)	0.70
Balance issues	32.4% (12)	27.0% (17)	29.0% (29)	0.58
Change in memory	32.4% (12)	36.5% (23)	35.0% (35)	0.68
Psychiatric symptoms	18.9% (7)	23.8% (15)	22.0% (22)	0.57
Loss of consciousness	59.5% (22)	58.7% (37)	59.0% (59)	0.94
Hospitalized	43.2% (16)	47.6% (30)	46.0% (46)	0.67
Amnestic to event	13.5% (5)	14.3% (9)	14.0% (14)	0.91

[1] % (N)
[2] Fisher's exact test; Pearson's Chi-squared test

Table 2. Summary of TBI Symptoms of the Study Population by Symptom Duration

- The long recovery group (LRG) (2+ years) was significantly older than the short recovery group (SRG) (<2 years). Otherwise, demographic characteristics between the two groups were similar (Table 1)
- There were no significant differences in etiology and symptoms at diagnosis, indicating that TBI severity was similar for the groups (Table 2)
- LRG patients were more likely to walk/hike as their primary mode of exercise vs. SRG patients. No significant differences in exercise modality, intensity, frequency, or duration (Table 3)
- There were no significant differences between recovery groups and worsening symptoms with exercise (Table 4)

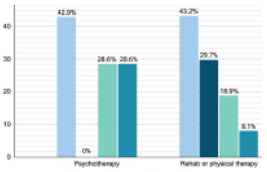

Figure 2. Therapy Utilization Frequency by Race

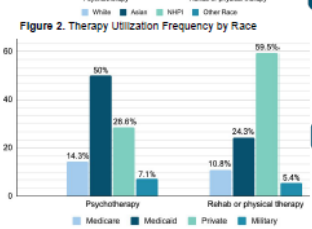

Figure 3. Therapy Utilization Frequency by Insurance Type

Conclusions/Discussion

Emerging research focusing on recovery recommendations for traumatic brain injury has shed new light on conventional literature. However, these studies included younger participants and their results are not generalizable to other ages.

The mean age of our study cohort was 46 years old. No significant differences between time-to-exercise, exercise modalities, frequencies, durations, and intensities with recovery times were found, suggesting that exercise was not a significant predictor of recovery time, and that exercise would not negatively impact patients' recovery. If encouraged to exercise following a TBI, it appears that patients will self-regulate a regimen that will not exacerbate their symptoms or recovery time. Additionally, most patients expressed satisfaction with their decision to exercise following TBI (90.9%) and nearly all patients said that they would recommend exercise to others recovering from a TBI (98.9%).

This research also highlights worrying trends in access to TBI recovery resources, such as psychotherapy, rehabilitation, and medications (Figures 2 and 3). The study found clear inequalities in access to resources when comparing both race and insurance type. Our research also indicates a notable trend of employment status change following TBI, with 64% of patients employed at the time of TBI but only 38% currently employed.

This study has a few limitations. Our research only includes TBI patients seen in a neuroscience clinic, which are possibly those who have suffered TBIs of greater than average severity, limiting the generalizability of the study. Additionally, retrospectively surveying patients may induce recall bias. However, this risk was minimized by only collecting data on TBIs occurring since 2020.

Future Directions

Conduct a prospective study of recovering TBI patients who exercise, and use exercise monitors such as apple watch and other technology to better track exercise, vitals, and recovery.

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Disclosure/Correspondence

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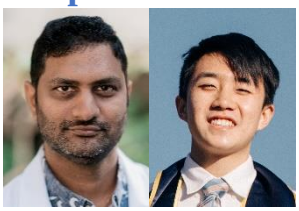
Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: Kent Yamamoto, MD, Jason Viereck, MD, PhD
Correspondence or reprints: kliow@hawaiineuroscience.com

Sleep Research Unit



Lead Investigator, Sriharsha Vajjala, MD, Director, *Sleep & Insomnia Center* ***, Clinical Educator of Medicine (Neurology)***

Research Assistants/Medical Students: Theodore Huo

Investigating CPAP Adherence Rates Among Sleep Apnea Patients in Hawaii

Continuous positive airway pressure (CPAP) is considered the gold standard treatment for patients with obstructive sleep apnea (OSA). Unfortunately, CPAP is known to be related to issues with adherence, with many patients abandoning the device or using it infrequently. However, adherence rates have not been described extensively in isolated, racially diverse island populations like those in Hawaii. The purpose of our project is to investigate CPAP adherence rates in Hawaii among patients with OSA who were treated at the Sleep and Insomnia Center at Hawaii Pacific Neuroscience

CPAP Adherence Among Obstructive Sleep Apnea Patients in Hawaii

Theodore Huo[1,2], Kalawena Kalehuawehe[1,3], Brooke Suzuki[1,4], Lorraine Sim[1,5], Connor Goo[1,2], Sriharsha Vajjala, MD[1], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2], Devashri Prabhudesai, MS[6], John J Chen, PhD[6]

[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, [3]University of Hawai'i- West Oahu, Kapolei, HI, [4]University of Hawai'i, Honolulu, HI, [5]University of California, Los Angeles, Los Angeles, CA, [6]JABSOM Biostatistics Core Facility, Department of Quantitative Health Sciences, University of Hawai'i John A Burns School of Medicine

Background

Obstructive sleep apnea (OSA) is a condition characterized by the obstruction or collapse of the upper airway while still maintaining respiratory effort during sleep.[1-3] Sleep-related breathing disorders like OSA increase all-cause mortality and negatively impact people's quality of life.[4,5] Implementing positive airway pressure (PAP) therapy is commonly used to treat patients with OSA and improve respiration.[6] The Hawaii Pacific Neuroscience (HPN) clinic utilizes three types of machines: continuous (CPAP), bi-level (BiPAP), and automatic (APAP).

It is important to continually assess patient adherence to PAP therapy. A patient is generally considered compliant to their therapy when they use the device at least 4 hours a night and 70% of the time.[7,8] Understanding the CPAP adherence rates in Hawai'i will improve therapeutic approaches and ensure that OSA patients receive optimal and manageable treatment.

This study establishes a foundational understanding of CPAP adherence rates of OSA patients in Hawai'i, while offering an opportunity to investigate other social, environmental, economic, and health-related correlations.

Objective

- To investigate and evaluate the CPAP adherence and compliance of patients diagnosed with OSA in Hawaii
- To determine any associations between variables - namely OSA severity - and CPAP adherence.

Methods

A retrospective chart review was conducted on patients diagnosed with OSA in the (HPN) *eClinicalWorks* database. 600 patients were identified using the ICD 10 code for OSA (G47.33). This cross-sectional data was collected from the most recent patient chart note between January 1, 2021- December 31, 2021.

Exclusion Criterion:

- Patients with coexisting diagnosis/ICD-10 codes for:
  - Unspecified Insomnia (G47.00)
  - Insomnia due to a medical condition (G47.01)
  - Central Sleep Apnea (G47.37)
- Patients not treated by Dr. Sriharsha Vajjala
- Patients with unclear or insufficient compliance ratings
- Patients with a compliance rating that fell outside of the 2021 timeframe

195 observations were made across 22 variables. Variables include sex, age, race/ethnicity, social history, cardiac history, BMI, weight, height, severity of OSA, type of PAP therapy, PAP adherance rate, and PAP compliance.

Compliance followed Medicare guidelines and was based around four ratings of adherence consistent in Dr. Vajjala's notes:

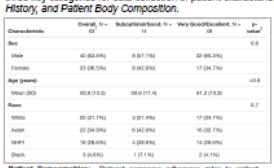
Compliant	Not Compliant
• Excellence ○ use machine over 4 hours a night for over 70% all nights night • Very Good ○ use at least 4 hours a night for only 70% of all nights	• Good ○ use machine over 4 hours a night for less than 70% all nights night • Suboptimal ○ uses less than 4 hours a night for less than 70% of all nights

Statistical data was analyzed using a Pearson's Chi Squared, Wilcoxon ranked sum test, and Fisher's exact test. Patients with missing values in any variables were excluded from the analysis of that particular variable. Alpha = 0.05 determined statistical significance.

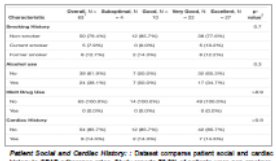
Results

Patient Characteristics vs CPAP Adherence

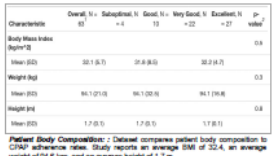
Patient characteristics were collected and reported by differentiating CPAP Adherence rates amongst OSA patients. The three key categories for data collection of patient characteristics were *Patient Demographics, Patient Social and Cardiac History, and Patient Body Composition.*



Patient Demographics: *Dataset compares adherence rates to patient demographics. Study reports 67.5% male representation, an average age of 59 y/o, and an ethnically well represented sample set.*



Patient Social and Cardiac History: *Dataset compares patient social and cardiac history to CPAP adherence rates. Study reports 78.2% of patients were non-smokers, 64.5% do not drink alcohol, 96.9% were not drug users, and 85.2% had no known history of cardiac complications.*



Patient Body Composition: *Dataset compares patient body composition to CPAP adherence rates. Study reports an average BMI of 32.4, an average weight of 94.6 kgs, and an average height of 1.7 m.*

- No significant association was observed between CPAP therapy adherence and patient characteristics
- CPAP therapy adherence was **significantly associated** with severity of OSA ($p = 0.02$)

Adherence to CPAP Therapy

Approximately 65% of patients (n= 126) with OSA (obstructive sleep apnea) were on CPAP (continuous positive airway pressure) therapy (Table 1), out of which almost 41% of patients (n = 51) showed *excellent adherence* to CPAP therapy (Figure 2).

Characteristic	N = 126[7]
Adherence to CPAP therapy	
Suboptimal	11 (8.7%)
Good	21 (16.7%)
Very Good	43 (34.1%)
Excellent	51 (40.5%)

[7] n (%)

CPAP: Continuous Positive Airway Pressure

Table 1: Adherence rates of patients on CPAP therapy based on determined compliance. N=126

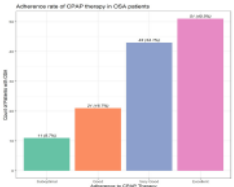


Figure 2: Adherence rates of patients on CPAP therapy based on determined compliance. N=126

Adherence to CPAP Therapy vs Severity of OSA

CPAP adherence was significantly associated with severity of OSA ($p = 0.02$). A reported 49% of patients with severe OSA has excellent compliance, while 85.7% of patients with mild/moderate OSA had poor compliance.

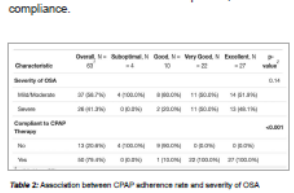


Table 2: Association between CPAP adherence rate and severity of OSA

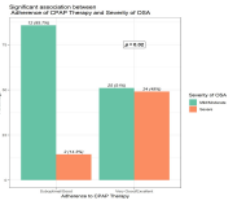


Figure 3: Association between CPAP adherence rate and severity of OSA

Conclusions/Discussion

This was the first study that evaluated CPAP adherence rates in Hawai'i. Our main finding showed that OSA severity was directly associated with improved adherence to CPAP therapy; this is consistent with similar studies done globally.[9] We found a significant difference in adherence rates among those who experience mild/moderate OSA, in comparison to those with severe cases of OSA. Likewise, previous studies have reported that having a higher frequency of observed interrupted breathing correlated with better adherence to CPAP therapy.[10]

The unique and ethnically diverse demographics of Hawai'i led the study to investigate possible correlations between factors such as BMI and social history, as they relate to CPAP adherence. The data collected showed no significant correlation between CPAP therapy compliance and BMI. The data also reports no significant correlation between social history, weight, or cardiac history when determining patient CPAP adherence. This data remains consistent with other retrospective chart review studies done in Singapore, and across the U.S.[9]

Because this was a single center and single physician case study, we had limited accessibility to medical records for any treatment done outside of HPN. Additionally, because we used a retrospective case review methodology, information of CPAP adherence could not be accurately reported if patients did not come in for their routine compliance check. Thus, many patients were excluded from the dataset. This study provides valuable insight into CPAP compliance across the population of Hawai'i, while paving way towards understanding how we may begin improving adherence rates amongst apnea patients.

Future Directions

Future directions should aim to explore:

- Differentiating and circumstantial variables affecting poor or suboptimal adherence rates to CPAP therapy. Follow-up phone interviews with poor or suboptimal adherence to CPAP therapy could potentially provide an explanation for poor apposition and pave the way for the development of innovative solutions.
- Ethnic, social, and economic correlations between CPAP adherence rates. Collecting information such as socioeconomic status, education, occupation, family/marital status, and cultural identity/background, could potentially present symbolic disparities amongst the population, and identify key themes in the evaluation of poor adherence rates.
- The inclusion of CSA, insomnia, and other apnea diagnosed patients. This incorporation of a wide-range of sleep disordered patients would increase the sample size and representation of patients on CPAP therapy.

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Disclosure/Correspondence

All authors reported no conflicts of interest.

Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: (Faculty Mentor) Sriharsha Vajjala, MD

Correspondence or reprints: kliow@hawaiineuroscience.com

Hawaii Pacific Neuroscience Summer Internship Program
Honolulu, HI | August 13, 2022

Parkinson's Research Unit

Lead Investigator: Jason Viereck, MD, PhD,
Neurologist & Director, *Parkinson's & Movement Disorders Center,*
Clinical Assistant Professor of Medicine (Neurology)
Research Assistants/Medical Students: ZoeAnn Kon

Does Parkinson's Disease Patients with Depression have a Worse Outcome Compared to Those without Depression?

In patients with Parkinson's disease (PD), depression is the most common psychiatric comorbidity and is often under-diagnosed and under-recognized. This can lead to worsened outcomes for patients and caregivers. To find the prevalence of depression in patients with PD at our institution using the Patient Health Questionnaire (PHQ-2). We retrospectively reviewed patients at the Hawaii Parkinson's Disease & Movement Disorders with PD. Including patients on sleeping medications and antidepressants using two self-rating scales (Zung Self-rating Depression Scale and 15-item Geriatric Depression Scale).

COVID-19 Impact on Depressive Symptomatology Among the Parkinson's Disease Population within Hawaii

Ana Tavares[3], ZoeAnn Kon[2], Brennan Lee[2], Richard Kainalu Rista[4], Jason Viereck, MD, PhD[1]
[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]Chaminade University of Honolulu, Honolulu, HI, [4]Creighton University School of Medicine, Phoenix, AZ

Background

Parkinson's disease (PD) is a progressive neurodegenerative disease that is associated with a breakdown of dopaminergic neurons in the substantia nigra of the brain. Salient characteristics of PD involve body rigidity, rest tremors, and a slowing of movement. Additionally, PD is associated with a high prevalence of psychopathology in individuals, including an increased risk for cognitive deterioration and a 30-40% prevalence rate for depression. Those who have comorbid affective disorders, like depression, are more likely to experience poorer health outcomes. Despite this, only 20% of all depressed PD patients receive treatment for their depression.

Hawaii's diverse cultural landscape is unlike that of other locations which may yield different scientific findings and outcomes. Unfortunately, a study that identifies the correlation between depression and severity of PD has never been done here before. This research is vital for improving intervention plans that lead to better health outcomes for the PD population of Hawaii.

Objectives

To identify the prevalence of depression in the PD population among our institution (Hawaii Pacific Neuroscience), to determine if depression is positively correlated with PD severity, and to clarify the impact the COVID-19 pandemic has had on the depressive symptomatology of the PD population of Hawaii.

Methods

We conducted a retrospective review of patient records from the Hawai'i Pacific Neuroscience (HPN) eClinicalWorks 11e software with a diagnosis of PD from June 18th, 2017, to June 18th, 2022, via International Classification of Diseases 10th Revisions, Clinical Modification (ICD-10) codes for PD: G20. Recorded data included: sex, age at diagnosis, gender, self-reported race (White, Hispanic, Asian, Native Hawaiian or Other Pacific Islanded [NHPI]) marital status, insurance, comorbidities (HTN, HLD, DM, Dementia, Anxiety, Depression), illicit drug use, alcohol use, smoking history, Parkinson's medications and dosages, and PHQ-2 scores from preCOVID-19 and most recent scores that were received during or post 2020. Socioeconomic variables were also recorded including insurance type and Zone Improvement Plan (zip) code of the patient's residence, with zip code serving as a proxy for other variables. To be included in this study, patients had to have PHQ-2 scores recorded before 2020 and during/after 2020, and they had to be taking medication to treat PD.

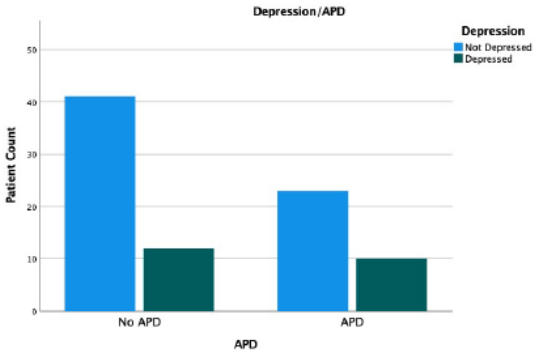
Depression was defined as a recorded PHQ-2 score of 3 or more during or after the year 2020 or having a diagnosis of depression. Severity of PD was measured by medication dosage amount and frequency, and presence of Dementia. ≥700 mg/day of a Levodopa and/or a Levodopa Equivalent Dosage (LED), ≥ 5 doses of an LED per day, and/or an ICD-10 code for Dementia (any subtype) was necessary for Advanced PD (APD) classification. <700 mg LED per day was classified as mild/moderate PD. LEDs were calculated based on a previously published algorithm from a systematic review by Tomlinson et al (2010).

Results

- In our sample (*N* = 33 , 86), 38.4% were assigned APD status based on the LED ≥700 MG cut-off, ≥ 5 dosing frequency, and/or a medical diagnosis of dementia. While (N = 22, 86) 25.6% were classified as depressed based on a PHQ-2 score of ≥3 and/or a medical diagnosis of depression.
- A paired samples t-test was run to evaluate the impact of COVID-19 on patient's PHQ-2 scores. There was no significant difference in PHQ-2 scores from before COVID-19 (M = 0.93, SD = 1.79) to during COVID-19 (M = 0.84, SD = 1.92). The mean decrease in PHQ-2 scores during COVID-19 was 0.09, with a 95% confidence interval ranging from -0.17 to 0.36.
- A Chi-square test for independence was used to understand the relationship between depression and APD. 45.5% of those with depression also had APD while 54.5% did not have APD. 35.9% of those with APD did not have depression and 64.1% did not have APD or depression.

Depression * APD Crosstabulation

			APD		
			No APD	APD	Total
Depression	Not Depressed	Count	41	23	64
		% within Depression	64.1%	35.9%	100.0%
		Adjusted Residual	.8	-.8	
	Depressed	Count	12	10	22
		% within Depression	54.5%	45.5%	100.0%
		Adjusted Residual	-.8	.8	
Total		Count	53	33	86
		% within Depression	61.6%	38.4%	100.0%



Conclusions/Discussion

This study aimed to build upon COVID-19 research on the affective consequences of the pandemic and identifying how these impacts have potentially caused more severe PD pathology at our facility. While our results suggested that there were no significant differences in PHQ-2 scores from before the pandemic to now, future researchers should continue to explore potential protective factors in this population here in Hawaii. Using an LED threshold of ≥700 mg, we found that 38.4% of our sample were classified as having the advanced disease, while the remaining 61.6% were classified as having mild/moderate disease. Our approach was similar to a study by Dahodwala et al., (2020) who used LED ≥ 1000 and ≥800 mg to identify individuals with advanced Parkinson's disease in Medicare claims data. We chose to increase APD sensitivity by lowering the threshold to LED ≥700 mg due to having a smaller sample size.

Our results suggest that the proportion of those who are depressed and have APD is not significantly different from the proportion of those without depression and APD. There appears to be no association between depression and APD classification.

Future Directions

Future studies may want to explore the impact of exercise and climate on depressive symptomology. Frequency, type, and location of exercise may have played an important role in lessening the effects of depression. Hawaii's sunny and warm climate may have also been a factor in these results as people living in warmer climates are more likely to spend time outdoors and in nature.

It is possible that the PHQ-2 was too sensitive of a measure, and we accounted for more people than were depressed. A more specific measure should be used next time. The PHQ-9 or Beck Depression Inventory Scale are two examples on what could be used in place of the PHQ-2.

Using a measure to help determine APD like the Unified Parkinson's Disease Rating Scale (UPDRS) would have been beneficial in ensuring more accurate APD classification.

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Disclosure/Correspondence

All authors reported no conflicts of interest.

Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: (Faculty Mentor), MD, Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com

Alzheimer's Research Unit

Lead Investigator, Kore Liow, MD,
Neurologist & Director, *Memory Disorders Center*
Clinical Professor of Medicine (Neurology)

Analyzing Barriers & Methods to Improve Clinical Trial Participation among Minority Population especially Asians and Native Hawaiian & Pacific Islands in Alzheimer's Disease Research

Research Assistants/Medical Students: Anson Lee

Alzheimer's disease (AD) is the most common neurodegenerative disorder in the United States and disproportionately burdens minority populations. However, clinical AD trials regularly face a shortage of eligible participants numbering in the thousands and this number is set to increase in the next several years. Previous research into barriers to clinical trial participation has found that economic constraints, structural and logistical obstacles, a lack of trust in medical institutions, or a scarcity of information about clinical trials, all negatively impact recruitment efforts. Amongst ethnic minority populations, Native Hawaiians and Pacific Islanders (NHPI), as well as Asians are the most underrepresented with Pacific islanders frequently found absent in AD clinical research. Minority representation is a key part of the generalizability of trial results, so identifying how ethnic minority engagement can be bolstered is crucial. This study explores the barriers to AD clinical trial participation in patients diagnosed with AD or mild cognitive impairment (MCI) in Hawai'i, the state with the largest relative population of Asian and NHPI individuals in the U.S.

Barriers & Methods to Improve Alzheimer's Disease Clinical Trial Participation Among Asian American and Native Hawaiian Populations

Anson Y Lee[1,2], Darrell Guittu[1,3], Rexton Suzuki[1,4], Lauren Pak[1,5], Kyle M Ishikawa, MS[2,6], Connor Goo[1,2], John J Chen, PhD[1,6], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore K Liow, MD, FACP, FAAN[1,2]

[1]Memory Disorders Center & Alzheimer's Research Unit, Hawai'i Pacific Neuroscience, Honolulu, HI, [2]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, [3]University of Hawai'i at Mānoa, Honolulu, HI, [4]Creighton University, Omaha, NE, [5]University of Oregon, Eugene, OR, [6]JABSOM Biostatistics Core Facility, Department of Quantitative Health Sciences, University of Hawaii John A. Burns School of Medicine, Honolulu, HI

Background

Alzheimer's disease (AD) is the most common neurodegenerative disorder in the United States and disproportionately burdens minority populations.[1] Yet, clinical AD trials regularly face a shortage of eligible participants numbering in the thousands and this number is set to increase in the next several years.[2,3] More than a quarter of clinical trials in the U.S. fail to recruit even a single participant, and only one-third of multicenter trials achieve their planned enrollment goals oftentimes leading many to prematurely close citing insufficient recruitment.[4,5] As such, recruitment barriers have been noted as the primary factor negatively impacting AD clinical research progress.[6]

While research has been conducted to assess the primary reasons for the lack of clinical trial participation in minority groups, most of these studies investigated African American patients.[7-9] Amongst minority populations, Asians and Native Hawaiians are the most understudied.[2,7,10] This study explores the barriers to AD clinical trial participation in patients diagnosed with AD or mild cognitive impairment (MCI) in Hawai'i, the state with the largest relative population of Asian and NHPI individuals in the U.S.

Objectives

Understanding barriers to Alzheimer's Disease (AD) clinical trial participation in Asian and Native Hawaiian (NH) patients diagnosed with AD or mild cognitive impairment (MCI) at a single institution.

Methods

This retrospective study included 187 (134 AD, 53 MCI) patients with a Mini-Mental State (MMSE) score ≥14 between 01/2022-06/2022. A 15-question telephone survey was conducted assessing demographics, barriers to participation, and improvement methods. Descriptive statistics were performed using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Incomplete surveys were included for analysis.

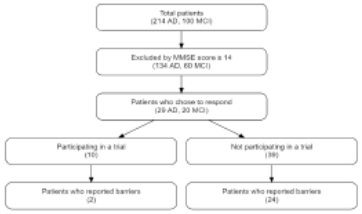

Figure 1. Diagram of surveyed patient breakdown

Results

49 patients responded (29 AD, 20 MCI) with 47 surveys incomplete having one or more questions unanswered. The mean patient age was 77 years with 51% being male and the mean MMSE score being 23.2. Surveys identified that the decision to participate in trials to help others differed by race (91% White, 80% NH, 29% Asian; p=0.023). Additionally, 5.6% of Asian, 22% of NH, and 32% of White patients surveyed were in an active AD clinical trial. The main reported barriers to participation were a lack of information about clinical trials and logistical complications (30% Asian, 80% NH, 45% White and 30% Asian, 20% NH, 27% White respectively). The top two most popular improvement methods were additional trial information given to family members (64% Asian, 88% NH) and patients (64% Asian, 88% NH). However, Asian patients chose increased financial compensation to be the third most important trial change (36%) whereas NH patients chose additional clinical trial hours (50%). White patients on the other hand listed additional patient trial information as their top change (62%) with a tie between additional trial information provided to family, complimentary transportation, and financial compensation (46%) as the second most important trial adjustment.

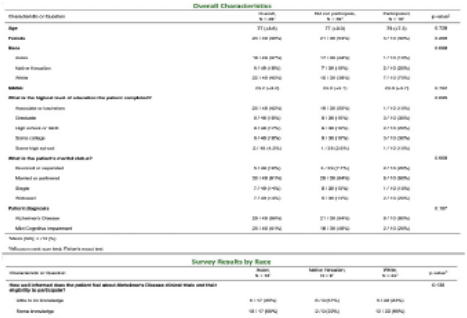

Table 1. Overall characteristics of surveyed patients

Table 2. Select survey results by patient race

Conclusions/Discussion

The results of this study reflect that Asian and NH patients feel they are often lacking information and face logistical obstacles when it comes to AD clinical trial participation. Previous research to increase minority trial participation had similar findings listing lack of information, lack of trial awareness, and time and resource constraints as among the top five barriers.[9] Interestingly, White patients shared similar barriers indicating that all three groups had similar impediments to involvement potentially indicating similar priorities and problems with how trials are run across across all three races.

The top two trial improvement methods were consistent across Asian and NH populations (additional information provided to family members and patients), but White patients were equally concerned with financial burdens, transportation logistics, and information provided to family members when considering their second most important trial change. Past studies which identified preferred incentives in aging AD trial patients, found transportation as the most popular incentive overall and financial compensation as being especially important in minority populations.[12] Both of these conclusions were contrary to the findings of this study.

Overall, a deficiency in information about AD clinical trials is the primary barrier to participation amongst Asian and NH patients followed by difficulty with coordinating transportation and time for trials. Increased outreach, education, and assistance with trial logistics in these communities should be pursued to improve rates of participation.

Future Directions

Future research should look into a larger cohort spanning a wider range of time to better generalize results and provide a more complete dataset.

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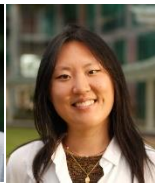
Disclosure/Correspondence

All authors reported no conflict of interests

Principal Investigator: Kore K Liow, MD, FACP, FAAN

Correspondence or reprints: kliow@hawaii.edu



Headache Research Laboratory

Lead Investigator, Vimala Vajjala, MD,

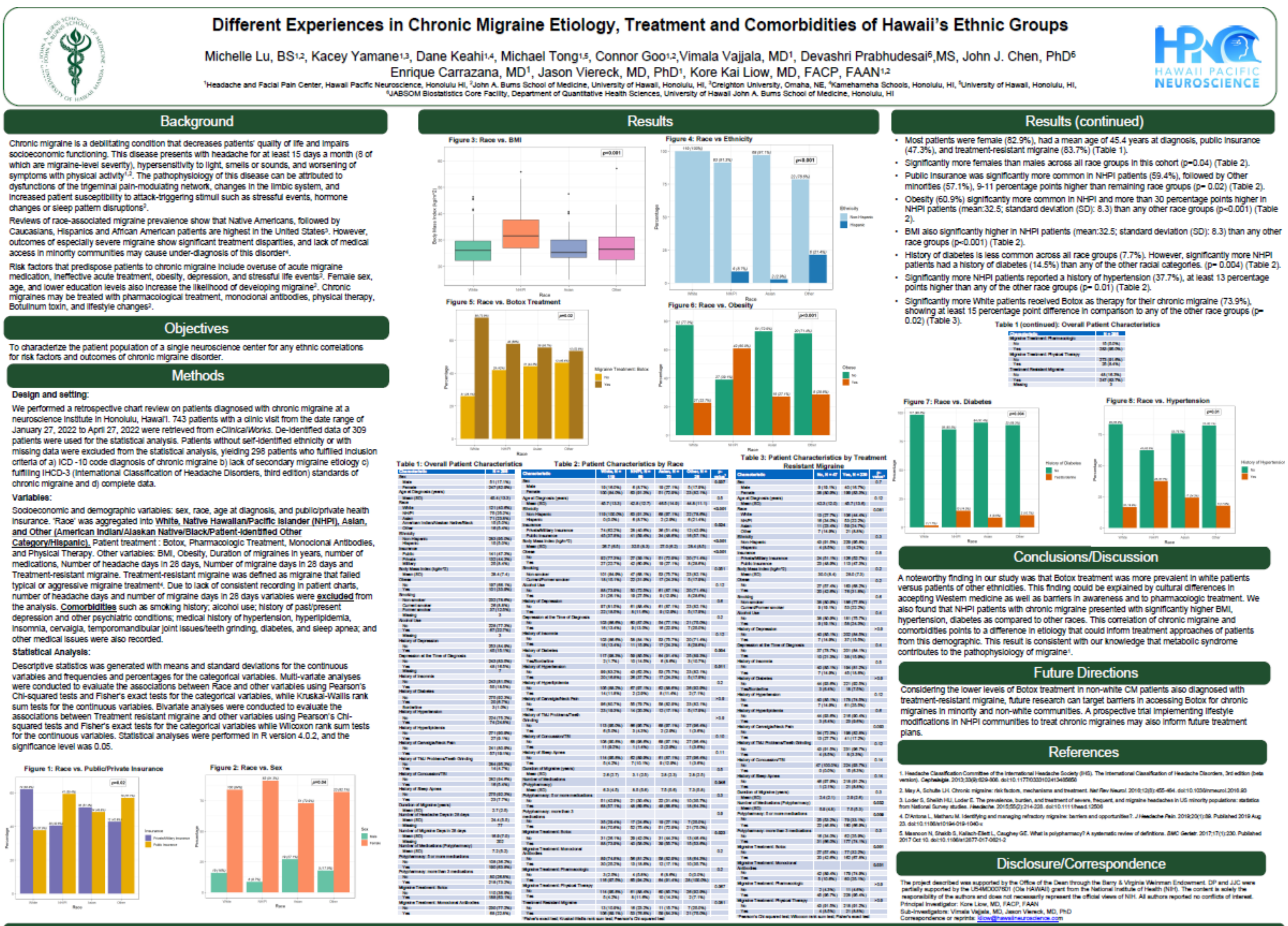
Neurologist & Director, [Headache & Facial Pain Center,](#)

Clinical Educator of Medicine (Neurology)

Does Headaches Disrupt Quality of Life Different in Minority Population?

Research Assistants: Medical Students Michelle Lu

Headaches of all kinds, including tension headaches, cluster headaches, migraines, trigeminal neuralgia and headaches that are refractory to treatment can be extremely disruptive to patients' quality of life, and occur more frequently in women of all races. We would like to examine the profiles of minority patients in Hawai'i and see whether they are characterized differently from white populations.



Pain Research Unit

Lead Investigator, Jason Chang, MD,
Physiatrist & Director, *Spine & Pain Management Center*
Clinical Assistant Professor of Medicine (Neurology)

Evaluating the Relationship Between Pain and Disability in Lumbar Radiculopathy Patients in Hawaii Undergoing Conservative Pain Treatment

Research Assistants/Medical Students: Amanda Chau

While the numeric rating scale (NRS) is a commonly used in assessing pain intensity, it only captures one dimension of a patient's pain experience and may not necessarily reflect the extent of a patient's resulting disability and their actual capacity to participate in daily activities. Can a patient with lumbar radiculopathy be completely rid of pain, yet still only gain back minimal functional capacity? This retrospective study will investigate the relationship between traditional NRS questionnaires and patients' level of disability or dependence according to the Rankin Scale. Doing so can help us better identify patient outcomes related to functional capacity following conservative pain treatment in lumbar radiculopathy patients.

Implementation of the Modified Oswestry Disability Index (MODI) in Outcome Assessments for Chronic Back Pain Patients Undergoing Conservative Treatment: A Quality Improvement Project

Amanda Chau[2], Sophia Chun[4], Brandon Roy[4], Amelia Weintraub[3], Connor Goo[1,2], Jason Chang, MD[1,2], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]
[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]University of California Los Angeles, Los Angeles, CA [4]University of Hawaii, Honolulu, HI

HAWAII PACIFIC NEUROSCIENCE

Background

- The **Numerical Rating Scale (NRS)** is one of the most commonly used pain scales in medicine and captures pain intensity
- The **Modified Oswestry Disability Index (MODI)** is a self-reported tool score that measures functional status in activities of daily living and is used for evaluating disability caused by acute or chronic back pain
- National guidelines for conservative management of chronic back pain include: patient education, therapeutic exercises, +/- pharmacological therapy

Objectives

To evaluate the clinical utility of supplementing the traditional NRS pain scale with the MODI questionnaire in understanding a patient's chronic pain experience.

Methods

Study Design

- Single-centered study conducted at Hawaii Pacific Neuroscience from June to July 2022
- Pain measured by NRS, disability measured by MODI
- Baseline NRS and MODIs recorded
- Patients underwent 6 weeks of conservative pain treatment
- 6-week follow-up NRS and MODIs were recorded
- %Δ Pain and %Δ Disability calculated as:

$$\Delta = \frac{\text{post} - \text{pre treatment}}{\text{pre treatment}} \times 100\%$$

(+) correlation: Pain and disability increase or decrease in same direction
(-) correlation: Pain and disability change inversely or do not change w/ respect to the other

Participants

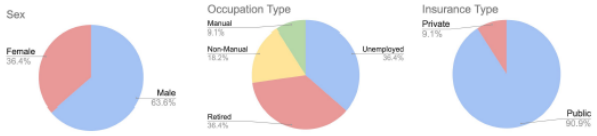
32 total participants
→ 2 patients without radiculopathy or lumbago w/ sciatica diagnosis excluded
30 participants
→ 6 patients lost to follow up excluded
24 participants
→ 10 patients who have not completed 6wks conservative treatment
14 participants
→ 3 patients with prior PT
11 participants

Analysis

- Partial correlation analysis
- Software: Stata Version 12.1
- Model adjusted for: age, sex, ethnicity, BMI, insurance type

Results

Sample Demographics



Correlation

Variable	Partial Correlation	p-value
ΔMODI	-0.9288	0.2417
Age	-0.2222	0.8574
BMI	-0.865	0.3346
Sex	0.9123	0.5492
Occupation	-0.7595	0.4509
Ethnicity	0.8012	0.4084
Insurance	0.7309	0.8239

Table 1. Partial correlations of ΔNRS

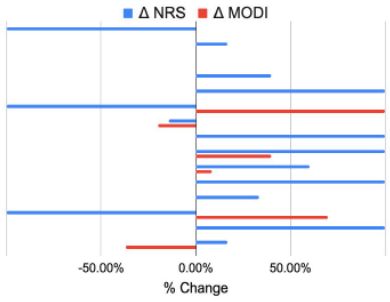
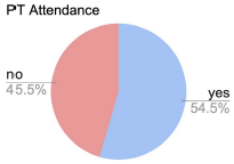


Figure 1. Change in NRS and MODI Scores Following 6 Week Conservative Treatment in Low Back Pain Patients

Current Treatment Guidelines as a Potential Barrier to Care



45% of patients were **unable to attend PT**

Of those who attended, each patient attended an **average of 9.6 hours of PT**

Conclusions/Discussion

- Our findings support prior literature that there is no correlation between pain and functional disability (p<.05)
- Both direction and magnitude of change in pain and functional disability widely varied
  - 3 patients had a positive correlation
  - 8 patients had a negative correlation
- Majority of patients had public insurance and/or unemployed status
- Nearly half of patients referred to PT were unable to attend PT

- This study emphasize that chronic pain is a multidimensional phenomenon, encouraging providers to look beyond isolated assessment such as pain intensity
- Our exploratory findings of low PT attendance show that although there are established national guidelines for chronic back pain treatment, they are often barriers to care and providers should take into account patient lifestyle in treatment planning
- Limitations of the study include small sample size, short duration of treatment, pain can be intermittent

Future Directions

- Investigate patient barriers to PT attendance and follow-up appointments
- Measure effect of patient undergoing conservative treatment for longer duration
- Evaluate MODI and NRS scores to patients undergoing both invasive and conservative treatment

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Disclosure/Correspondence

All authors reported no conflicts of interest.

Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: (Faculty Mentor), MD, Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com


MS Research Unit

Lead Investigator: Jason Viereck, MD, PhD,
Neurologist & Director, *Comprehensive MS Center,*
Clinical Assistant Professor of Medicine (Neurology)

Investigating the Prevalence of Psychiatric Disorders in MS Patients with Immune Comorbidities?

Research Assistants/Medical Students: Shin Chang

The immune system plays a vital role in the onset and progression of multiple sclerosis (MS). Studies have shown that certain immune comorbidities such as Hashimoto's thyroiditis, Type I diabetes, and psoriasis are more prevalent in patients with MS. Other studies have also indicated a higher rate of anxiety and depression among patients with MS. In this study, we will research the patterns of immune comorbidities in patients with MS and how they may correlate with diagnoses of depression and anxiety.

Psychiatric Disorders Associated with Comorbid Autoimmune Diseases in Multiple Sclerosis

Shin Chang[1,2], Donovan Roy[1,3], Jenna Okazaki[1,4], Plyfaa Suwanamalik-Murphy[1,5], Masako Matsunaga, PhD[2], Connor Goo[1,2], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]
[1]MS Research Unit, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]University of Hawaii at Manoa, Honolulu, Hawaii, [4]University of Portland, Portland, OR, [5]University of California, Davis, CA

Background

Multiple Sclerosis (MS) is an autoimmune inflammatory disease that affects the central nervous system. It is also the most common chronic disabling neurological disease in young adults, affecting nearly 1 million people in the US.

Recent studies have highlighted the high prevalence of comorbidities in patients with MS, in particular, autoimmune diseases such as immune thyroiditis, rheumatoid arthritis, and Sjogren's syndrome, and psychiatric disorders such as depression and anxiety. These comorbidities are important to consider because they may drastically impact the outcomes and quality of life of patients with MS.

Previous studies have found positive associations between autoimmune diseases and psychiatric disorders, but have not looked at how co-existing autoimmune diseases in patients with MS may further influence their risks of having psychiatric disorders. By collecting information such as demographics, socioeconomic factors, and clinical characteristics, our study hopes to analyze how environment factors may influence the prevalence of comorbid autoimmune diseases in MS and the types of health disparities associated with comorbid autoimmune diseases in MS.

Objectives

This study aims to understand the relationship between comorbid autoimmune diseases and psychiatric disorders in patients with MS, and to elucidate associated environment and health disparities within this relationship.

Methods

A retrospective chart review was conducted on patient records using the eClinicalWorks software at the Hawaii Pacific Neuroscience (HPN) in Honolulu, Hawaii, from January 2000 to June 2022. 147 patient records were identified using the ICD-9 (340) and ICD-10 (G35) codes for MS. 38 patients were excluded due to insufficient medical information or unclear MS diagnoses.

Information collected includes demographics such as sex, race, employment status, zip codes, and health insurance type; social history such as tobacco use, alcohol use, illicit drug use, and occupation status; and clinical characteristics such as co-existing cardiovascular conditions, autoimmune diseases, and psychiatric conditions. The zip codes were classified by socioeconomic need based on the 2021 Health Equity Index created by the Conduent Healthy Communities Institute. Autoimmune diseases considered include psoriasis, autoimmune thyroiditis, Sjogren's syndrome, inflammatory bowel disease, celiac disease, systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, vasculitis, and immune thrombocytopenia purpura. Psychiatric conditions collected were classified into depression, anxiety, and others, which included conditions such as dysthymic disorder, bipolar disorder, and attention deficit disorder.

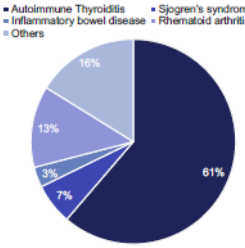
Information about the MS characteristics such as age at the time of MS diagnosis, the patient's ambulatory status, and the types of MS (Clinically isolated syndrome, relapsing-remitting MS, primary-progressive MS, secondary-progressive MS), were collected. 4 patients were previously diagnosed to have MS but later found to have neuromyelitis optica (NMO). NMO is also an autoimmune disease of the CNS that presents with clinical manifestations similar to that of MS, and was therefore traditionally classified as a type of MS. Given this similarity, NMO was added as a variable alongside the types of MS in our study.

Socio-demographic characteristics, clinical characteristics, and psychiatric/neurological conditions between the autoimmune disease status groups were compared using the Wilcoxon rank sum test for continuous variables and Pearson's Chi-squared test or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant. R (version 4.0.2) was used for all analyses.

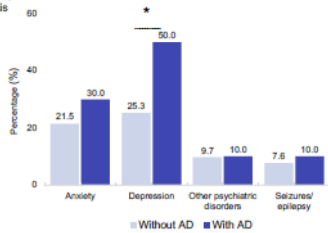
Results

- Of the 109 patients analyzed, 30 (27.5%) patients with MS had co-existing autoimmune diseases (ADs). A comparison between patients with and without comorbid ADs was made.
- The AD group was more likely to be female (86.7% vs. 67.1%; p=0.04) and older (median 54y vs. 45y; p=0.01). There was also a higher proportion of ADs found in patients with the primary progressive type of MS (30.8% vs. 10.5%), however, the difference in MS type did not reach statistical significance (p=0.13).
- The AD group had a higher proportion of depression (50.0% vs. 25.3%; p=0.014) and a higher proportion of anxiety (30.0% vs. 21.5%), however, the difference between the anxiety groups was not statistically significant (p=0.35).
- The AD group was also more likely to have one or more psychiatric/neurological conditions than the non-AD group (63.3% vs. 39.2%; p=0.024).

Prevalence of different comorbid ADs



Psychiatric/ Neurological conditions with and without AD



Type of MS or NMO, n (%)	Overall n = 109 (100%)	Without AD n = 79 (72%)	With AD n = 30 (28%)	p-value
Clinically isolated syndrome	12 (11.8%)	9 (11.8%)	3 (11.5%)	0.13
Relapsing-remitting	54 (52.9%)	41 (53.9%)	13 (50.0%)	
Primary progressive	16 (15.7%)	8 (10.5%)	8 (30.8%)	
Secondary progressive	16 (15.7%)	14 (18.4%)	2 (7.7%)	
Neuromyelitis Optica	4 (3.9%)	4 (5.3%)	0 (0.0%)	
(Missing)	7	3	4	

Comparison of other clinical characteristics factors between the AD and non-AD groups

- The AD group had a higher proportion of coronary artery disease (CAD) (13.3% vs. 2.5%; p=0.048), and as well as asthma (26.7% vs. 10.1%; p=0.038).

Clinical characteristics	Overall n = 109 (100%)	Without AD n = 79 (72%)	With AD n = 30 (28%)	p-value
Asthma				**0.038**
No	93 (85.3%)	71 (89.9%)	22 (73.3%)	
Yes	16 (14.7%)	8 (10.1%)	8 (26.7%)	
Coronary Artery Diseases				**0.048**
No	103 (94.5%)	77 (97.5%)	26 (86.7%)	
Yes	6 (5.5%)	2 (2.5%)	4 (13.3%)	
Hypertension, n (%)				0.076
No	82 (75.2%)	63 (79.7%)	19 (63.3%)	
Yes	27 (24.8%)	16 (20.3%)	11 (36.7%)	
Stroke, n (%)				0.063
No	105 (96.3%)	78 (98.7%)	27 (90.0%)	
Yes	4 (3.7%)	1 (1.3%)	3 (10.0%)	

Conclusions/Discussion

Our results showed that comorbid ADs in MS were more prevalent in female and older patients, but did not seem to be associated with other factors such as socioeconomic status, health insurance type, and alcohol use.

Overall, depression was found in a significantly higher proportion of MS patients with comorbid ADs. And although anxiety was not significantly more prevalent in MS patients with comorbid ADs, it still presented in a higher proportion. These results support previous studies about the positive associations between autoimmune diseases and depression but also suggest the increased risk of depression beyond the risks already posed by MS, by having comorbid ADs.

Other health disparities were also found in MS patients with comorbid ADs. Asthma and coronary artery diseases were significantly more common in the AD group, while hypertension and stroke, although not significantly more prevalent in the AD group, were found to be in a higher proportion.

Our research elucidates the need of addressing comorbid ADs in MS, given the higher prevalence of debilitating psychiatric disorders and cardiovascular diseases it is associated with. By showing these adverse health disparities, we hope to influence the treatment choices and cross-specialty care management of these patients, to help increase their treatment outcomes.

There are several limitations to this study. The small sample size may not represent the population as a whole and may have skewed or obscured trends. Another limitation is due to the retrospective chart review nature of this study. Our data relied on the information that is often self-reported by patients and depended on accurate patient charting. There may be instances where charting was incomplete or varied between different physicians.

Future Directions

Several factors that were collected, such as race, tobacco use, and frequency of exercise, could not be properly analyzed due to missing data from > 10% of the patients. Future steps in this study could include surveying patients to obtain these missing information to see how these factors influence the health disparities in patients. The sample size of the data can also be increased by expanding the data set to include MS patients from other health systems.

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Disclosure/Correspondence

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Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: (Faculty Mentor), MD, Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com

Epilepsy Research Unit

Lead Investigator, Vimala Vajjala, MD,
Neurologist, *Comprehensive Epilepsy Center*
Clinical Educator of Medicine (Neurology)

Investigating the Etiologies of Seizures in Patients Undergoing Video-EEG at Hawaii Comprehensive Epilepsy Center *Research Assistant/ Medical Students: Julia Jahansooz*

Routine electroencephalograms (EEG) are a first-line diagnostic tool used to detect abnormalities in brain waves. Outpatient Video-EEG monitoring (vEEG) is a more extensive, multi-day procedure that helps to determine the cause of these abnormalities. The distribution of etiologies of Hawaii Comprehensive Epilepsy Center patients who underwent an vEEG is currently unknown. This project aims to identify the percentage of patients with vEEG abnormalities and whether they experienced an epileptic versus a non-epileptic event. Other factors that will be considered include age, gender, duration of epilepsy, types of seizures, and number of anti-epileptic drugs (AED) used.

Investigating the Etiologies of Seizures in Patients Undergoing Video-EEG at Hawaii Comprehensive Epilepsy Center

Julia Jahansooz, MS[1,2], Corey Nishimura[1,3], Uiyeol Yoon[1,4], Taylor Matsubara[1,5], Kyle Ishikawa[2], Connor Goo[1,2], Vimala Vajjala, MD[1], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]
[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]University of Notre Dame, Notre Dame, IN, [4]Hawaii Pacific University, Honolulu, HI, [5]Wheaton College, Norton, MA

Background

Seizures are characterized by alterations in behavior or motor abilities and are diagnosed with an electroencephalogram (EEG), an ambulatory procedure used in the diagnosis of epilepsy.[2,5] Video-EEG (vEEG) monitoring is classically used to confirm, diagnose, and classify epilepsy.[2,3,6] Parnell et al. showed that the use of inpatient vEEG monitoring altered the epilepsy classification in 47.5% of patients, classified previously non-diagnostic studies in 20% of patients with epilepsy, and provided useful information in ~72% of patients studied.[6]

Hawaii is a diversified state for which there is limited research available on Native Hawaiians and Pacific Islanders. Collecting data from Hawaii Comprehensive Epilepsy Center will help to identify risk factors and guide diagnoses in these under-represented populations.

Objectives

To identify the percentage of patients with vEEG abnormalities and whether they experienced an epileptic versus a non-epileptic event. Other factors that were considered include age, gender, age at onset, seizure types, MRI findings, psychiatric comorbidities, and number of anti-epileptic drugs (AED) used.

Methods

We analyzed patient data from Hawaii Comprehensive Epilepsy Center between 2015-2022. We selected individuals 18 years or older at the time of vEEG. 248 subjects were identified. One was excluded for lack of a report. For patients who had multiple vEEG procedures, each report was considered independently totalling 294 vEEG reports. IRB exemption was granted by the University of Hawai'i at Manoa's Office of Research Compliance (protocol number: 2020-01010).

Data were collected from available medical records. Data included the presence of a vEEG abnormality, photic stimulation and hyperventilation procedure abnormalities, and the number of AEDs used. Abnormalities were considered an epileptic event if there was an EEG anomaly or if it correlated to an ictal event. Non-epileptic events were denoted by an event without a corresponding change on EEG. Events were subcategorized as focal, generalized, non-epileptic, or non-diagnostic. Additionally, magnetic resonance imaging (MRI) reports were examined for any structural abnormalities.

Epilepsy risk factors were recorded including family history of epilepsy and history of head trauma, developmental delay, abuse, and febrile seizures. Pre-existing epilepsy diagnosis, age at onset, and psychiatric comorbidities were noted as well. Psychiatric comorbidities included depressive disorder, anxiety disorder, psychosis, bipolar disorder, attention-deficit/hyperactivity disorder, post-traumatic stress disorder (PTSD), and somatoform disorder.

Characteristics of the vEEG reports were compared by Wilcoxon rank-sum tests for numeric variables and Fisher's exact tests for categorical variables. A p-value of <.05 was considered statistically significant for hypothesis testing. All analyses were conducted in R version 4.0.2 (R Core Team, 2020).

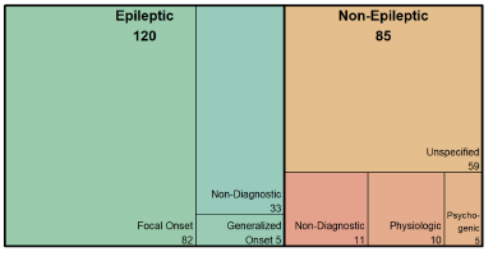
Results

Of the 294 vEEG reports derived from 247 unique individuals, 209 (84.6%) vEEGs were abnormal. Subjects with an abnormal vEEG were significantly more likely to have epilepsy ($p < 0.001$) and be taking an AED ($p < 0.001$).

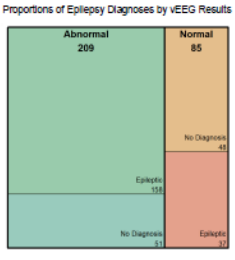
Of the abnormal vEEGs, 123 (58.9%) elicited epileptic events which were subcategorized into focal onset (69%), generalized onset (4.1%), and non-diagnostic (27%). Those with an epileptic event were significantly more likely to have epilepsy ($p < 0.001$) and be taking an AED ($p = 0.002$) than those with a non-epileptic event.

Of the 86 (41.1%) non-epileptic seizures, 6 (7.0%) were psychogenic, 11 (13.0%) were physiologic, 59 (69%) were unspecified non-epileptic, and 11 (13%) were non-diagnostic. Those with a non-epileptic seizure were significantly more likely to be Asian ($p = 0.046$) or Other ($p = 0.031$) race, have depression ($p = 0.003$), and have anxiety ($p = 0.035$).

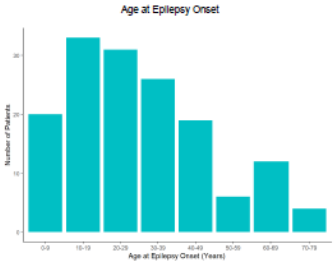
Types of Seizures



Proportions of Epilepsy Diagnoses by vEEG Results



Age at Epilepsy Onset



Conclusions/Discussion

-Of the 84.6% abnormal vEEGs, 21% were non-diagnostic and 77.6% of diagnosable non-epileptic events were classified as unspecified non-epileptic. Still, having a non-epileptic diagnosis can prevent the use of unnecessary AEDs.

-Our distribution of epilepsy onset peaks with the 10-19 year old age group which differs from epilepsy's typical bimodal distribution.[7] This unimodal arrangement could be due to the referral pattern of young adult patients to Hawaii Pacific Neuroscience.

-Our psychiatric comorbidity results align with previously conducted studies using EEGs. In a study by Ho et al., significant psychiatric disorder (PTSD, anxiety) correlations were found in patients with psychogenic non-epileptic seizures (PNES), other non-epileptic seizure disorders, and epilepsy. We further identified anxiety as a risk factor for non-epileptic seizures. A review by Asadi-Pooyaa and Sperling found individuals with PNES are significantly more likely to have major depression.[1] The increased likelihood of psychiatric comorbidities in non-epileptic seizures could be attributed to the increased time taken to attain a non-epileptic seizure diagnosis.[4]

-Our study was limited by the inclusion of multiple vEEG reports from the same patient. As each vEEG report was treated as a unique report, patient comorbidities and ethnicity information were duplicated for those patients. A second limitation was the use of non-standardized patient charts. Some information such as ethnicity was not always available.

Future Directions

Future studies could explore the relationship between PNES and epilepsy, risk factors for PNES, or risk factors in psychiatric comorbidities for PNES.

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Disclosure/Correspondence

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Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: Vimala Vajjala, MD, Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com

Neuromodulation & Brain Computer Interface Laboratory

Lead Investigator, Kore Liow, MD,
Neurologist & Director, *Hawaii Center for Neuromodulation*
Clinical Professor of Medicine (Neurology)
Research Assistants/Medical Students: ZoeAnn Kon

Is Neuromodulation like Vagal Nerve Stimulator Improving the Quality of Life, Reducing HealthCare Utilization in Geographic Island State like Hawaii?

Neuromodulation-based therapies such as vagal nerve stimulation (VNS) is used for patients with refractory epilepsy. Many studies have shown VNS reduces seizure frequency and the impact on quality of life (QOL) in patients implanted with VNS treatment in many epilepsy centers. However, the efficacy, utilization and QOL of life in VNS patients has not been looked at in geographic isolated island populations like those in the state of Hawaii and whether they are any different from other epilepsy centers. Our project seeks to investigate the efficacy, utilization and QOL impacts of patients implanted with VNS at the Hawaii Comprehensive Epilepsy Center and Hawaii Center for Neuromodulation.

Quality of Life in Patients with Refractory Epilepsy with Implanted Vagal Nerve Stimulation Using QOLIE-10

Ana Tavares[3], Richard Rista[4], Brennan Lee[2], ZoeAnn Kon[2], Connor Goo[2],
Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore Kai Liow, MD, FACP, FAAN[1,2]
[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu, HI, [2]John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [3]Chaminade University of Honolulu, Honolulu, HI, [4]Creighton University School of Medicine, Phoenix, AZ

Background

Vagal nerve stimulation (VNS) is a neuromodulation-based surgical treatment option that involves the implantation of a device that electrically stimulates the vagus nerve. It is commonly used as an adjunctive treatment in epilepsy when refractory to antiepileptic medications. The exact mechanism of which VNS achieves its effects is not known, but hypothesized to be afferent vagal projections to seizure-generating regions of the brain with desynchronized cortical activity. Many studies have shown VNS reduces seizure frequency,[1] and the impact on quality of life (QOL) in patients implanted with VNS treatment in the US cities,[6-8] However, the efficacy, utilization, and QOL of life in VNS patients has not been looked at in geographic isolated island communities like in the state of Hawaii.

Objectives

To evaluate the efficacy, utilization, and QOL impacts of patients residing in urban and rural communities implanted with VNS at Hawaii Comprehensive Epilepsy Center.

Methods

A voluntary telephone survey was conducted on new and follow-up patients seen at Hawaii Pacific Neuroscience (HPN) institution between July 1st, 2022 and August 1st, 2022, to investigate their quality of life (QOL) following insertion of the neuromodulation-based therapy of vagal nerve stimulation (VNS).

We administered a Quality of Life in Epilepsy-10 (QOLIE-10) questionnaire consisting of questions designed to assess the patients' rating of their memory, level of physical and mental well-being, energy, depression, worries about seizures and work, social limitations, and overall quality of life on VNS treatment.

Interviewers were trained in survey administration to ensure consistency of data collection and followed a pre-written telephone script. Surveys lasted about 15 minutes, and the surveyor documented patient responses to the survey in a de-identified online form in Google Docs (Google, Mountain View, CA). All patients gave verbal consent and acknowledged the right to decline the survey at any point. Patients were not offered incentives for survey completion. The inclusion criteria were the patients seen at HPN either in-person or via video conferencing within the past seven years. Patients who declined or failed to complete the survey were excluded from the study. When appropriate, the principal caregiver for the patient was interviewed.

Results

Among 37 epilepsy patients who underwent VNS implantation consecutively at our epilepsy center, 12 patients completed the interview and were included in the analysis. The mean age of participants was 45.25 years with a range of 11 - 73 years. More than half (83.3%) of respondents were female, and 100% were from an urban area based on zip code. The detailed description of patient clinical comorbidity characteristics of the study participants is shown in Figure 1.

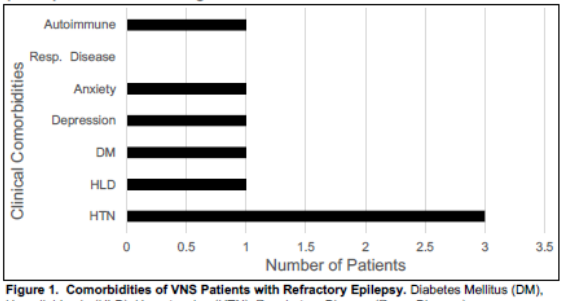

Figure 1. Comorbidities of VNS Patients with Refractory Epilepsy. Diabetes Mellitus (DM), Hyperlipidemia (HLD), Hypertension (HTN), Respiratory Disease (Resp. Disease)

Participants mean quality of life in epilepsy-10 (QOLIE-10) score was 29.33, with a minimum and maximum score of 21 and 44, respectively. By choosing a QOLIE-10 total score of > 25 as a impaired quality of life, 8 (66.67%) of participants fulfilled this criteria. Majority of patients reported rarely to never feeling downhearted and blue, and many also reported feeling a little to not at all fearful of having a seizure within the next month (shown in Table 1).

Table 1. Response of patients for quality of life assessment questions.

QOLIE-10 questions	All the time N (%)	Most of the time N (%)	Sometimes N (%)	Rarely N (%)	Never N (%)
Did you have enough energy for the last 4 weeks?	0 (0)	3 (25)	5 (42)	3 (25)	1 (8)
Have you felt down-hearted and blue?	0 (0)	1 (8)	2 (17)	6 (50)	3 (25)
	Not at all N (%)	**A little N (%)**	**Somewhat N (%)**	**A lot N (%)**	**A great N (%)**
How much are you bothered by work limitation?	5 (42)	0 (0)	0 (0)	2 (17)	5 (42)
How much are you bothered by social limitation?	1 (8)	3 (25)	7 (58)	1 (8)	0 (0)
How much are you bothered by memory difficulty?	1 (8)	0 (0)	5 (42)	3 (25)	3 (25)
How much are you bothered by physical effect?	3 (25)	4 (33)	4 (33)	0 (0)	1 (8)
How much are you bothered by mental effect?	3 (25)	3 (25)	4 (33)	1 (8)	1 (8)
How fearful are you of having seizure during the next month?	3 (25)	5 (42)	2 (17)	2 (17)	0 (0)

Conclusions/Discussion

At our institution in twelve patients, we observed improvement in various metrics of QOL through the self-reported QOLIE-10 questionnaire. Improvement in QOL metrics was significantly related to more favorable seizure outcome. With VNS, previous literature notes approximately 50-60% of epileptic patients achieve over 50% seizure reduction after 12 to 24 months of treatment. Here, ten (83.33 %) reported a reduction in their seizures with all (100%) patients reporting they tolerate the neuromodulatory device. Complete seizure freedom has been noted as the single most important factor of QOL in epileptic patients. Despite the significant improvements in seizure reduction, only four (33.3%) reported a good quality of life. Given the deleterious effects of recurrent seizures on the QOL in patients with refractory epilepsy, improved QOL metrics is an important treatment goal in this disorder.

Future Directions

Future directions can include follow-up to help determine whether improvements are sustained as they continue to use the VNS device. In addition, this patient population may have a baseline QOL and possibly completing this survey incrementally in the future could see how their baseline is changing as they continue treatment on the VNS device.

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Principal Investigator: Kore Liow, MD, FACP, FAAN
Sub-Investigators: Jason Viereck, MD, PhD

Correspondence or reprints: kliow@hawaiineuroscience.com

HAWAII PACIFIC NEUROSCIENCE

Clinical Research Center
Brain Research, Innovation & Translation Laboratory (BRITL)

Recent Publications & National Presentations

2021 Graduating Hawaii BRITL Scholars

2022 Graduating Hawaii BRITL Scholars

Student or Resident Involved PubMed Peer Reviewed Neuroscience Publications

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Evaluating Whether EEG Could Predict Alzheimer's Disease Onset in Preclinical Patients with the ApoE4 Allele: An Update. Kim N, Tan C, Ma E, Kutlu S, Mitchell C, Carrazana E, Viereck J, Vajjala V, Liow K. 2022 **American Epilepsy Society** Meeting, Nashville, TN December 2022

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Safety and Time to Second Doses in Pediatric and Adult Patients With Seizure Clusters Treated With Diazepam Nasal Spray in a Phase 3, Open-Label, Repeat-Dose Safety Study. James W. Wheless, R. Edward Hogan, Michael R. Sperling, Kore Liow, Daniel Tarquinio, Jay Desai, Dennis Dlugos, Gregory D. Cascino, Enrique Carrazana, and Adrian L. Rabinowicz, for the DIAZ.001.05 Study Group. 2nd **North American Epilepsy Congress,** May 2022

Timing to Administration and Ease of Dosing of Diazepam Nasal Spray Rescue Therapy for Seizure Clusters: Results from a Phase 3, Long-Term Open-Label, Repeat-Dose Safety Study. Jay Desai, MD; R. Edward Hogan, MD; James W. Wheless, MD; Michael R. Sperling, MD; Kore Liow, MD; Daniel Tarquinio; Dennis Dlugos, MD; Gregory D. Cascino, MD; Sunita N. Misra, MD, PhD; Adrian L. Rabinowicz, MD; and Enrique Carrazana, MD for the DIAZ.001.05 Study Group. **American Academy of Neurology Annual Meeting**, Seattle, WA, April 2022.

Safety of a Second Dose of Diazepam Nasal Spray Within 4 Hours in Patients with Seizure Clusters: Final Results From a Long-Term, Phase 3, Open-Label, Repeat-Dose Safety Study. Gregory D. Cascino, MD; Jay Desai, MD2; Daniel Tarquinio, DO; James W. Wheless, MD; R. Edward Hogan, MD; Michael R. Sperling, MD; Kore Liow, MD; Sunita N. Misra, MD, PhD; Enrique Carrazana, MD; and Adrian L. Rabinowicz, MD for the DIAZ.011.05 Study Group. **American Academy of Neurology Annual Meeting**, Seattle, WA, April 2022.

Positive Clinical Outcomes in Two Phase 2a Studies; ADAS-Cog in Alzheimer's and UPDRS in Parkinson's patients plus Markers of Toxic Cascade that Leads to Nerve Cell Death
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Safety Profile of Valtoco® (diazepam nasal spray) in Patients with Epilepsy: Final Results From a Phase 3, Open-Label, 12-Month Repeat Dose Safety Study. Wheless JW, Sperling MR, **Liow K**, Vazquez B, Segal EB,

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