HAWAII PACIFIC NEUROSCIENCE

Annual Report 2022-2023

Alzheimer's Neural Network EEG

Our Commitment to Excellence in Neuroscience Care, Research & Services in Hawaii

HONOLULU

2230 Liliha Street #104
Honolulu, Hawaii 96817, USA

WEST OAHU

94849 Lumiaina Street #203
Waipahu, Hawaii 96797

Call or Text (808) 261-4476 Fax (808) 263-4476
Dedicated Research Line (808) 564-6141, Fax (808) 443-0774
www.HawaiiNeuroscience.com Online Referral Form

About the Neuroscience Institute

Hawaii Pacific Neuroscience (HPN) is made up of over 20 different disease-specific, “one stop shop” centers of excellence provided by interdisciplinary collaborative team in neuroscience where the patient is the center and focus of all we do here.

Our mission is focused on:

- Care and services of highest quality including groundbreaking innovative research therapies
- Convenient access & locations
- Cost efficient care delivery pathways with measurable quality outcome data
- Culture of servant leadership – to teach & mentor and to care for all regardless of payment abilities

Click to View Video Introduction

https://www.youtube.com/watch?v=YTaER2HbiAg

History

Hawaii Pacific Neuroscience was founded in 2009 by Kore Kai Liow, MD and his wife, Michelle Liow after they moved to the island to retire only discover that patients must wait a long time to have access to quality neuroscience care especially those underserved populations in Hawaii. See full story featured on Hawaii KITV News Station.

https://www.youtube.com/watch?v=I5I4s_WCFl8

HAWAII PACIFIC NEUROSCIENCE

2023 is *our BEST Year yet….*

Lives changed because of our compassionate care	> 18,000 & Growing
Underserved, uninsured patient visits	>10,000 & Growing
Uncompensated care we provided	>$2 million & Growing
Mainland Travel for Advanced care & research avoided	> 1000 & Growing
Unique Lives & hope restored because of Clinical Trials	226 & Growing
Groundbreaking research brought to Hawaii	16 & Growing
Research investments brought to Hawaii	> $2.5 million & Growing
Local partners & economy we support	29 & Growing
Local Doctors, staff careers we nurture & support	47 & Growing
Residents, Med & Research Students we nurture	86 & Growing
PubMed Peer reviewed full length scientific publication	10 & Growing
Patients turned away because of payment ability or “quota”	0
Types of health Insurance not accepted	0
Trust YOU, our patients, local & global partners have in us	Priceless
Difference made in precious lives of patients & families	Priceless

CLINICAL

RESEARCH CENTER

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

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

Department of Quantitative Health Sciences

SEMINAR QHS 646

What's Needed for a Successful Clinical Research Career in Hawaii

The "Why", "What" and "How" with Real Life Experience

Kore Kai Liow, MD, FACP, FAAN

Neuroscience Chair & Principal Investigator, Clinical Research Center & Brain Research, Innovation & Translation labs (BRITL), Hawaii Pacific Neuroscience, Clinical Professor, Dept. of Medicine (Neurology), Affiliate Graduate Faculty, Quantitative Health and Clinical Research, Dept. Quantitative Health Sciences, University of Hawai`i John Burns School of Medicine

Dr. Liow is an NIH-trained research neurologist and PI (Principal Investigator) for the Brain Research, Innovation and Translation Lab and Clinical Research Center at Hawaii Pacific Neuroscience, Honolulu located on St Francis Liliha campus. He completed neurology training at the University of Utah in Salt Lake City before a research fellowship in cortical neurophysiology at NIH in Bethesda, Maryland. Dr. Liow spends the majority of his time in research and has served as PI for over 180 phase I-IV clinical trials sponsored by the NIH, CDC, and the industries for the past 25 years collaborating with global partners. In addition, investigating neurologic therapeutics. Dr. Liow is a Clinical Professor of Medicine (Neurology), Graduate Faculty in Quantitative Health and Clinical Research at the University of Hawaii John A. Burns School of Medicine where his team currently mentors over 20 medical students in neuroscience research projects. He has published over 70 PubMed-indexed peer-reviewed publications.

Thursday, October 26, 2023
12:00 – 1:00 PM HST

Zoom Link: https://hawaii.zoom.us/j/94719670015
Meeting ID: 947 1967 0015
Passcode: QHS646

For more information, contact Dr. Chathura Siriwardhana at: Tel. 692-1487 or Email: cksiri@hawaii.edu

HAWAII PACIFIC
NEUROSCIENCE
Center for
Neuroscience
DIVERSITY

Hawaii leads US in Caring for Underserved Alzheimer's Patients including NHPI and Rural Island Populations

Creative Methods (Hula Dance, EEG) to Improve Alzheimer's Care

HONOLULU (HI Now) NBC TV Station- November 7th, 2023

Despite Native Hawaiians and Pacific Islanders (NHPI) especially those with low social economic status are at an increased risk for earlier onset, more severe Alzheimer's disease with higher vascular comorbidities. They are often diagnosed later, undertreated, less well managed leading to poor long-term outcome. If we go "upstream," risk factors are associated with socioeconomic factors, such as financial hardship, food insecurity, and stressors associated with economic deprivation. There are sociocultural and psychosocial factors, such as racism, acculturation-related stressors, and social isolation. In a randomized controlled trial (RCT) of 240 adult NHPI, the 6-month hula-based intervention, called Ola Hou I ka Hula (retorting health through hula), was found superior to an education-only waitlist control group in improving blood pressure control and reducing 10-year CVD risk

NHPI has less access to advanced care like clinical trials, spinal tap and PET. As of 2023 November, Patients in Hawaii has to travel out of state for Amyloid PET or undergo invasive spinal tap. Access to readily available, noninvasive, cost-effective diagnostic tool like using Neural Network EEG may encourage early, timely diagnosis and intervention especially in underserved and rural (or island) communities This innovative diagnostic tool is being developed at Honolulu based ANNE (Alzheimer's Neural Network EEG) Lab.

More information: University of Hawaii Hula Lessons To Reduce Dementia Risk in Native Hawaiians, ANNE (Alzheimer's Neural Network EEG) Lab, Memory Disorders Center & Alzheimer's Research Unit, Center for Neuroscience Diversity

2023 Hawaii Neuroscience Research Plenary Sessions Keynote Lecture

August 19th, 2023
Honolulu, Hawaii

Hoʻi Hou iā Mauli Ola
Achieving Health Equity for Native Hawaiians and Pacific Islanders

Native Hawaiians and Pacific Islanders (NHPI) are at an increased risk for many neurological disorders (e.g., stroke and Alzheimer's disease and related dementias [ADRD]), and their vascular risk factors (e.g., hypertension, diabetes, and obesity). They are also diagnosed with these conditions at younger ages and are less likely to have these conditions well managed or treated than other racial/ethnic groups.

This keynote presentation highlighted the social and cultural determinants of NHPI health and the need for culturally responsive interventions aimed at preventing chronic diseases, such as cardiovascular disease (CVD) and ADRD. To illustrate these points, the adverse effects of racism on several cardiometabolic (i.e., hypertension and obesity) and mental health (e.g., depression)

conditions and physiological stress response, were presented based on research with NHPI communities. Also shared was a culturally grounded intervention that leveraged hula, the traditional dance of Native Hawaiians, to improve blood pressure control and 10-year CVD risk in Native Hawaiians and Pacific Islanders with previously uncontrolled hypertension.

In a randomized controlled trial (RCT) of 240 adult NHPI, the 6-month hula-based intervention, called Ola Hou I ka Hula (retorting health through hula), was found superior to an education-only waitlist control group in improving blood pressure control and reducing 10-year CVD risk. It was explained how this successful hula- based intervention is now being applied to improve the vascular risk factors of ADRD and cognitive functioning in NHPI participants of a current, ongoing RCT.

Key takeaways of this keynote lecture were:

1) NHPI are diverse in languages, cultures, and political statuses.

2) The need for NHPI data disaggregation in clinical research,

3) Racism is a significant social determinant of health impacting NHPI, and

4) Culturally grounded health promotion strategies are importance and effective in addressing the vascular factors associated with ADRD and other neurological disorders for NHPI communities.

Keaweʻaimoku Kaholokula, PhD
Professor and Chair of Native Hawaiian Health
Multiple Principal Investigator, Center for Pacific Innovations, Knowledge, and Opportunities
John A. Burns School of Medicine
University of Hawai'i at Mānoa

BRAIN RESEARCH

INNOVATION & TRANSLATION LABS

Brain Research, Innovation & Translation Laboratory (BRITL) 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 Hawaii Neuroscience Scholar Program -
Brain Research, Innovation and Translation Lab (BRITL) &
Summer Internship Program (SIP)
Alzheimer's Neural Network EEG Research Lab

2023 BRITL Graduates (Click for more pictures)

2023 BRITL Scholars and Interns (click for more pictures)

2023-2024 BRITL Scholars

2022 Summer Internship Program (SIP)

Brain Research, Innovation & Translation Labs (BRITL)

2230 Liliha Street #104
HONOLULU, HI 96817

FINALS POSTER PRESENTATION

Aug 13 Saturday, 2022

9:00AM-1:30PM

7:30-8:30AM Poster Set up

9:00AM

Introduction
Kore Liow, MD
Principal Investigator, BRITL
Clinical Professor Medicine (Neurology)
Graduate Faculty, Clinical & Translational Research

9:15AM

Keynote Speakers – Neurosurgery
Novel Treatments for Brain Tumors-Counteracting Immune Evasion and Killing Mitochondria".
David Baskin, MD Professor & Vice Chair, Residency Program Director, Dept. of Neurosurgery, Houston Methodist Hospital and Cornell University

10:00AM

Keynote Speakers – Basic Science
Food as Medicine: Action Targets & Effects of Selected Phytochemicals Against Alzheimer's & Obesity
Qing Li, PhD, Professor, Dept. Molecular Biosciences & Bioengineering

10:30AM BREAK
Breakfast & Refreshments Served

10:45AM

Keynote Speaker – Neurology
Rho kinase Inhibition: Potential treatments for Cerebral Cavernous Angiomas
Enrique Carrazana, MD, Publication Director, Neurology, Hawaii Pacific Neuroscience

11:30AM POSTER PRESENTATION & JUDGES ROUNDS

Jason Viereck, MD, PhD
Head Judge
Academic Director, BRITL
Clinical Assistant Professor Medicine (Neurology), Graduate Faculty, Clinical & Translational Research

Panel of Judges: Jason Vierek, MD, PhD (Head) Lawrence Burgess, MD, Qing Li, PhD, David Baskin, MD, Enrique Carrazana, MD, Eliza Hagen, MD, Chathura Siriwardhana, PhD, Kore Liow, MD

12:30PM

Presentation of Award & Conclusions
Lawrence Burgess, MD
Director, Student Affairs
Professor of Surgery

12:45PM Announcement of 2022 Hawaii Neuroscience Poster of the Year

1:00PM Dismissal and Clean up

Summer Internship Program (SIP)

Brain Research, Innovation & Translation Labs (BRITL)

2022 Hawaii Neuroscience Posters Presentations

Aug 13 Saturday, 2022

Download Abstracts, Download Posters

2022 BRITL SIP Faculty and Students

Dr. Lawrence Burgess, Director of Student Affairs quizzing Epilepsy Research Group (Led by Julia Johansooz, MS2)

Posters of the Year: TBI Research Group (led by Edward Weldone IV, MS2) with neurosurgeon David Baskin, MD, Professor & Director of Neurosurgery Residency Program, Houston Methodist Hospital.
MS Research Group (led by Shin Chang, MS2) with neurologist Jason Viereck, MD, PhD, HI Pacific Neuroscience, Clinical assistant professor of Medicine (neurology)

Acknowledgements

Mahalo to our patients and their precious families
whom we get to humbly serve and learn from every day!

BRITL Clinical & Research Faculty Mentors

Kore Liow, MD	Neurology, Principal Investigator, Neuroscience Chair
Jason Viereck, MD, PhD,	Neurology, Academic Director
Enrique Carrazana, MD,	Neurology, Publication Director
Vimala Vajjala, MD	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, PM & R
Kent Yamamoto, MD	Neurorehabilitation, PM & R
David Baskin, MD	Neurosurgery, Professor and Residency Program Director, Houston Methodist
Ricardo Burgos, MD	Neuroradiology
Qing Li, PhD	Neuroscience, Molecular Biosciences & Bioengineering
Paul Smith, MD	Brain Health, Lifestyle Medicine & Wellness, Sub-Investigator
Sriharsha Vajjala, MD	Sleep Medicine, Sub-Investigator
Lawrence Burgess, MD	Surgery, Director of Student Affairs, JABSOM
Chathura Siriwardhana, PhD	Biostatistics, Dept. Quantitative Health, JABSOM
John Chen, PhD	Biostatistics, Chair, Dept. Quantitative Health, JABSOM
Kimberly Ko,	Clinical Research Center Lead
Ena Zhu, CCRC	Certified Clinical Research Coordinator
Catherine Mitchell, CCRC	Certified Clinical Research Coordinator

2022 Hawaii Pacific Neuroscience Summer Internship Program

Project Leader:
Connor Goo, MS3, John A. Burns School of Medicine

Graduate Team Leaders:
Shin Chang, MS2, John A. Burns School of Medicine
Theodore Huo, MS2, John A. Burns School of Medicine
Amanda Chau, MS2, John A. Burns School of Medicine
Julia Jahansooz, MS2, John A. Burns School of Medicine
Edward Weldon IV, MS2, John A. Burns School of Medicine
ZoeAnn Kon, MS2, John A. Burns School of Medicine
Stephanie Matsuura, MS2, John A. Burns School of Medicine
Hannah Bulosan, MS2, John A. Burns School of Medicine
Nathan Kim, MS2, John A. Burns School of Medicine
Vanessa Rubel, University of Hawai'i at Manoa Graduate Program
Michelle Lu, MS2, John A. Burns School of Medicine
Anson Lee, MS2, John A. Burns School of Medicine

Undergraduate Co-Leaders:
Tracy Van, Skaggs School of Pharmacy, University of Colorado
Michael Tong, University of Hawai'i at Manoa

Brandon Roy, University of Hawai'i at Manoa
Donovan Roy, University of Hawai'i at Manoa
Richard Rista, MS2, Creighton Medical School Phoenix
Uiyeol Yoon, Hawai’i Pacific University
Anna Fan, University of Hawai'i at Manoa
Ana Tavares, Chaminade University
Jonathan Aoki, University of Hawai'i at Manoa
Matthew Calumpit, Drexel University
Dariann Davis, Hawai’I Pacific University
Weintraub, Amelia, University of California, Los Angeles
Keahi, Dane, Kamehameha Schools
Rexton Suzuki, Creighton University
Renzelle Ponce, Hawai’i Pacific University
Kalawena Kelehuawehe, University of Hawai'i at Manoa West Oahu
Jenna Okazaki, University of Portland
Lauren Pak, University of Oregon
Brooke Suzuki, University of Hawai'i at Manoa
Lorraine Sim, University of California, Los Angeles
Sophia Chun, University of Hawai'i at Manoa
Kacey Yamane, Creighton University
Corey Nishimura, University of Notre Dame
Brennan Lee, MS2, John A. Burns School of Medicine
Michael Tong, University of Hawai'i at Manoa
Ana Nakamura, University of California, Santa Barbara
Tefaiha Ashe, McMaster University
Darrell Matthew Guittu, University of Hawai'i at Manoa
Plyfaa Suwanamalik-Murphy, University of California, Davis
Taylor Matsubara, Wheaton College
Chancen Law, Kamehameha Schools

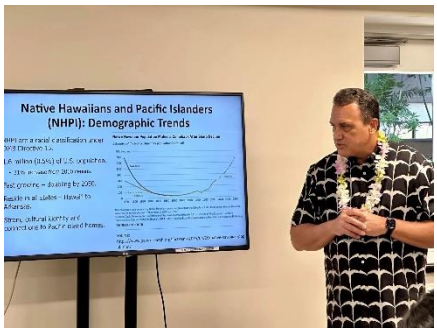
HAWAII PACIFIC NEUROSCIENCE

Hawaii BRITL

Brain Research, Innovation & Translation Labs (BRITL)
2230 Liliha Street #104, HONOLULU, HI 96817

JOHN A. BURNS SCHOOL OF MEDICINE · UNIVERSITY OF HAWAII MANOA

2023 Neuroscience Research Summer Symposium



Mahalo **to Keaweʻaimoku Kaholokula, Ph.D.**
Professor and Chair of Native Hawaiian Health,
University of Hawaii, John A. Burns School of Medicine on keynote lecture

Hoʻi Hou iā Mauli Ola, Achieving Health Equity for Native Hawaiians and Pacific Islanders

First place $1000

Characterizing Small Vessel Disease in Native Hawaiian and Other Pacific Islanders with Dementia: A Retrospective Pilot Study, Michelle Trinh, Elise Wong, Megan Baldemor, Sarah Song, Tyson Wu, Julia Jahansooz, Edward Weldon, Anson Lee, Chathura Siriwardhana

Runner ups $500

Exploring Radiculopathy in Underserved Communities: A Focus on AANHPI Populations and Risk Factors
Anita Cheung MPH, Matthew K. Nishimura, Kai J. Miyaki, Tea A. Stephens, Edward J. Weldon, Julia R.Jahansooz MS, Anson Y. Lee, Masako Matsunaga

(Lawrence Burgess, MD, Director of Student Affairs with Med student Bradon Hong and Group)

Runner ups $500

Use of Optimal Treatment Modalities for Spasticity and Stiffness in Post-Stroke and Cerebral Palsy Patients in Native Hawaiian Pacific Islanders and Underserved Populations in Hawaii, Bradon Hong, Michael Garvin, Connor Weldon, Yuewen Ding, Julia Jahansooz, Edward Weldon, Anson Lee, Masako Matsunaga

Abstracts Online Posters Online Event Photos Questions kliow@hawaii.edu

HAWAII PACIFIC NEUROSCIENCE

Brain Research, Innovation & Translation Laboratory (BRITL)

2230 Liliha Street #104
Honolulu, HAWAII 96817

Hawaii BRITL

Recent PubMed Publications & International Presentations

Hawaii Pacific Neuroscience (HPN) is committed to helping residents and students pursue their passion in neuroscience, research and develop leadership in this field to make an impact in the local community. HPN is proud to recognize exceptional medical students and scholars who have demonstrated exemplary academic abilities in neuroscience, leadership qualities, passion, and commitment to the pursue of excellence in research and a commitment to make a difference in the local and global community.

University Hawaii JABSOM medical students may sign up for UH elective Neuroscience research credit as MD5 MED 599, inquire with David Horio, MD dhorio@hawaii.edu

Core Neurology/Neuroscience Faculty

Kore Kai Liow, MD,	Neurology, Neuroscience Chair, Clinical Professor
Jason Viereck, MD, PhD,	Neurology, Academic Director, Assistant Professor
Enrique Carrazana, MD,	Neurology, Publications Director, Clinical Educator
Janette Abramowitz, MD,	Neurology, Psychiatry, Assistant Professor
Eliza Hagen, MD,	Neurology

Core Biostatistics & Research Faculty

John Chen, PhD	Professor & Chair, Dept. Quantitative Health Sciences
Chathura Siriwardhana, PhD	Assistant Professor and Biostatistician
Lawrence Burgess, MD	Professor and Director of Student Affairs
Russell Woo, MD	Professor and Director of Medical Student Research

Questions, contact Kore Kai Liow, MD, Principal Investigator, kliow@hawaii.edu

2023 BRITL Scholars/Medical Students

Julia Jahansooz, MS2, *Project Leader*
Ward Weldon, MS2, *Project Leader*
Anson Lee, MS2, *Student Editor*
Joo Won Choi, MS3
Richard Ho, MS3
Kyung Moo Kim, MS3
Charissa Tan, MS3
Shin Chang, MS2
Michelle Lu, MS2
Nathan Kim, MS2
Chloe Delos Reyes, MS2
Hailey Bao, MS2
D-Dré Wright, MS1
Anita Cheung, MS1
Michelle Trinh, MS1
Ho Hyun Lee, MS1
Elizabeth Rooks, MS1
Shay Nakahira, MS1
April Hamachi, MS1
Ryan Nakamura, MS1
Kirra Borrello, MS1
Cierra Nakamura, MS1
Jeff Hayashi, MS1
Bradon Hong, MS1
Jonathan Carino, MS1
Nina Krupa, MS1
Tamlyn Sasaki, MS1
Justin Abe, MS1
Eli Snyder, MS1
Johanna Mandl, Med U Innsbruck, Austria
Ana Tavares

Hawaii BRITL

UH JABSOM MD5 MED 599 Credit available

2023 BRITL Interns

Reyn Yoshioka, USD
Darrell Guittu, UH
Tyson Wu, UH
Chanel Hunter, UH
Shalita Areeyaphan,, UC Irvine
Timothy Ignacio Bowdoin C
Matthew Calumpit, Drexel U
Isabella Kostecki, Yale U
Megan Baldemor Santa Clara U
Zoe Mia, Exeter U
Michael Garvin, UC Berkeley
Connor Weldon, UC Santa Cruz
Yuewen Ding, UH
Courtney Yuen, U Rochester
Audrey Herman U Michigan
Ysabelle Bondocoy UH
Kaylin Bersamin UH
Tyler Shimabukuro Lewis Clark
Miriya Ogawa BYU, Utah
Alyson Hayashi, Macalester C
Matthew Nishimura, Pitzer C
Mariel Gonzales, UC Merced
Tea Stephens, UH
Sarah Song, Pomona C
Man Ian Woo, UH
Lana Liquard, McGill U
Natalie Gibson, UCLA
Shari Ho, U Notre Dame
Kaylie Kaneshiro, Tufts U
Paul Fontana, U Michigan
Kai Justin Miya, Boston U
Volet Nguyen, UH
Crystal Kanoa, UH
Elise Wong, Punahou
Chancen Law, Kamehameha

HAWAII PACIFIC NEUROSCIENCE

Hawaii BRITL

Brain Research, Innovation & Translation Labs (BRITL)

2230 Liliha Street #104, HONOLULU, HI 96817

June 17th-August 5th, 2023

June 17th Sat ORIENTATION Spring Presentation
Myasthenia Gravis Symposium Register Online

Introduction
Kore Liow, MD
Neuroscience Chair
Clinical Professor Medicine (Neurology)
Graduate Faculty, Clinical & Translational Research

Visiting Professor Keynote Speaker

Richard Nowak, MD, MS
Director, Yale Myasthenia Gravis Clinic
Director, Program in Clinical & Translational Neuromuscular Research,
Assistant Professor of Neurology,
Yale University School of Medicine

June 20, 27 Tues 5:00-6:30PM

Research Bio Statistics I and II
Chathura Siriwardhana, PhD,
Assistant Professor,
Biostatistics Core Facility,
Dept. Quantitative Health Services

July 8th Saturday MID TERM Oral Presentation

Keynote Speakers
Jason Viereck, MD, PhD
Academic Director, BRITL, Clinical Assistant Professor of Med (Neurology)

July 11 Tues 5:00-6:00PM **Writing up Your Abstract and Poster**

Enrique Carrazana, MD
Publication Director, Neurology, Hawaii Pacific Neuroscience, Clinical Educator

July 18th, 25th -Tues 5:00-6:00PM

How to Get Your Posters Ready
How to Submit to National Meetings
How to Submit for Full length Publications
Julia Jahansooz, MS3
Ward Weldon, MS3
Anson Lee, MS3
2023 BRITL Academic Scholars & Leaders

Aug 19th Sat 9-2:00PM FINAL Poster Presentation
Native Hawaiian & Pacific Islanders Health Disparity

Keaweʻaimoku Kaholokula, PhD
Professor and Chair of Native Hawaiian Health, University Hawaii John A. Burns School of Medicine

Visiting Professor Keynote Speaker

Advances in Spasticity, Dystonia & Blepharospasm Treatments
Zoltan Mari, MD
Ruvo Family Chair for Parkinson's Disease & Movement Disorders
Cleveland Clinic Lou Ruvo Center for Brain Health

Presentation Research Award
2023 HI Neuroscience Best Posters Presentations

Lawrence Burgess, MD
Director, Student Affairs
Russell Woo, MD
Director, Med Student Research,

Acknowledgements

Mahalo to our patients and their precious families
whom we get to humbly serve and learn from every day!

BRITL Clinical & Research Faculty Mentors

Kore Liow, MD	Neurology, Neuroscience Chair HPN
Jason Viereck, MD, PhD	Neurology, Academic Director
Enrique Carrazana, MD	Neurology, Publication Director
Michael Slattery, MD	Neurology
Eliza Hagen, MD	Neurology
Janette Abramowitz, MD	Neurology
Chris Larrinaga, APRN	Neurology
L. Nicole Little, PA-C, PhD	Neurology
Nicole Evans, PA-C	Neurology
Jason Chang, MD	Neurorehabilitation, Physical Medicine & Rehabilitation
David Baskin, MD	Neurosurgery, Professor and Residency Program Director, Cornell University
Tom Noh, MD	Neurosurgery, Assistant Professor
Ricardo Burgos, MD	Neuroradiology
Barlas Benkli, MD	Neurology
Paul Smith, MD	Brain Health, Lifestyle Medicine & Wellness, Preventive Medicine
Nicholas Anderson, MD	Sleep Medicine
Lawrence Burgess, MD	Director of Student Affairs, JABSOM
Russell Woo, MD	Associate Chair for Research
John Chen, PhD	Biostatistics, Chair, Dept. Quantitative Health
Chathura Siriwardhana, PhD	Biostatistics, Dept. Quantitative Health, JABSOM

2023 BRITL Scholars, Interns & Faculty

2023 Hawaii Pacific Neuroscience Summer Internship Program

Project Leaders:
Julia Jahansooz, MS3, John A. Burns School of Medicine
Edward Weldon IV, MS3, John A. Burns School of Medicine
Anson Lee, MS3, John A. Burns School of Medicine

BRITL Scholar Group Leaders:
Cierra Nakamura, MS2, John A. Burns School of Medicine
Bradon Hong, MS2, John A. Burns School of Medicine
Jonathan Carino, MS2, John A. Burns School of Medicine
Shay Nakahira, MS2, John A. Burns School of Medicine
Ryan Nakamura, MS2, John A. Burns School of Medicine
Michelle Trinh, MS2, John A. Burns School of Medicine
Kirra Borrello, MS2, John A. Burns School of Medicine
D-Dre Wright, MS2, John A. Burns School of Medicine
Ho Hyun Lee, MS2, John A. Burns School of Medicine
Elizabeth Rooks, MS2, John A. Burns School of Medicine
April Hamachi, MS2, John A. Burns School of Medicine
Anita Cheung, MS2, John A. Burns School of Medicine
Ana Tavares, Chaminade University

SIP Student Leaders:
Nina Krupa, MS2, John A. Burns School of Medicine
Tamlyn Sasaki, MS2, John A. Burns School of Medicine
Eli Snyder, MS2, John A. Burns School of Medicine
Reyn Yoshioka, University of San Diego

Elise Wong, Punahou School
Chancen Law, Kamehameha Schools Kapalama
Darrell Matthew Allen Guittu, University of Hawai‘i at Mānoa
Tyson Wu, University of Hawai‘i at Mānoa
Chanel Hunter, University of Hawai‘i at Mānoa
Johanna Mandl, Medical University of Innsbruck
Shalita Areeyaphan, University of California, Irvine
Timothy Ignacio, Bowdoin College
Matthew Calumpit, Drexel University
Isabella Grace Kostecki, Yale University
Megan Baldemor, Santa Clara University
Zoe Mia, Exeter University
Michael Garvin, University of California, Berkeley
Connor Arthur Weldon, University of California, Santa Cruz
Yuewen Ding, University of Hawai‘i at Mānoa
Courtney Kalanoweoikapoliokala'i Yuen, University of Rochester
Audrey Herman, University of Michigan
Ysabelle Bondocoy, University of Hawai‘i at Mānoa
Kaylin Bersamin, University of Hawai‘i at Mānoa
Miriya Ogawa, Brigham Young University, UT
Matthew Ki'ai O Ke Kuku'i Nishimura, Pitzer College
Mariel Grace Gonzales, University of California, Merced
Tea Stephens, University of Hawai‘i at Mānoa
Sarah Song, Pomona College
Man Ian Woo, University of Hawai‘i at Mānoa
Lana Liquard, McGill University
Natalie Gibson, University of California, Los Angeles
Shari Ho, University of Notre Dame
Kaylie Kaneshiro, Tufts University
Paul Fontana, University of Michigan
Kai Justin Miyaki, Boston University

MEMORY

DISORDERS CENTER

ALZHEIMER'S RESEARCH UNIT

Hawaii Memory Disorders Center is the only facility in Hawaii with a dedicated multidisciplinary team of clinical neurologists, research neurologists, cognitive rehabilitation specialists and brain health and wellness specialists trained in diagnosing and treating memory disorders and dementia.

The evaluation to diagnose memory disorders and dementia may include an MRI of the Brain, EEG, laboratory tests and neuropsychology testing. Each patient is unique and medical workups will vary depending on the patient's medical history and clinical presentation. Once the evaluation for the patient is complete, the multidisciplinary team will discuss the findings with the patient and family.

Together we formulate an individualized plan for treatment and management. Plans can include medications and lifestyle recommendations. Teaching includes nutritional counseling, physical exercise, and brain stimulation exercises that focus on improving brain health. Memory Disorders Center staff are dedicated to continued support those living with memory disorders. Care for the caregivers is a vital part of the Memory Disorders Center program and includes education, counseling, coordination of care and access to resources in the community.

The Memory Disorders Center and Alzheimer's Research Unit is a part of the global network of top neuroscience centers involved in Alzheimer's research funded by NIH and other organizations. Our Neuroscience Center of Excellence is recognized nationally for its work not only in providing most advanced cutting edge treatments, but also work with other centers in US and global to offer groundbreaking Clinical Research.

Clinical Trials available at Hawaii Memory Disorders Center & Alzheimer's Research Unit

Publications by specialists & researchers at the Hawaii Memory Disorders Center and Alzheimer's Research Unit

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and have local resources available to you. Therefore, we work closely with and support Hawaii's local support group.

alzheimer's association

Kore Kai Liow, MD, FACP, FAAN
Director, Memory Disorders Center
Principal Investigator, Alzheimer's Research Unit
Hawaii Pacific Neuroscience
Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawaii John Burns School of Medicine
Neurology Residency: University of Utah School of Medicine
Fellowship: Cortical Neurophysiology & Clinical Research, NINDS, NIH

MEMORY CTR

Hawai‘i 2035

STATE STRATEGIC PLAN

On Alzheimer’s Disease & Related Dementias





Hawai‘i State Department of Health

Executive Office on Aging

September 2023


Kuakini Honolulu Heart Program Offspring Study

other midlife experiences contribute to the development of disorders of the elderly. At the "Third World Congress on Vascular Factors in Alzheimer's Disease" held in Kyoto, Japan, in April 2002, the Kuakini HAAS presented findings from the analyses of autopsied brain specimens donated by Kuakini HHP participants, who identified vascular and non-vascular pathogenic processes associated with poor cognitive function. In 2022, the published article on "Late-life social networks and incident Alzheimer's disease: The Kuakini HAAS" presented the study findings on longitudinal associations between social networks and incidence of all-cause dementia, Alzheimer's disease, and vascular dementia in 2,636 Kuakini HHP participants who were dementia-free at baseline, over a 10-year follow-up period. Those with strong social networks at baseline were less likely to develop all-cause dementia. Therefore, prevention of social isolation of older adults should be considered a priority. Another outgrowth of the Kuakini HHP is the Kuakini Honolulu Heart Program Offspring Study, which is designed to collect data (including demographics, health conditions, lifestyle, and genetics) from the sons and daughters of the original Kuakini HHP participants. The goal of the study is to conduct multi-generational research on several diseases, health conditions, and healthy aging, including heart disease, stroke, high blood pressure, diabetes, age-related disability, memory loss, dementia, Alzheimer's disease, Parkinson's disease, cancer, longevity, and related genetic research. Kuakini believes that the linkage of the Kuakini HHP Offspring Study to the Kuakini HHP research will result in major scientific contributions that will benefit the Hawai'i and global communities, as well as future generations.

Hawaii Memory Disorders Center and Alzheimer's Research Unit

Hawaii Memory Disorders Center and Alzheimer's Research Unit at Hawai'i Pacific Neuroscience is 1 of 48 top neuroscience centers in the U.S. For over a decade now, our Hawai'i memory & Alzheimer's specialists and researchers worked tirelessly collaborating with other researchers around the world to develop innovative and novel treatments for this devastating neurological condition affecting more than 6 million Americans, including over 35,000 in Hawai'i. Our mission is to provide options to patients who suffer from dementia, mild cognitive impairment, or preclinical state whose conditions are not satisfactory controlled on approved therapies, or who are seeking advanced, innovative or research treatments. Our hope is that this will meet unmet needs of patients and their precious families in need of options and hope; Hawai'i physicians who want to incorporate research options as part of their comprehensive approach; local awareness; education on conditions; and empowering patients, families, and caretakers. Individuals with mild cognitive impairment or mild to moderate Alzheimer's disease (AD) may be eligible to participate in one of the following studies: ATH-1017 LIFT (Synaptic Plasticity), Buntanetap (Axonal Transport), PRX012 (Next Generation Amyloid), Aducanumab ENVISION (Amyloid), GLP1-RA EVOKE (Glucose), or BIIB080 CELIA (Tau).

HAWAII PACIFIC NEUROSCIENCE

LIFT-AD (Synaptic Plasticity). Enhancing signaling between receptors in the brain has the potential to protect existing neurons from damage, reduce inflammation, promote regeneration, and positively modulate

Hawaii Pacific Neuroscience staff

brain activity. Results are being monitored not just with memory testing or CSF/PET biomarkers, but also by measuring brain network and connectivity using Quantitative EEG and P300 Event related potential.

Buntanetap (Axonal Transport) is administered via oral capsule. Its unique mechanism of action allows it to simultaneously inhibit multiple neurotoxic proteins which are at play in all neurodegenerative diseases. Buntanetap is the only drug so far to show improvement in cognition in AD patients and motor function in Parkinson's disease patients. Buntanetap has shown to reduce inflammation and preserve axonal integrity and synaptic functions, as well as neurotoxic proteins in previous Phase 2a studies. Buntanetap-treated AD patients showed a statistically significant cognitive improvement of 30% as measured by ADAS-Cog11 and in the WAIS Coding Scale when compared with baseline results.

PRX012 is a next-generation, high binding potency antibody designed to enable subcutaneous dosing on a patient-friendly, convenient administration schedule, potentially providing greater accessibility for patients and caregivers. Preclinical data have shown that PRX012 binds to beta amyloid plaques and oligomers with high avidity, enabling effective levels of Aβ plaque occupancy at relatively lower dose ranges. Additional pre-clinical data demonstrated clearance of both pyroglutamate modified and unmodified Aβ plaque in brain tissue at concentrations of PRX012 estimated to be clinically achievable in the central nervous system with subcutaneous delivery.

Aducanumab ENVISION (Amyloid). The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. Clinical trials show the effect of ADUHELM on reducing amyloid beta plaques, a surrogate biomarker that is reasonably likely to predict clinical benefit, in this case a reduction in clinical decline. ADUHELM can cause serious side effects, including Amyloid Related Imaging Abnormalities (ARIA). ARIA is a common side effect that does not usually cause any symptoms but can be serious. Although most people do not have symptoms, some people may have symptoms such as: headache, confusion, dizziness, vision changes and nausea.

GLP1-RA EVOKE (Glucose). Type 2 diabetes almost doubles the risk of developing AD and is associated with accelerated cognitive decline in people with mild cognitive impairment. Semaglutide has specifically been shown to reduce measures of neuro-inflammation which may affect cognition and function. In a post-hoc analysis of data from three large cardiovascular outcomes trials conducted by Novo Nordisk, the rate of developing dementia statistically significantly reduced by 53% in favor of GLP-1. Oral semaglutide (7 mg

and 14 mg) is approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes in the US, EU and Japan. This randomized double-blind placebo-controlled clinical trial investigates the effect and safety of Oral Semaglutide in Subjects With Early AD (EVOKE).

BIIB080 CELIA (Tau) is an antisense oligonucleotide (ASO) that may reduce production of the tau protein and its accumulation in brain cells, potentially slowing the progress of the disease. BIIB080 is an investigational antisense therapy designed to target microtubule-associated protein tau mRNA and prevent production of tau protein. This is a study to assess if BIIB080 can change clinical dementia rating-sum of boxes scores, and BIIB080 safety and tolerability when injected into the cerebrospinal fluid of participants with mild cognitive impairment due to AD or mild AD dementia between 50 to 80 Years of age (CELIA).

Lecanemab (Leqembi) is an intravenous antibody designed to remove amyloid deposits that have not yet clumped together. Leqembi should be initiated in patients with MCI (mild cognitive impairment) or in the mild dementia stage of AD. Leqembi demonstrated a statistically significant and clinically meaningful reduction of decline from baseline to 18 months on the primary endpoint, the Clinical Dementia Rating Scale Sum of Boxes score, compared to placebo. People on the medication experienced side effects such as brain swelling and tiny bleeds common with similar amyloid-targeting drugs called ARIA. The study reported that 17% of people experienced small brain bleeds, compared to 8.7% in the placebo group. The side effects were detected in brain images but rarely caused symptoms. Since 2019, patients have been closely monitored for these side effects after receiving Leqembi at Hawai'i's first outpatient ambulatory Infusion Center by the experienced onsite infusion and neuroscience team.


Kore Liow, MD, FACP

"Our team of neurologists, neuroscience specialists, and researchers in Hawai'i cannot be more proud of many of our Hawai'i patients and their 'ohana who have contributed to so many of these important Alzheimer's research studies and many who continue to do so in the future, without which, we have no way of developing better options to those affected," says Kore Liow, MD, FACP, Principal Investigator, Memory Disorders Center & Alzheimer's Research Unit, Founder & CEO, Neurologist & Neuroscience Chair at Hawai'i Pacific Neuroscience & Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Medicine, University of Hawai'i John A. Burns School of Medicine.

For more information, visit hawaiineuroscience.com. Or call the Hawaii Alzheimer's Research Unit Hotline at (808) 564-6141 or email info@HawaiiNeuroscience.com.

Racial/Ethnic Disparities in the Alzheimer's Disease Link with Cardio and Cerebrovascular diseases, based on Hawaii Medicare Data

Chathura Siriwardhana1, Enrique Carrazana2, Kore Liow1,2,3, John J. Chen1

1 Clinical & Translational Research, Department of Quantitative Health Sciences; 2Department of Medicine, University of Hawaii John Burns School of Medicine, Honolulu, HI 96813, USA, 3Memory Disorders Center, Stroke & Neurologic Restoration Center, Hawaii Pacific Neuroscience, Honolulu, Hawaii 96817, USA

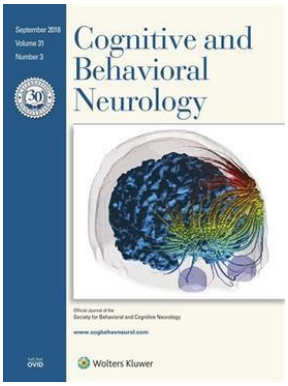
(Accepted for Publication Journal of Alzheimer's Disease Reports)

Background: There is an expanding body of literature implicating heart disease and stroke as risk factors for Alzheimer's disease (AD). Hawaii is one of the six majority-minority states in the US and has significant racial health disparities. Native-Hawaiians/Pacific-Islander (NHPI) population is well-known as a high-risk group for a variety of disease conditions.

Objective: We explored the association of cardiovascular disease with AD development based on the Hawaii Medicare data, focusing on racial disparities. Methods: We utilized nine years of Hawaii Medicare data to identify subjects who developed heart failure (HF), ischemic heart disease (IHD), atrial fibrillation (AF), acute myocardial infarction (AMI), stroke, and progressed to AD, using multistate models. Propensity score-matched controls without cardiovascular disease were identified to compare the risk of AD after heart disease and stroke. Racial/Ethnic differences in progression to AD were evaluated, accounting for other risk factors.

Results: We found increased risks of AD for AF, HF, IHD, and stroke. Socioeconomic (SE) status was found to be critical to AD risk. Among the low SE group, increased AD risks were found in NHPIs compared to Asians for all conditions selected and compared to whites for HF, IHD, and stroke. Interestingly, these observations were found reversed in the higher SE group, showing reduced AD risks for NHPIs compared to whites for AF, HF, and IHD, and to Asians for HF and IHD.

Conclusion: NHPIs with poor SE status seems to be mostly disadvantaged by the heart/stroke and AD association compared to corresponding whites and Asians.



Barriers to Alzheimer Disease Clinical Trial Participation in a Minority Population

Anson Y Lee [1 2], Julia R Jahansooz [1 2], Darrell Guittu [1], Rexton Suzuki [1], Lauren Pak [1], Kyle M Ishikawa [2 3], Connor Goo [1 2], John J Chen [2 3], Enrique Carrazana [1 2], Jason Viereck [1 2 3], Kore K Liow [1 2 3]

1Memory Disorders Center & Alzheimer's Research Unit, Hawaii Pacific Neuroscience, Honolulu, Hawaii.
2John A. Burns School of Medicine, University of Hawaii, Honolulu, Hawaii.
3Biostatistics Core Facility, Department of Quantitative Health Sciences, John A. Burns School of Medicine, University of Hawaii, Honolulu, Hawaii.

Background: Alzheimer disease (AD), the most common neurodegenerative disorder in the United States, disproportionately burdens minority populations.

Objective: To explore barriers to AD clinical trial participation by Asian and Native Hawaiian patients diagnosed with AD or mild cognitive impairment.

Method: We surveyed 187 patients with a Mini-Mental State Examination score ≥14 between January 2022 and June 2022. The score cutoff for clinical trial eligibility was set by the institution. Individuals also completed a 15-question telephone survey that assessed demographics, barriers to clinical trial participation, and clinical trial improvement methods.

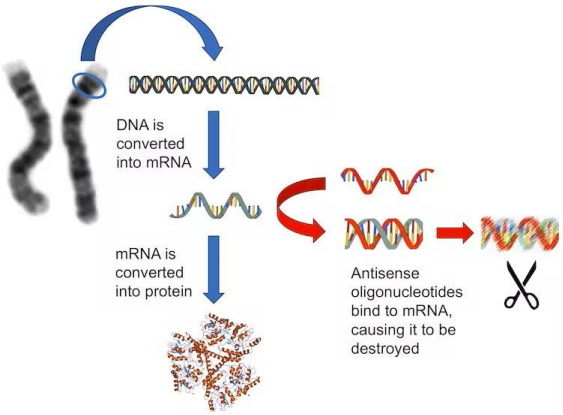
Results: Forty-nine patients responded, with a response rate of 26%. Asian and Native Hawaiian patients were less likely than White patients to participate in AD trials. The main barrier to participation was a lack of information about AD trials. Providing additional information regarding AD trials to patients and family members were listed as the top two reasons patients would consider participating in a clinical trial.

Conclusion: Insufficient information about AD clinical trials is the primary barrier to participation among Asian and Native Hawaiian patients, followed by difficulty coordinating transportation and, in the case of Asians, the time required for clinical trials. Increased outreach, education, and assistance with logistics in these populations should be pursued to improve rates of participation in clinical trials.

Lee AY, Jahansooz JR, Guittu D, Suzuki R, Pak L, Ishikawa KM, Goo C, Chen JJ, Carrazana E, Viereck J, Liow KK. Barriers to Alzheimer Disease Clinical Trial Participation in a Minority Population. Cogn Behav Neurol. 2023 Oct 24. doi: 10.1097/WNN.0000000000000359. Epub ahead of print. PMID: 37878413.

Phase 1 Novel Alzheimer's Therapy Targeting Tau using ASO (Antisense Oligonucleotide Therapy) underway at 1 of 7 US sites including Hawaii Memory Center & Hawaii Alzheimer's Research Unit

24th February 2023 Honolulu



According to Biogen website, Alzheimer's disease (AD) is a progressive neurodegenerative disease that damages healthy cells in the brain causing cognitive impairment and functional disability.

The memory loss and functional decline of Alzheimer's disease have been linked to amyloid plaques and tau tangles, abnormal protein deposits that build up in the brain and in the brain cells. BIIB080 (tau ASO) is an antisense oligonucleotide (ASO) that may reduce production of the tau protein and its accumulation in brain cells, potentially slowing the progress of the disease.

BIIB080 is an investigational antisense therapy designed to target microtubule-associated protein tau (MAPT) mRNA and prevent production of tau protein.

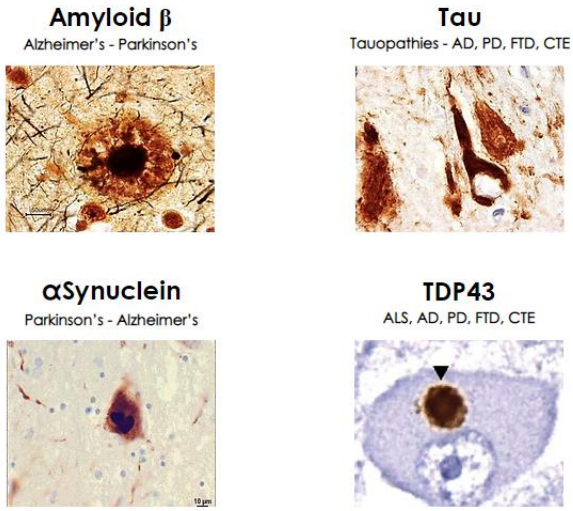
This is a Study to Assess if BIIB080 Can Change Clinical Dementia Rating-Sum of Boxes Scores, and BIIB080 Safety and Tolerability When Injected Into the Cerebrospinal Fluid of Participants With Mild Cognitive Impairment Due to Alzheimer's Disease (AD) or Mild AD Dementia Between 50 to 80 Years of Age (CELIA). More information: NIH Website

"Our Hawaii patients, caregivers, families, neurologists & researchers are honored to be able to play a role to contribute to this important ground breaking research" Kore Kai Liow, MD, Neurologist & Principal Investigator, Hawaii Memory Disorders Center & Alzheimer's Research Unit, Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawai`i John Burns School of Medicine

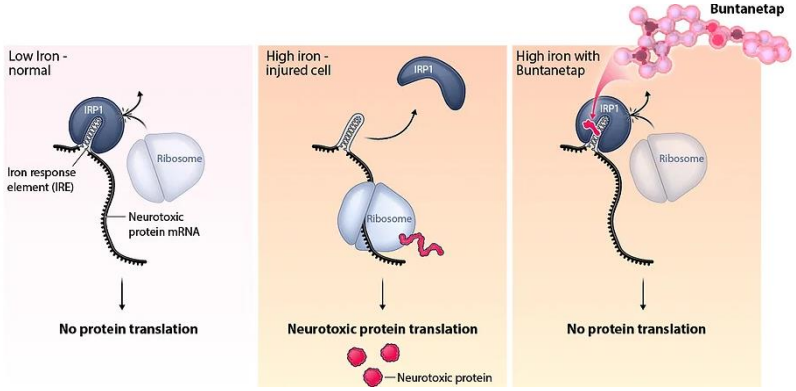
Dedicated Hawaii Alzheimer's Research Hotline (808) 564-6141

Hawaii Alzheimer's Researchers and Doctors investigates Buntanetap, reducing APP, tau and αSYN levels, Improving Axonal Transport and Impedes the Toxic Cascade Leading to Neurodegeneration.

According to Annovis Website, Buntanetap is a translational inhibitor of neurotoxic aggregating proteins (TINAPs). Different from monoclonal antibody therapies, buntanetap is an orally available small molecule, and its unique mechanism of action allows it to inhibit multiple neurotoxic proteins at once. Recent research has shown that multiple neurotoxic proteins are at play in all neurodegenerative diseases. Buntanetap is the only drug to attack multiple neurotoxic proteins simultaneously.



Buntanetap has shown to reduce inflammation and preserve axonal integrity and synaptic functions as well as neurotoxic proteins in previous Phase 2a studies. In this study we plan to measure plasma GFAP, NFL and potentially TDP43. (Photo credits: www.annovisbio.com)



Buntanetap inhibits the translation of neurotoxic proteins by increasing the binding of a special mRNA sequence that is preserved among neurotoxic aggregating proteins and its binding protein that keeps it from going to the ribosome and being translated.

Buntanetap-treated AD patients showed a statistically significant cognitive improvement of 30% as measured by ADAS-Cog11 and in the WAIS Coding Scale, when compared with baseline results. Buntanetap is the only drug so far to show improvement in cognition in AD patients and motor function in PD patients.

See Website to see Who is Eligible for Study, Publications by HI Researcher

"Our team of neurologists, neuroscience specialists and researchers in Hawaii cannot be more proud of our Hawaii Patients who have contributed to and many who will contribute to this important research study" says Kore Liow, MD, Principal Investigator, Hawaii Memory Disorders Ctr and Alzheimer's Research Unit, Neurologist & Neuroscience Chair at Hawaii Pacific Neuroscience & Clinical Professor of Medicine (Neurology), University Hawaii JABSOM

Phase 1 Research on Next Generation High Binding Potency Potential Best-in-Class Anti-Amyloid Beta Antibody underway at Hawaii Memory Center & Hawaii Alzheimer's Research Unit

October 2023 Honolulu

According to Prothena website, PRX012 is a next-generation, high binding potency antibody, designed to enable subcutaneous dosing on a patient-friendly, convenient administration schedule, potentially providing greater accessibility for patients and caregivers.

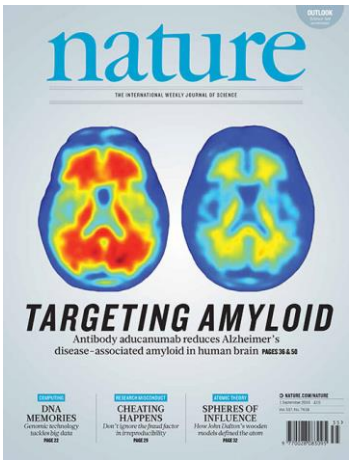
Preclinical data have shown that PRX012 binds to beta amyloid plaques and oligomers with high avidity, enabling effective levels of Aβ plaque occupancy at relatively lower dose ranges, which are optimal for subcutaneous delivery. Additional preclinical data demonstrated clearance of both pyroglutamate modified and unmodified Aβ plaque in brain tissue at concentrations of PRX012 estimated to be clinically achievable in the central nervous system with subcutaneous delivery. Compared to first generation anti-Aβ antibodies, PRX012 is expected to result in less variance of antibody concentrations in the brain.

The Phase 1 single ascending dose (SAD) study of PRX012 is a randomized, double-blind, placebo-controlled study to evaluate safety, tolerability, immunogenicity, and pharmacokinetics in healthy volunteers and patients with Alzheimer's disease. In this Phase 1 SAD study, healthy volunteers and patients will be randomized to receive a single subcutaneous injection of either PRX012 or placebo. ***Qualified Hawaii patients must be willing to travel to partner Amyloid PET Imaging facility in Los Angeles, California.***

"Our Hawaii patients, caregivers, families, neurologists & researchers are honored to be able to play a role to contribute to this important ground breaking research" Kore Kai Liow, MD, Neurologist & Principal Investigator, Hawaii Memory Disorders Center & Alzheimer's Research Unit, Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawai`i John Burns School of Medicine

Dedicated Hawaii Alzheimer's Research Hotline (808) 564-6141

ADUHELM (Aducanumab) ENVISION Phase 3b study awarded to Hawaii Memory Disorders Center and Alzheimer's Research Unit, only site in Hawaii & 30th US site to participate in FDA Post Marketing Confirmatory study *Honolulu September 2022*



According to Biogen website, ADUHELM is a monoclonal antibody directed against amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. The accelerated approval of ADUHELM has been granted based on data from clinical trials showing the effect of ADUHELM on reducing amyloid beta plaques, a surrogate biomarker that is reasonably likely to predict clinical benefit, in this case a reduction in clinical decline.

ADUHELM can cause serious side effects including: Amyloid Related Imaging Abnormalities or "ARIA". ARIA is a common side effect that does not usually cause any symptoms but can be serious. Although most people do not have symptoms, some people may have symptoms such as: headache, confusion, dizziness, vision changes and nausea.

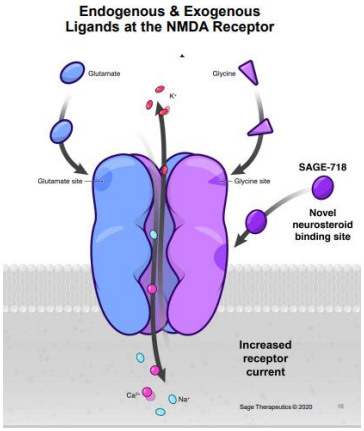
The study plans to enroll total of 1521 participants in US with early Alzheimer's (confirmation of amyloid beta pathology by CSF or PET), monthly IV Infusions with close monitoring at Hawaii Memory Disorders Center & Alzheimer's Research Unit, Honolulu, currently the only site in Hawaii and as of September 2022, the 30th site in US to offer Aducanumab at no cost to qualified participants:

- 60-85 years old
- MMSE between 22 and 30 inclusive

"Our neurologists & researchers at Hawaii Memory Disorders Center & Alzheimer's Research Unit are honored to be selected to contribute to this important confirmatory study and making available this option to our local island populations who no longer has to travel to Mainland" Kore Kai Liow, MD, Neurologist & Principal Investigator.

Information: Dedicated research hotline (808) 564-6141 or info@HawaiiNeuroscience.com

Hawaii Memory Disorders Ctr and Alzheimer's Research Unit selected for LIGHTWAVE Study - Phase 2 SAGE-718 NMDA Receptor Positive Allosteric Modulator (PAM) effect on Cognitive Functions in Alzheimer's Disease



According to Sage website, SAGE-718, Sage's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). Ongoing studies aim to evaluate whether SAGE-718 may have the potential to improve cognitive symptoms for these difficult-to-treat disorders.

Phase 2 LUMINARY Study that showed SAGE-718, a first-in-class, oral, positive allosteric modulator of the NMDA receptor, was generally well-tolerated and associated with improvement

on multiple tests of executive performance and learning and memory in patients with mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD). The LUMINARY Study is part of CogNEXT, Sage's early-stage trial platform designed to evaluate the therapeutic potential of SAGE-718 to treat cognitive deficits across a range of brain health disorders. The data presented during the Emerging Science Session on Tuesday, April 5, at the 74th Annual Meeting of the American Academy of Neurology (AAN) in Seattle.

Randomized, Double-blind, Placebo-controlled Study to Evaluate the Effects of SAGE-718 in Participants With Mild Cognitive Impairment or Mild Dementia Due to Alzheimer's Disease

Eligible patients: 50-80 years, MoCA 15-25 See Website for more information.

"Our team of neurologists, neuroscience specialists and researchers in Hawaii cannot be more proud of our Hawaii Patients who have contributed to and many who will contribute to this important research study" says Kore Liow, MD, Principal Investigator, Hawaii Memory Disorders Ctr and Alzheimer's Research Unit, Neurologist & Neuroscience Chair at Hawaii Pacific Neuroscience, Graduate faculty, Clinical & Translational Research, Clinical Professor of Medicine (Neurology), University Hawaii JABSOM

nature
SCIENTIFIC REPORTS

Scientific Reports is the 5th Most-Cited Journal in the World with 5-Year Impact Factor (2021) of 5.516

Demographic Recruitment Bias of Adults in United States Randomized Clinical Trials by Disease Categories Between 2008 to 2019: A Systematic Review and Meta-Analysis. Sci Rep. 2023 Jan 2;13(1):42.

Buffenstein I, Kaneakua B, Taylor E, Matsunaga M, Choi SY, Carrazana E, Viereck J, Liow KK, Ghaffari-Rafi A.
John A. Burns School of Medicine: Center for Neuroscience Diversity, Hawaii Pacific Neuroscience

Objectives: To promote health equity within the United States (US), randomized clinical trials should strive for unbiased representation. Thus, there is impetus to identify demographic disparities overall and by disease category in US clinical trial recruitment, by trial phase, level of masking, and multi-center status, relative to national demographics.

Methods: A systematic review and meta-analysis were conducted using MEDLINE, Embase, CENTRAL, and ClinicalTrials.gov, between 01/01/2008 to 12/30/2019. Clinical trials (N = 5,388) were identified based on the following inclusion criteria: study type, location, phase, and participant age. Each clinical trial was independently screened by two researchers. Data was pooled using a random-effects model. Median proportions for gender, race, and ethnicity of each trial were compared to the 2010 US Census proportions, matched by age. A second analysis was performed comparing gender, race, and ethnicity proportions by trial phase, multi-institutional status, quality, masking, and study start year.

Results: 2977 trials met inclusion criteria (participants, n = 607,181) for data extraction. 36% of trials reported ethnicity and 53% reported race. Three trials (0.10%) included transgender participants (n = 5). Compared with 2010 US Census data, females (48.3%, 95% CI 47.2-49.3, $p < 0.0001$), Hispanics (11.6%, 95% CI 10.8-12.4, $p < 0.0001$), American Indians and Alaskan Natives (AIAN, 0.19%, 95% CI 0.15-0.23, $p < 0.0001$), Asians (1.27%, 95% CI 1.13-1.42, $p < 0.0001$), Whites (77.6%, 95% CI 76.4-78.8, $p < 0.0001$), and multiracial participants (0.25%, 95% CI 0.21-0.31, $p < 0.0001$) were under-represented, while Native Hawaiians and Pacific Islanders (0.76%, 95% CI 0.71-0.82, $p < 0.0001$) and Blacks (17.0%, 95% CI 15.9-18.1, $p < 0.0001$) were over-represented. Inequitable representation was mirrored in analysis by phase, institutional status, quality assessment, and level of masking. Between 2008 to 2019 representation improved for only females and Hispanics. Analysis stratified by 44 disease categories (i.e., psychiatric, obstetric, neurological, etc.) exhibited significant yet varied disparities, with Asians, AIAN, and multiracial individuals the most under-represented.

Conclusions: These results demonstrate disparities in US randomized clinical trial recruitment between 2008 to 2019, with the reporting of demographic data and representation of most minorities not having improved over time.

PubMed Full Length Publication:
Smith M, Van N, Roberts A, Hosaka KRJ, Choi SY, Viereck J, Carrazana E, Borman P, Chen JJ, Liow KK. Disparities in Alzheimer Disease and Mild Cognitive Impairment Among Native Hawaiians and Pacific Islanders. Cogn Behav Neurol. 2021 Sep 2;34(3):200-206. doi: 10.1097/WNN.0000000000000279.
PubMed PMID: 34473671.

Disparities in Alzheimer Disease and Mild Cognitive Impairment Among Native Hawaiians and Pacific Islanders

Maiya Smith [1], Nicholas Van [2], Alyssa Roberts [2], Kalei R J Hosaka [1], So Yung Choi [3], Jason Viereck [1 4 5], Enrique Carrazana [1 6], Pat Borman [7 5], John J Chen [3], Kore Kai Liow [1 4 5]

- [1]Departments of Medicine.
- [2]Undergraduate Education, University of Hawaii at Mānoa, Honolulu, Hawaii.
- [3]Quantitative Health Sciences.
- [4]Clinical and Translational Research, John A. Burns School of Medicine, Honolulu, Hawaii.
- [5]Alzheimer's Research Unit and Memory Disorders Center, Hawaii Pacific Neuroscience, Honolulu, Hawaii.
- [6]Epilepsy Research Unit, Hawaii Pacific Neuroscience, Honolulu, Hawaii.
- [7]Geriatrics, John A. Burns School of Medicine, Honolulu, Hawaii.

Background: Previous studies of racial differences in Alzheimer disease (AD) presentation have not included Native Hawaiians and Pacific Islanders (NHPI).To explore the presentation of AD and mild cognitive impairment (MCI) in NHPI.

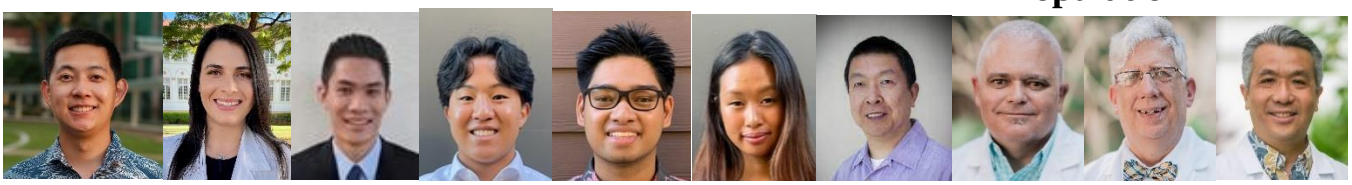
Method: We conducted a retrospective review of patient records from Hawaii with a diagnosis of unspecified AD or MCI from September 2000 to September 2019. Variables of interest included age at diagnosis, gender, race, marital status, insurance, comorbidities, and scores on the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA).

Results: We reviewed the medical records of 598 patients, including 224 Asians, 202 Whites, 87 NHPI, and 85 Other. AD was more dominant than MCI across all of the groups, with the highest percentage in NHPI. Among the mean ages of diagnosis, NHPI were the youngest. Across all groups, a higher proportion of women than men had AD, with the highest female prevalence among NHPI. Hypertension, hyperlipidemia, and type II diabetes were highest among NHPI compared with the other groups. Of individuals with MMSE/MoCA scores, there were significant variations in scores by racial group. The mean MMSE/MoCA score was highest among Whites and lowest among NHPI.

Conclusion: Compared with other racial groups, NHPI have a higher proportion of AD than MCI at diagnosis, are diagnosed at a younger age, have a higher female prevalence, have more comorbidities that may contribute to AD/MCI onset, and present with lower MMSE scores.

AD/PD™ 2023
ADVANCES IN SCIENCE & THERAPY
March 28 - April 1, 2023 | Gothenburg, Sweden • HYBRID

Barriers To Alzheimer's Disease Clinical Trial Participation in Hawaii's Minority-Majority Population



Anson Y Lee, Julia R Jahansooz, Darrell Guittu, Rexton Suzuki, Lauren Pak, Kyle M Ishikawa, Connor Goo, John J Chen, Enrique Carrazana , Jason Viereck, Kore K Liow

Center for Neuroscience Diversity, Hawaii Pacific Neuroscience, U of Hawaii John Burns School of Medicine,

Background: Alzheimer's disease (AD) is the most common neurodegenerative disorder in the United States and disproportionately burdens minority populations. 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. As such, recruitment barriers have been noted as the primary factor negatively impacting AD clinical research progress. While research has been conducted to assess the primary reasons for the lack of clinical trial participation in minority groups, amongst minority populations, Asians and Native Hawaiians are the most understudied. 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 in U.S.

Objectives: Understanding barriers to Alzheimer's Disease (AD) clinical trial participation in underrepresented Asian and Native Hawaiian (NH) patients diagnosed with AD or mild cognitive impairment (MCI) in Hawaii.

Methods: Patients and caregivers completed a 15-question telephone survey that assessed demographics, barriers, 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.

Results: Forty-nine patients responded (29 AD, 20 MCI). The mean patient age was 77 years, 51% were male, and the mean MMSE score was 23.2. Compared to the clinic population (20.0% Asian, 30.7% NH, 39.7% White), 5.6% Asian, 22% NH, and 32% White patients were in an active trial. More NH and White patients participated in trials than Asian patients. The decision to participate in trials to help others significantly differed by race (91% White, 80% NH, 29% Asian; p=0.023), with other reasons being statistically insignificant. Asian (30%) and NH (80%) patients reported the main barrier to participation was a lack of information about trials, with psychosocial conflicts and financial burdens as the least important barrier. Additional trial information given to family members (64% Asian, 88% NH, 62% White) and patients (64% Asian, 88% NH, 46% White) were listed as the most popular trial improvements.

Conclusions: Asian and NH patients were less likely to participate in AD trials compared to White patients. A deficiency in information was the primary barrier amongst minority patients. To overcome this barrier, increased outreach and education to patients and their families should be pursued. 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. Interestingly, White patients shared comparable barriers indicating that all three groups had similar impediments to involvement potentially indicating problems with how trials are run 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. A primary limitation to this study was the small sample size of completed responses, and as such, future research should investigate these barriers in a larger cohort spanning a wider range of time to better generalize results and provide a more complete dataset.

EEG Slowing and CSF Amyloid Status: Implications for Alzheimer's Disease Detection and Progression

Nathan N. Kim[1,2], Shay Nakahira[1,2], Anson Y. Lee[1,2], Eliza Hagen[2], Enrique Carrazana[2], Jason Viereck[1,2], Kore K. Liow[1,2]

[1]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, USA

[2]Hawai'i Pacific Neuroscience, Brain Mapping EEG Laboratory, Alzheimer's Research Unit, Honolulu,

Background: Cerebrospinal fluid (CSF) biomarkers amyloid-β and tau proteins play a significant role in diagnosing Alzheimer's disease (AD). However, alternative non-invasive biomarkers are still being investigated for the early detection of the disease. Electroencephalogram (EEG) findings, particularly the slowing of brain wave patterns, have been observed in AD patients, but their relationship with CSF amyloid status has yet to be characterized.

Methods: This was a retrospective cohort study that investigated the association between CSF amyloid status, EEG findings, and AD stage. Logistic regression analysis was employed to examine the relationship between the presence of abnormal slowing and CSF amyloid status. Demographic information, MMSE scores, CSF amyloid status, and MRI reports were collected for each participant. EEG recordings were analyzed through visual analysis and manual counting.

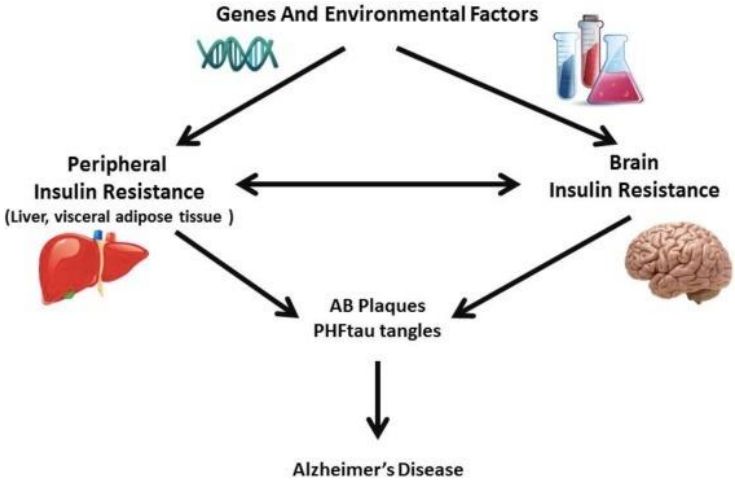
Results: In total 19 participants were included, of which 13 were CSF amyloid positive and 6 were CSF amyloid negative. Among the CSF amyloid positive individuals, 8 (61.5%) displayed evidence of diffuse background slowing, while 2 (33.3%) of the CSF amyloid negative individuals exhibited diffuse background slowing. Logistic regression analysis revealed a statistically significant association between positive CSF amyloid status and the presence of diffuse background slowing (odds ratio = 6.667; p-value = 0.039).

Conclusion: This study provided evidence of an association between abnormal diffuse background slowing observed in EEG recordings and positive CSF amyloid status. Integrating EEG analysis may enhance AD diagnosis and facilitate means of early intervention in disease progression.

Hawaii Memory Disorders Ctr & Alzheimer's Research Unit ranked #1 of 70 US Sites Investigating Semaglutide GLP-1 RA (Glucagon Like Peptide 1-Receptor Agonist) in Alzheimer's EVOKE study

According to Novo Nordisk Website, Alzheimer's disease represents a rapidly growing public health concern causing significant detrimental consequences to the affected people and their families and has led to substantial and increasing global socioeconomic impact. Worldwide, 70-100 million people are estimated to have early Alzheimer's disease (mild cognitive impairment and mild dementia stages). Photo credit: Science direct

Is Alzheimer's an Insulin Signaling Problem?



Animal studies highlight the key effects of GLP-1 relevant for Alzheimer's disease including improved memory function and reduced phospho-tau accumulation. According to Evaluate, study testing the hypothesis that neurodegeneration is linked to low insulin and insulin resistance, and thus that a GLP-1 analogue diabetes drug like Novo's Victoza could improve cognitive function. A correlation between blood glucose levels and rate of cognitive decline can be seen even without clinical diabetes, some have suggested, but type 2 diabetes almost doubles the risk of developing Alzheimer's and is associated with accelerated cognitive decline in people with mild cognitive impairment. Others have suggested that insulin plays a role beyond glucose metabolism and could be involved in memory and learning. One paper describes the function of insulin receptors in the brain,and says defects in these receptors have been identified in neurons from Alzheimer's brains.

Randomized Double-blind Placebo-controlled Clinical Trial Investigating the Effect and Safety of Oral Semaglutide in Subjects With Early Alzheimer´s Disease (EVOKE) (NIH Info) Semaglutide has specifically been shown to reduce measures of neuro-inflammation which may affect cognition and function. Finally, in a post-hoc analysis of data from three large cardiovascular outcomes trials conducted by Novo Nordisk (LEADER, SUSTAIN 6 and PIONEER 6), which included 15,820 patients with type 2 diabetes with median follow-up of 3.6 years, a total number of 47 people were identified with development of dementia, of which 32 were on placebo and 15 on GLP-1 (liraglutide or semaglutide). The rate of developing dementia was statistically significantly reduced by 53% in favour of GLP-1. Oral semaglutide (7 mg and 14 mg) is approved as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes in the US, EU and Japan.

"Thanks to the support of our community, our team of neurologists, dementia specialists and investigators and dedicated research staff at the Memory Disorders Center & Alzheimer's Research Unit at Hawaii Pacific Neuroscience, in Honolulu cannot be more proud of the work we do here in Hawaii to contribute to the worldwide effort to meet unmet needs in this exciting field in Neurodegeneration", says Kore Liow, MD, Principal Investigator and Neurologist, Hawaii Pacific Neuroscience. info@HawaiiNeuroscience.com or Alzheimer's Research Unit Hotline (808) 564-6141 or NIH Info

anne

Alzheimer's Neural Network EEG

ANNE (Alzheimer's Neural Network EEG) Lab Developing Noninvasive, Easily Accessible and Cost-Efficient EEG (Electroencephalogram) Biomarker for Early Detection and Monitoring of Alzheimer's Disease

There is currently no widely available biomarker to measure someone's memory or cognitive abilities to look for early signs of Alzheimer's or monitor the efficacy of treatment or progression. Traditional memory testing are subjective and depends on patients' performance thus we rely on invasive test like spinal tap and use of radioactive substance injected into body to look for Alzheimer's biomarker in the brain which are not readily accessible in island communities such as Hawaii state and many rural communities in US. Lack of readily available testing often leads to delayed diagnosis & intervention and eventually poor long-term outcome. *(2023 ANNE Research Team (front) medical students Kirra Borrelo, Shay Nakahira, Neurologist Kore Kai Liow, MD, research staff Ena Zhu, Baylee Valenzuela (back) Jason Schroeder, REEG tech, Sam Kim and Sarah Hogue)*

The Hawaii Memory Disorders Center & Alzheimer's Research Unit collaborates with the EEG Lab & Brain Research Innovation & Translation Labs to launch the Hawaii ANNE (Alzheimer's Neural Network EEG) Biomarker Lab dedicated to develop an easily accessible, noninvasive and cost effective biomarker to measures synaptic neuronal network brain electrical activities, measuring the frequency as well as specific brain waves to access the health of the brain and its function like memory and cognitive abilities?

ANNE

alzheimer's association AAIC 21

Denver, CO, July 2021

Evaluating Whether EEG could Predict Alzheimer's Disease Onset in Preclinical Patients with the ApoE41

Hawaii NBC News HInow 2023, Nov

AES AMERICAN EPILEPSY SOCIETY

Nashville, TN, Dec 2022

EEG Predicting Alzheimer's Disease Onset in Preclinical Patients with the ApoE4 Allele: ***An Update on EEG Findings***

Peer Reviewed Pub Med Publication: *Abnormal Temporal Slowing on EEG Findings in Preclinical Alzheimer's Disease Patients with the ApoE4 Allele: A Pilot Study Kim N, Tan C, Ma E, Kutlu S, Carrazana E, Vimala V, Viereck J, Liow K. (October 28, 2023) Cureus 15(10): e47852. DOI 10.7759/Cureus.47852.*

"Our Hawaii patients, caregivers, families, neurologists & researchers are honored to be able to play a role to contribute to this important ground breaking research to develop a noninvasive, widely available and cost effective tool for Alzheimer's Disease to serve our island and rural populations, " Kore Kai Liow, MD, Director, Hawaii Memory Disorders Center Principal Investigator, Alzheimer's Neural Network EEG (ANNE) Research Lab, Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawai`i John Burns School of Medicine. Dr. Liow is a research neurologist trained in clinical neurophysiology & EEG at National Institutes of Health (NIH), Bethesda, Maryland. ***Info: kliow@hawaii.edu***

Abnormal Temporal Slowing on EEG Findings in Preclinical Alzheimer's Disease Patients With the ApoE4 Allele: A Pilot Study

Enze Ma1, Selin Kutlu1, Nathan Kim1, Vimala Vajjala, MD1,2, Enrique Carrazana, MD1,2, Jason Viereck, MD, PhD1,2 and Kore Liow, MD1,2,
(1) John A. Burns School of Medicine, Honolulu, HI, USA,
(2) ANNE (Alzheimer's Neural Network EEG) Research Lab, Hawaii Pacific Neuroscience, Honolulu, HI, USA

Introduction: Currently, there are limited accessible and cost-effective biomarkers for preclinical Alzheimer's disease (AD) patients. However, the apolipoprotein E (ApoE) polymorphic alleles can predict if someone is at high (e4), neutral (e3), or low (e2) genetic risk for developing AD. This study analyzed electroencephalogram (EEG) reports from individuals with various ApoE genotypes, aiming to identify EEG changes and patterns that could potentially serve as predictive markers for preclinical AD progression.

Methods: Participants aged 64-78 were selected from the patient database at an outpatient neurology clinic. Genotype studies were performed to determine ApoE status, followed by EEG analysis to identify any apparent trends. A case-control design was used, categorizing participants into cases (e2e3, e2e4, e3e4, e4e4) and controls (e3e3). EEG recordings were compared between the groups to identify potential differences in EEG characteristics, including abnormal temporal slowing, frequency, and ApoE genotype association.

Results: Among 43 participants, 49% demonstrated evidence of abnormal temporal slowing on EEG. Of these, 48% displayed focal left temporal slowing, and 52% displayed bilateral temporal slowing. The right-sided temporal slowing was not observed. Among participants with abnormal slowing, 95% exhibited theta frequency (4-8 Hz) slowing, while only 4.8% displayed delta frequency (0-4 Hz) slowing. Among participants with the ApoE4 allele, 61.5% demonstrated evidence of abnormal slowing, compared to 43.3% without it. Furthermore, the presence of an ApoE4 allele was associated with a significantly higher proportion of males (54%) compared to those without it (13%) ($p=0.009$).

Conclusions: Although we did not find a statistically significant difference in temporal EEG slowing among different ApoE genotypes, our findings suggest a potential association between temporal slowing on EEG and the presence of an ApoE4 allele in individuals with preclinical AD. These observations highlight the need for further exploration into the potential influence of the ApoE4 allele on EEG findings and the utility of EEG as a complementary diagnostic tool for AD. Longitudinal studies with large sample sizes are needed to establish the precise relationship between EEG patterns, ApoE genotypes, and AD progression.

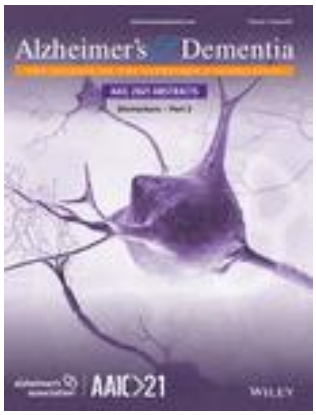
DOI: 10.1002/alz.049677

BIOMARKERS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Evaluating whether EEG could predict Alzheimer's disease onset in preclinical patients with the ApoE4 allele



Enze Ma1, Selin Kutlu1, Nathan Kim1, Catherine Mitchell3, Vimala Vajjala, MD1,2, Enrique Carrazana, MD1,2, Jason Viereck, MD, PhD1,2 and Kore Liow, MD1,2,
(1) John A. Burns School of Medicine, Honolulu, HI, USA,
(2) ANNE (Alzheimer's Neural Network EEG) Research Lab, Hawaii Pacific Neuroscience, Honolulu, HI, USA

Background: 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.

Method: 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.

Result: 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.

Conclusion: 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.

2022 American Epilepsy Society Meeting
Nashville, TN December 2022

Evaluating Whether EEG Could Predict Alzheimer's Disease Onset in Preclinical Patients with the ApoE4 Allele: An Update

Kim N1, Tan C2, Ma E2, Kutlu S3, Mitchell C3, Carrazana E1,3, Viereck J1,3, Vajjala V1,3 Liow K1,3
1. John A. Burns School of Medicine at the University of Hawaii, 2. University of Hawaii at Manoa, 3. Alzheimer's Research Unit Neurodiagnostic lab, Hawaii Pacific Neuroscience

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease and the leading cause of dementia in the elderly. AD is diagnosed primarily through clinical examination, but mental status exams, supportive imaging, and/or laboratory tests are often used as well. Although no predictive biomarkers or tests are currently available for preclinical patients, the Apolipoprotein E (ApoE) polymorphic alleles are the strongest genetic risk factor for indicating if a patient is at high (e4 allele), neutral (e3 allele), or low risk (e2 allele) for developing AD. Previous studies have also shown that there may be electrical changes in the brains of mild cognitive impaired (MCI) patients as memory loss progresses. In this study, electroencephalogram (EEG) analysis was used in preclinical patients with 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 (HPN) patient database. Participants had a Mini-Mental Status Exam (MMSE) score no lower than 28 and were asymptomatic at the time of the study. A genotype study was performed to determine the ApoE genotype for each participant (1 e2e4; 3 e2e3; 26 e3e3; 7 e3e4; 3 e4e4). EEG was performed to determine any apparent trends via visual analysis for each participant.

Results: This study included EEG and genotype data from a previous study that examined 18 preclinical participants and introduced data for 22 additional participants from the same database. Of the combined 40 participants, 19 (47.5%) displayed evidence of abnormal temporal slowing of some kind. Of these 19 participants, 10 displayed focal left temporal slowing and 9 displayed bilateral temporal slowing of some kind. The remaining 21 participants showed no abnormalities in their EEG study. Of all participants, 2 e2e3 participants (67%) 1 e2e4 participant (100%), 10 e3e3 participants (38%) 5 e3e4 participants (71%), and 1 e4e4 participant (33%) displayed abnormal slowing. Of the participants with an ApoE4 allele present in their genotype, 7 (64%) displayed abnormal slowing. Of the participants without an ApoE4 allele present in their genotype, 12 (41%) displayed abnormal slowing.

Conclusion: This study suggests that EEG has potential to serve as a prognostic tool for the progression to AD in patients, particularly those with the presence of the ApoE4 allele. Our data showed that individuals with an ApoE4 allele present in their genotype had a higher percentage of abnormal temporal slowing being present on their EEG compared to individuals without an ApoE4 allele present. However, the small sample sizes for certain genotype groups are a limitation of this study and may have influenced our findings. Future studies may involve examining EEG data in this same patient population over time to determine if our EEG data correlates with the future onset of cognitive symptoms. If successful, EEG may be an additional, noninvasive, affordable tool that could aid in the early diagnosis and intervention of AD to delay the progression of permanent memory loss.

Stroke & Neurologic Restoration Center

Stroke Research Unit

Stroke & Neurologic Restoration Center & Stroke Research Unit

The Hawaii Stroke and Neurologic Restoration Center focuses all of our efforts on the goal significantly improving the chances of an excellent recovery after a stroke and the prevention of another stroke.

We strongly believe that our patients deserve high quality, compassionate care after their stroke. Therefore, we work laulima together using a holistic multidisciplinary approach team includes fellowship trained stroke and vascular neurologist, neurorehabilitation specialists, brain health wellness physician, speech, physical and occupational therapist to includes a comprehensive stroke work up to tailor individual treatment and stroke recovery plans for our patients.

This includes optimizing:

1. Preventive measures with use of medications and advanced procedure to reduce risk of another stroke
2. Rehabilitation efforts and use of new and innovative therapies like Botox injections and neuromodulation to help restore function and improve quality of life and function.
3. Holistic approach addressing mental concerns as well as diet and healthy activities with our board certified lifeline wellness physician especially reducing preventable lifestyle like smoking cessation program.

Clinical Trials available at Hawaii Stroke Research Unit

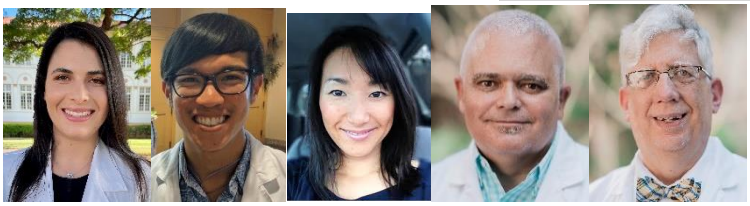
Publications by our specialists and researchers at the Hawaii Stroke Restoration Research Unit

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and encourage our patients to seek out credible resources with local and national support groups.

American Stroke Association.
A division of the American Heart Association.

Jason Viereck, MD, PhD
Director, Stroke and Neurologic Restoration Center
Sub investigator, Stroke Research Unit
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine,
University of Hawaii John Burns School of Medicine
Stroke Fellowship: Boston University Medical School
Neurology Residency: Boston University Medical School, Boston

PubMed Full Length Publications



Correlation Between Intracranial Calcification and Extracranial Stenosis of the Internal Carotid Artery

Julia R Jahansooz 1 2, Andrew Ko 1 2, Ryoko Hiroi 1 2, Masako Matsunaga 3, Enrique Carrazana 1 2, Jason Viereck 2 3
1Neurology, John A. Burns School of Medicine, Honolulu, USA. 2Brain Research, Innovation & Translation Laboratory, Hawaii Pacific Neuroscience, Honolulu, USA. 3Quantitative Health Sciences, John A. Burns School of Medicine, Honolulu, USA.

Rationale: Intracranial artery calcification is a marker of vascular atherosclerosis and has a high prevalence worldwide. Both atherosclerosis of the internal carotid artery at the carotid sinus in the neck and intracranial calcification have been associated with ischemic stroke. The relationship between the two has not been well studied.

Methods: The present study investigated how carotid sinus narrowing could relate to calcification located in the distal intracranial artery at the cavernous carotid. We examined a population not selected for cerebral disease. This retrospective study contained 179 subjects aged 18 years and older from the Hawaii Diagnostic Radiology database. Extracranial internal carotid artery stenosis was determined using the absolute diameter, North American Symptomatic Carotid Endarterectomy Trial, and common carotid artery methods. Calcification was scored using the modified Woodcock method.

Results: A positive correlation between intracranial calcification and extracranial carotid stenosis was found using all three methods. Individuals with intracranial calcification were more likely to be older, have a smaller internal carotid artery diameter, and have a greater percent stenosis at the internal carotid artery than those without intracranial artery calcification ($p<0.001$ for all).

Conclusions: These results may help refocus interest in calcification in studies of cerebral vasculature and its correlation with extracranial carotid stenosis.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10332851/
Free Full text PMC

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications

Journal of Stroke and Cerebrovascular Diseases

Native Hawaiian And Other Pacific Islanders' Leading Risk Factors For Ischemic Stroke: A Comparative Ethnographic Study

Ogasawara R, Kang E, Among J, Oyadomari K, Capitaine J, Regaspi N, Borman P, Viereck J, Carrazana E, Liow KK. Native Hawaiian and Other Pacific Islanders' Leading Risk Factors for Ischemic Stroke: A Comparative Ethnographic Study. J Stroke Cerebrovasc Dis. 2022 Jun;31(6):106433.
doi: 10.1016/j.jstrokecerebrovasdis.2022.106433. Epub 2022 Mar 24. PMID: 35339856.

Hawaii is a multicultural state with many different ethnicities, including Native Hawaiians and other Pacific Islanders (NHOPI). This demographic has not been thoroughly studied, despite its significantly higher prevalence of stroke. This study aimed to characterize risk factors for ischemic stroke in NHOPI compared to other ethnicities.

Methods:
An Institutional Review Board (IRB) sanctioned retrospective chart review was conducted at a multi-site community neurology clinic from June 2017 through June 2019. Prospective patients were identified from the database using the International Classification of Diseases 10th Edition (ICD-10) codes for ischemic stroke. 326 patients (99 NHOPI, 116 Asian, 111 Caucasian) with a history of ischemic stroke met the inclusion criteria. Risk factors were determined based on the American Stroke Association guidelines; ethno-racial grouping was based on self-identification; and average household income levels were estimated based on patient zip codes US Census Bureau data. Continuous variable risk factors were analyzed using an analysis of variance (ANOVA) and post-hoc pairwise comparisons using Tukey-Kramer; a multivariate analysis was conducted.

Results:
Compared to Asians and Caucasians, NHOPI patients were on average 11 years younger at the onset of stroke and more likely to be women. The NHOPI group also had the highest rates of diabetes and obesity. NHOPI average income was significantly lower compared to the Caucasian group. Hypertension and hyperlipidemia were found to be higher in the Asian population. Alcohol consumption was reported more frequently among Caucasian patients.

Conclusions:
These results better-characterized risk factors for ischemic stroke among NHOPI in Hawaii. The younger age of stroke onset in NHOPI patients is likely due to the higher burden of cardiovascular risk factors like obesity, smoking, and diabetes. Identifying such disparities in associated risk for NHOPI and other ethnicities can allow targeted stroke prevention and outpatient care in a multicultural setting

PubMed Full Length Publication:

Identification Of Associations and Distinguishing Moyamoya Disease from Ischemic Strokes Of Other Etiologies: A Retrospective Case-Control Study

Annals of Medicine and Surgery, Volume 78, June 2022,103771, ISSN 2049-0801

Cori Xiu Yue Sutton a, Enrique Carrazana a,b, Catherine Mitchell b, Jason Viereck a,b, Kore Kai Liow a,b, Arash Ghaffari-Rafi a,c,*

a University of Hawai‘i at M¯anoa, John A. Burns School of Medicine, Honolulu, HI, USA
b Hawai‘i Pacific Neuroscience, Stroke & Neurologic Restoration center, Brain Research, Innovation and Translation Lab, Honolulu, HI, USA
c University of California Davis, School of Medicine, Department of Neurological Surgery, Sacramento, CA, USA

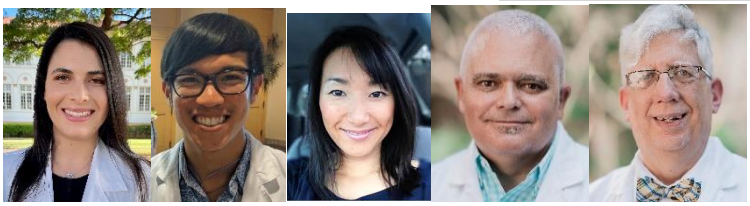
Introduction
Better characterizing moyamoya disease (MMD) from ischemic strokes of other etiologies may facilitate earlier diagnosis by raising suspicion for a diagnostic work-up.

Methods
To identify associated variables, MMD cases (n = 12) were compared against three sets of controls: age-, sex-, and race-matched controls of patients with general neurological disorders (n = 48), unmatched general controls (n = 48), and unmatched non-MMD ischemic stroke controls (n = 48).

Results
MMD patients were 32 years ($p < 0.0001$) younger than ischemic stroke controls. Relative to non-MMD ischemic strokes, MMD patients had greater odds of presenting with visual field defects (OR: 9.13, $p = 0.09$) or dizziness (OR: 9.13, $p = 0.09$), as well as being female (OR: 8.04, $p = 0.008$), Asian (OR: 3.68, $p = 0.087$), employed (OR: 6.96, $p = 0.02$), having migraines (OR: 21.61, $p = 0.005$), epilepsy (OR: 6.69, $p = 0.01$), insomnia (OR: 8.90, $p = 0.099$), and a lower Charlson Comorbidity Index (CCI; $p = 0.002$). Patients with MMD, compared to non-MMD ischemic strokes, also had a 4.67 kg/ greater body mass index (BMI) and larger odds (OR relative to normal BMI: 21.00, $p = 0.03$) of being from obesity class III (>40 kg/), yet reduced odds of coronary artery disease (OR: 0.13, $p = 0.02$). Relative to general controls, MMD patients had greater odds of diabetes mellitus type 2 (OR: 10.07, $p = 0.006$) and hypertension (OR: 7.28, $p = 0.004$).

Conclusion
MMD not only has a unique clinical presentation from other ischemic strokes, but also unique comorbidities, which may facilitate earlier work-up and treatment.
Moyamoya patients are 32 years younger than ischemic strokes of other etiologies.
Moyamoya patients are 4.67 kg/ heavier than those with ischemic strokes.
Moyamoya patients are at greater odds of type 2 diabetes mellitus and hypertension.
Moyamoya patients are at reduced odds of coronary artery disease.
Moyamoya patients present more often with visual field deficits or dizziness.

PubMed Full Length Publications



Correlation Between Intracranial Calcification and Extracranial Stenosis of the Internal Carotid Artery

Julia R Jahansooz 1 2, Andrew Ko 1 2, Ryoko Hiroi 1 2, Masako Matsunaga 3, Enrique Carrazana 1 2, Jason Viereck 2 3
1Neurology, John A. Burns School of Medicine, Honolulu, USA. 2Brain Research, Innovation & Translation Laboratory, Hawaii Pacific Neuroscience, Honolulu, USA. 3Quantitative Health Sciences, John A. Burns School of Medicine, Honolulu, USA.

Rationale: Intracranial artery calcification is a marker of vascular atherosclerosis and has a high prevalence worldwide. Both atherosclerosis of the internal carotid artery at the carotid sinus in the neck and intracranial calcification have been associated with ischemic stroke. The relationship between the two has not been well studied.

Methods: The present study investigated how carotid sinus narrowing could relate to calcification located in the distal intracranial artery at the cavernous carotid. We examined a population not selected for cerebral disease. This retrospective study contained 179 subjects aged 18 years and older from the Hawaii Diagnostic Radiology database. Extracranial internal carotid artery stenosis was determined using the absolute diameter, North American Symptomatic Carotid Endarterectomy Trial, and common carotid artery methods. Calcification was scored using the modified Woodcock method.

Results: A positive correlation between intracranial calcification and extracranial carotid stenosis was found using all three methods. Individuals with intracranial calcification were more likely to be older, have a smaller internal carotid artery diameter, and have a greater percent stenosis at the internal carotid artery than those without intracranial artery calcification ($p<0.001$ for all).

Conclusions: These results may help refocus interest in calcification in studies of cerebral vasculature and its correlation with extracranial carotid stenosis.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10332851/
Free Full text PMC

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications

Investigating Young Atypical Stroke Risk Factors and Etiologies in Native Hawaiian and Pacific Islander Populations

D-Dre Wright[1,2], Michelle Lu[1,2], Anson Y. Lee[1,2], Edward J. Weldon[1,2], Julia R. Jahansooz[1,2], Kyle M. Ishikawa, MS[1,3], Enrique Carrazana, MD[1], Jason Viereck, MD, PhD[1], Kore K. Liow, MD, FACP, FAAN[1,2]

[1]Stroke and Neurologic Restoration Center, Hawaii Pacific Neuroscience, Honolulu, HI, [2]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, [3]Department of Quantitative Health Sciences, University of Hawai'i John A. Burns School of Medicine, Honolulu HI

Introduction: Ischemic and hemorrhagic strokes in patients ≤45 years old are uncommon and represent only 10%-15% of all stroke patients. Native Hawaiian/Pacific Islander (NHPI) populations in particular have a 30% higher occurrence of younger atypical stroke patients than non-Hispanic Whites, but a thorough analysis of differences in risk factors and etiologies has not been conducted. Hence, this study aimed to characterize distinctions in atypical stroke patient profiles among the NHPI population.

Methods: This retrospective study was a single-center analysis of all atypical stroke patients ≤45 years old from 2009-23. Patient charts were reviewed for demographics, risk factors, and stroke etiology. Descriptive statistics were performed using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.

Results: Of the 66 patients included, 25 were identified as NHPI. The mean patient age at the time of stroke was 38 years for both NHPI and non-NHPI cohorts. NHPI patients had higher rates of hypertension (p=0.022) and a positive family history of stroke (p=0.045). However, all other variables were insignificant between the two patient groups including known risk factors for stroke such as coronary artery disease (p>0.999), hyperlipidemia (p=.792), arrhythmias (p=0.396), and diabetes (p=0.724).

Conclusion: NHPI atypical stroke patients were significantly associated with higher rates of hypertension and a positive family history of stroke compared with non-NHPIs. This study identified key differences in atypical stroke risk among NHPIs that should be further investigated to guide preventative health guidelines.

CHARACTERIZING SMALL VESSEL DISEASE IN NATIVE HAWAIIAN AND OTHER PACIFIC ISLANDERS WITH DEMENTIA: A RETROSPECTIVE PILOT STUDY

Michelle Trinh[1,2], Elise Wong[1,3], Megan Baldemor[1,4], Sarah Song[1,5], Tyson Wu[1,6], Julia Jahansooz[1,2], Edward Weldon[1,2], Anson Lee[1,2], Chathura Siriwardhana PhD[2],
Yone-Kawe Lin[2], Jason Viereck, MD, PhD[1], Kore Liow, MD, FACP, FAAN[1,2], Enrique Carrazana, MD[1]
[1]Memory Dis Center Alz Research Unit, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, [3] Punahou School, Honolulu, HI, [4]Santa Clara University, Santa Clara, CA, [5]Pomona College, Claremont, [6]University of Hawaii at Manoa, Honolulu, HI

Objectives Small vessel disease (SVD), a major cause of age-related cognitive decline, affects small cerebral blood vessels, leading to cerebral hypoperfusion. Native Hawaiians and other Pacific Islanders (NHOPI) are reported to have higher rates of vascular risk factors of SVD, such as hypertension. This study aims to characterize the prevalence and severity of SVD in NHOPI dementia patients compared to their Caucasian and Asian counterparts.

Methods This retrospective chart review analyzed data from dementia patients ≥ 18 years old with a brain MRI and MMSE score between 23-27. Each NHOPI patient was matched with a Caucasian and Asian patient based on age, sex, and MMSE score. Patient charts were reviewed for demographics, comorbidities, medications, and SVD MRI findings at time of presentation of memory concerns.

Results Overall, 108 patients were included, with 36 patients in each racial group, a mean patient age of 72.1 years, and 72 (66.7%) females. NHOPI patients had a higher BMI ($p<0.001$) and higher rates of hypertension ($p=0.024$), diabetes mellitus ($p=0.020$), and coronary artery disease ($p=0.026$). NHOPI had higher rates of reporting attention deficits as a symptom of dementia ($p=0.015$). However, there were no significant differences in prevalence or severity of white matter lesions, subcortical infarcts, or brain atrophy among the racial groups.

Conclusion
NHOPI patients were significantly associated with higher rates of vascular risk factors and showed differences in presentation of dementia. Further investigation is needed to identify potential preventative targets and improve risk predictions for individuals with SVD.

CENTER FOR RARE

NEUROLOGICAL DISEASES

According to NIH Rare Diseases Clinical Research Network (RDCRN), an estimated 25 million Americans are affected by one of the more than 7,000 known rare diseases. Only a few hundred of these disorders have any treatments available.

Hawaii Pacific Neuroscience Center for Rare Neurological Diseases aim to:

-Hope through clinical and translational research

-Provide comprehensive compassionate care to patients affected

-Raise disease awareness and education

Our mission is to improve the lives of those affected by rare neurological disorders by leveraging insights from neuroscience and advantages in technology to meet unmet needs of those affected in Hawaii and Pacific Islands.

Our vision is to empower patient populations, their ohana and health care providers through collaboration, mentorship, and research to improve the lives of those affected.

We focus our effort in:

- Advancement of research through biological insights conducted at the Clinical Research Center
- Providing comprehensive multidisciplinary care at Center for Rare Neurological Diseases
- Education of other physicians and investigators interested in neurological rare diseases.
- Exploration of partnerships and collaborations with academia, patients groups, and industry

Center for Rare Neurological Diseases leverage the expertise of multidisciplinary neuroscience Team so that each patient workups and treatment is individually tailored to their presentations and needs involving input from their family/ohana. Plans can include medications, lifestyle recommendations and research options. Clinical Research Center is a part of the global network of top neuroscience centers involved in research in rare diseases recognized nationally.

Clinical Trials available in Hawaii

Publications by Hawaii's specialists & researchers

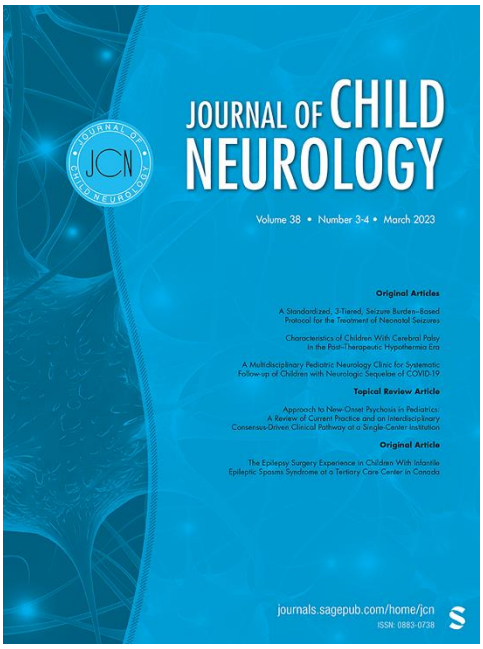
Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey we recommend resources at NIH- https://ncats.nih.gov/rdcrn

Kore Kai Liow, MD, FACP, FAAN
Director, Center for Rare Neurological Diseases
Principal Investigator, Clinical Research Center
Hawaii Pacific Neuroscience
Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawaii John Burns School of Medicine

PubMed Full Length Publication

The Gomez-Lopez-Hernandez Syndrome: The Contribution of 2 Hispanic Giants of Pediatric Neurology

Liang BX, Carrazana E, Viereck J, Liow KK. The Gomez-Lopez-Hernandez Syndrome: The Contribution of 2 Hispanic Giants of Pediatric Neurology. J Child Neurol. 2023 May 18:8830738231176057. doi: 10.1177/08830738231176057. PMID: 37203136.



Brain Research, Innovation, Translation Labs (BRITL), Hawaii Pacific Neuroscience, University of Hawaii, John A. Burns School of Medicine

The specialty of Pediatric Neurology emerged during the 20th century, a period in which many neurologists played significant roles in revolutionizing this field. Two acclaimed pediatric neurologists of Hispanic origin, Drs Manual Gomez and Arturo Lopez-Hernandez, made substantial contributions to the literature on pediatric neurology.

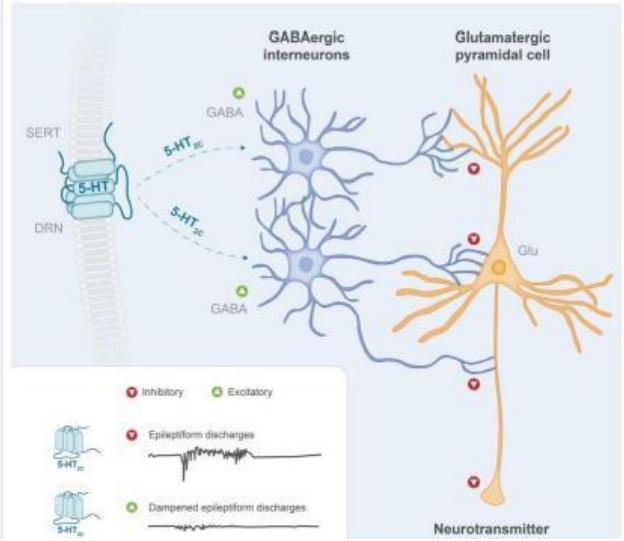
One of their remarkable contributions was their discovery of a new, rare neurocutaneous syndrome with variable phenotype, the Gomez-Lopez–Hernandez syndrome (GLHS). Here, we describe the current understanding of GLHS and the historical background of how 2 celebrated Hispanic pediatric neurologists discovered this rare, sporadic syndrome during a time when there was a limited representation of minorities in the medical profession.

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications

Center for Rare Neurological Diseases & Comprehensive Epilepsy Center, First among 25 US Epilepsy Centers to Investigate LP352 - next generation 5-HT2c receptor Superagonist in PACIFIC Study in Developmental and Epileptic Encephalopathies (DEE) Seizures

According to Longboard and its websites, Developmental and Epileptic Encephalopathy (DEE) syndromes (DEEs) refer to a group of severe heterogeneous epilepsies that are characterized by drug resistant seizures and significant developmental delay like Lennox Gastaut Syndrome. Importantly, if seizure control can be improved, developmental delay may slow. Most DEEs begin early in life, often starting in infancy. Children can have frequent and severe seizures which may be of multiple types. Epileptic spasms, tonic or atonic seizures and myoclonic seizures, among other seizure types, can be seen. In many cases, seizures are life long, although in some instances they can abate with time with certain syndromes or specific causes

LP352 is a highly selective, oral, centrally acting, next-generation 5-HT2c receptor superagonist in development for the potential treatment of seizures associated with developmental and epileptic encephalopathies (DEEs) such as Dravet syndrome, Lennox-Gastaut syndrome (LGS), tuberous sclerosis complex (TSC), CDKL5 deficiency disorder (CDD), and other epileptic disorders.



LP352 is designed to modulate GABA inhibition and, as a result, suppress the central hyperexcitability that is characteristic of seizures. LP352 has demonstrated negligible observed impact on 5-HT2b and 5-HT2a receptor subtypes in the Company's preclinical studies to date. 5-HT2b and 5-HT2a receptor agonism have been associated with significant adverse effects. LP352 has novel chemistry and attributes, and was designed to be more specific and selective for the 5-HT2c receptor subtype, giving it the potential to reduce seizures in DEE patients while overcoming the known or perceived safety limitations of available drugs in the 5-HT2 class. LP352 is currently being evaluated in the Phase 1b/2a PACIFIC Study in approximately 50 participants with a range of DEEs.

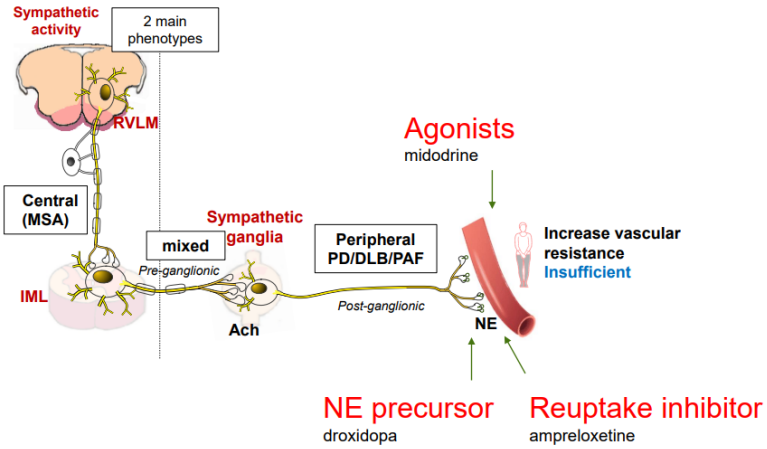
The PACIFIC Study is a Phase 1b/2a clinical study evaluating adult participants with DEEs.

An individual may qualify for the study if they:

- Are 17 to 65 years of age
- Have been diagnosed with a DEE, including Lennox-Gastaut Syndrome, Dravet Syndrome, or other DEEs
- Are currently taking 1 to 4 antiseizure medications at a stable dose

More information: info@HawaiiNeuroscience.com or Epilepsy Research Unit Hotline (808) 564-6141 or Comprehensive Epilepsy Center at Hawaii Pacific Neuroscience (808) 261-4476.

Center for Rare Neurological Diseases, Honolulu awarded Research Study on Rare Neurological Condition of Multiple System Atrophy (MSA) Multiple System Atrophy (MSA) and Symptomatic Neurogenic Orthostatic Hypotension (nOH).



According to Therevance MSA is a progressive brain disorder that affects movement and balance and disrupts the function of the autonomic nervous system. The autonomic nervous system controls body functions that are mostly involuntary. One of the most frequent autonomic symptoms associated with MSA is a sudden drop in blood pressure upon standing (nOH).1 There are approximately 50,000 MSA patients in the US2 and 70-90% of MSA patients experience nOH symptoms.3 Despite available therapies, many MSA patients remain symptomatic with nOH.

Neurogenic orthostatic hypotension (nOH) is a rare disorder defined as a fall in systolic blood pressure of >20 mm Hg or diastolic blood pressure of >10 mm Hg, within 3 minutes of standing. Severely affected patients are unable to stand for more than a few seconds because of their decrease in blood pressure, leading to cerebral hypoperfusion and syncope. A debilitating condition, nOH results in a range of symptoms including dizziness, lightheadedness, fainting, fatigue, blurry vision, weakness, trouble concentrating, and head and neck pain.

Ampreloxetine (TD-9855) is an investigational, once-daily norepinephrine reuptake inhibitor in development for the treatment of symptomatic nOH in patients with multiple system atrophy (MSA). Patients with MSA may benefit from ampreloxetine treatment due to the presence of central autonomic pathway degeneration and intact peripheral postganglionic fibers that is specific to MSA. As a NET re-uptake inhibitor, ampreloxetine may enhance the function of the residual sympathetic nerves resulting in increases in norepinephrine levels, standing BP, and reduction in symptoms of nOH in patients with MSA.

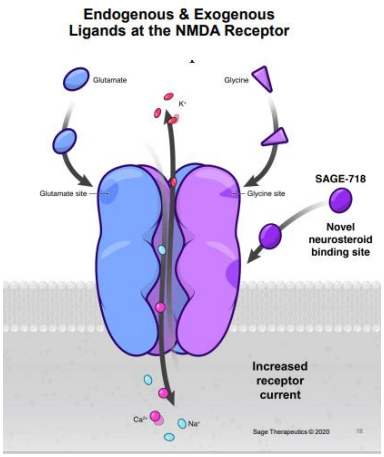
2022 November data presented at the American Autonomic Society 33rd International Symposium presented Phase 3 results (Study 0170) showed a benefit to MSA patients in the study that was observed in multiple endpoints including Orthostatic Hypotension Symptom Assessment (OHSA) composite, Orthostatic Hypotension Daily Activities Scale (OHDAS) composite, Orthostatic Hypotension Questionnaire (OHQ) composite and OHSA #1.

The CYPRESS Study is a Phase 3, Multi-center, Randomized Withdrawal and Long Term Extension Study of Ampreloxetine for the Treatment of Symptomatic Neurogenic Orthostatic Hypotension:

- at least 30 years old.
- MSA of the Parkinsonian subtype (MSA-P) or cerebellar subtype (MSA-C) according to The Gilman Criteria (2018)
- nOH, as demonstrated by a sustained reduction in BP of ≥20 mmHg (systolic) or ≥10 mmHg (diastolic) within 3 min of standing as part of orthostatic standing test or being tilted up ≥60o from a supine position as determined by a tilt-table test.

More information: info@HawaiiNeuroscience.com or Clinical Research Center Hotline (808) 564-6141 or Center for Rare Neurological Diseases at Hawaii Pacific Neuroscience (808) 261-4476.

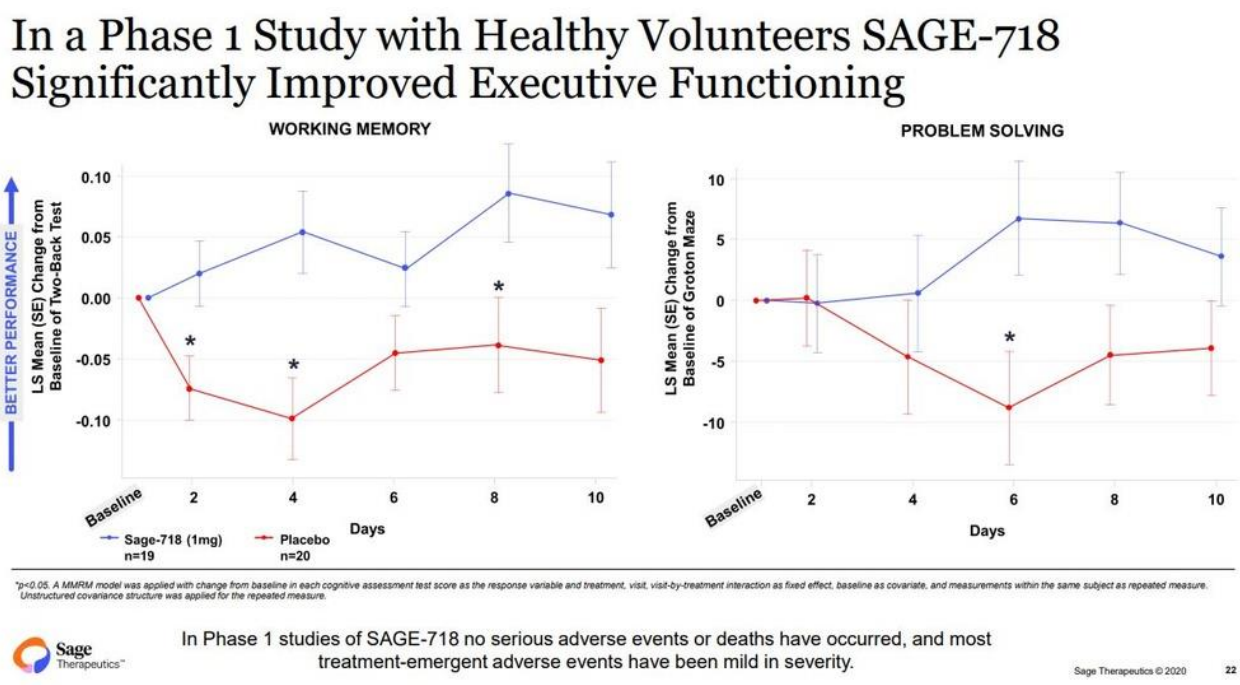
Hawaii Center for Rare Neurological Diseases 1 of 20 sites in US Selected for Hawaii's first study for Huntington's Disease Investigating NMDA Receptor Positive Allosteric Modulator effect on Cognitive Functions



According to Sage Therapeutic website, Huntington's disease (HD) is a rare, inherited neurodegenerative disease that progresses over time. Up to 30,000 adults are diagnosed with HD in the U.S. each year. Symptoms usually appear between ages 30–45, worsen over the following 15–20 years, and ultimately lead to death. Psychiatric and cognitive symptoms can severely affect people with HD. "HD is an autosomal dominant genetic disorder that impacts the brain and by nature numerous generations of a family. Cognitive decline is often one of the earliest signs of the disease and this decline, in addition to other symptoms, results in a devastating impact on independence, general functioning, and quality of life.

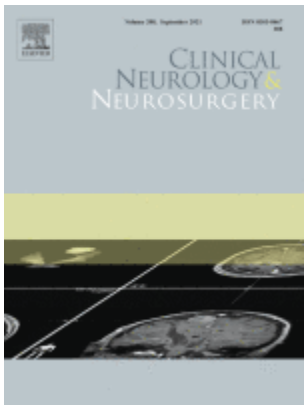
SAGE-718, Sage's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). Ongoing studies aim to evaluate whether SAGE-718 may have the potential to improve cognitive symptoms for these difficult-to-treat disorders.

In studies to date, treatment with SAGE-718 has been associated with improved cognitive performance, particularly in the domain of executive functioning. The FDA Fast Track Designation is an important milestone in the development of SAGE-718, as it provides opportunities to engage collaboratively with the FDA to further clinical development and future regulatory review of SAGE-718 for the treatment of HD



Photos credit: Sage

More information: info@HawaiiNeuroscience.com or Hawaii Parkinson's Research Unit Hotline (808) 564-6141 or Hawaii Parkinson's & Movement Disorders Center (808) 261-4476.



Characterizing idiopathic intracranial hypertension socioeconomic disparities and clinical risk factors: A retrospective case-control study, Clinical Neurology and Neurosurgery, Volume 208,2021,106894,ISSN 0303-8467

Frances Tiffany Cava Morden, Charissa Tan, Enrique Carrazana, Jason Viereck, Kore Kai Liow, Arash Ghaffari-Rafi

Introduction

Against the backdrop of the diverse minority-majority state of Hawaii, this study seeks to better characterize associations between idiopathic intracranial hypertension (IIH) with sociodemographic variables and medical comorbidities.

Methods

A retrospective case-control study was conducted by utilizing 54 IIH patients and 216 age-, sex-, and race-matched controls, 216 unmatched controls, and 63 age-, sex-, and race-matched migraine patients.

Results

Relative to controls, IIH were 25 years younger ($p < 0.0001$) and 10.18 kg/m2 heavier ($p < 0.0001$), as well as exhibited greater odds of the following variables ($p < 0.05$): female (odds ratio [OR]: 8.87), the lowest income quartile (OR: 2.33), Native Hawaiian or other Pacific Islander (NHPI; OR: 2.23), Native American or Alaskan Native (OR: 16.50), obesity class 2 (35.0–39.9 kg/m2; OR: 4.10), obesity class 3 (>40 kg/m2; OR: 6.10), recent weight gain (OR: 11.66), current smoker (OR: 2.48), hypertensive (OR: 3.08), and peripheral vascular disease (OR: 16.42). Odds of IIH were reduced ($p < 0.05$) for patients who were Asian (OR: 0.27) or students (OR: 0.30;). Unique from Whites, NHPI IIH patients exhibited greater odds ($p < 0.05$) for being from lower socioeconomic status and currently smoking, as well as potential association with seizures ($p = 0.08$). Compared to migraines, IIH headaches were at increased odds of occurring ($p < 0.05$) occipitally, for greater than 15 days per month, aggravated by postural changes, and comorbid with dizziness and tinnitus.

Conclusions

These results not only better characterize IIH, but also highlight socioeconomic and racial disparities in diagnosis

https://doi.org/10.1016/j.clineuro.2021.106894

NeuroCOVID CLINIC

NeuroCOVID RESEARCH

Hawaii Neuro COVID Clinic
Select site for NIH-NYU NeuroCOVID DataBank-Biobank

As of February 2022, Hawaii Neuro COVID Clinic is one of 20 US sites selected by NIH to serve as a participating site for the COVID-19 Neuro Databank-Biobank or NeuoCOVID Project to maintain a national resource studying neurological complications of COVID-19, project funded by the NINDS, NIH.

Hawaii Neuro COVID Clinic Interdisciplinary Specialists & Services

Specialists in memory, cognitive symptoms
Specialists in headache, facial & neck pain
Specialists in pain, muscle weakness and cognitive evaluation rehabilitation
Specialists in rehabilitation to minimize on-going damage and restore functions
Sleep specialist – specializes in evaluating "Covidsomnia", restless leg, sleep disorders associated with COVID
Wellness Physician - board certified in lifestyle medicine specializing in brain health

The goal is to provide patients with comprehensive neurologic long term whole-person health care. Based on the findings during the visit, the clinic may recommend further testing with other specialists, physical, occupational, and cognitive therapists. Patients visiting the clinic can expect a detailed neurologic history, physical & neurological examination which may include additional cognitive screenings, EEG, EMG and MRI brain.

"Recent study shows that at least one-third of people who have COVID-19 continue to experience neurological symptoms such as fatigue, brain fog, headache, decreased smell or taste, weakness, or pain. To address and treat neurological complications resulting from patients recovering from COVID-19, Hawaii Pacific Neuroscience has launched a interdisciplinary Neuro COVID clinic specifically to address the needs of these COVID "long haulers" Kore Kai Liow, MD, Neurologist & Director, Hawaii Neuro COVID Clinic, Hawaii Site Principal Investigator, NIH-NYU NeuroCOVID Project., Clinical Professor of Medicine (Neurology), University of Hawaii John Burns School of Medicine.

Hawaii NEURO NeuroCOVID Clinic NIH NeuroCOVID Databank-Biobank in Hawaii
Call or text (808) 261-4476

PubMed Full Length Publications

Mechanisms and Severity of Exercise Intolerance Following COVID-19 and Similar Viral Infections: A Comparative Review

Edward J. Weldon IV 1,2 , Bradon Hong1, 2 , Jeffrey Hayashi, 1,2 Connor Goo, 1,2 Enrique Carrazana 1,2, 3,Jason Viereck 1,2,3, Kore Liow 1,2,3
1 University of Hawaii John A. Burns School of Medicine, Honolulu, USA 2. Brain Research, Innovation, & Translation Laboratory, Hawaii Pacific Neuroscience, Honolulu, USA 3. Department of Neurology, Hawaii Neuro COVID Clinic, Honolulu, USA

Approximately 19% of the population is suffering from “Long COVID”, also known as post-acute sequelae of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (PASC), which often results in exercise intolerance. As COVID infections continue to be common, studying the long-term consequences of coronavirus disease (COVID) on physical function has become increasingly important. This narrative review will aim to summarize the current literature surrounding exercise intolerance following COVID infection in terms of mechanism, current management approaches, and comparison with similar conditions and will aim to define limitations in the current literature.

Multiple organ systems have been implicated in the onset of long-lasting exercise intolerance post-COVID, including cardiac impairment, endothelial dysfunction, decreased VO2 max and oxygen extraction, deconditioning due to bed rest, and fatigue. Treatment modalities for severe COVID have also been shown to cause myopathy and/or worsen deconditioning. Besides COVID-specific pathophysiology, general febrile illness as commonly experienced during infection will cause hypermetabolic muscle catabolism, impaired cooling, and dehydration, which acutely cause exercise intolerance.

The mechanisms of exercise intolerance seen with PASC also appear similar to post-infectious fatigue syndrome and infectious mononucleosis. However, the severity and duration of the exercise intolerance seen with PASC is greater than that of any of the isolated mechanisms described above and thus is likely a combination of the proposed mechanisms. Physicians should consider post-infectious fatigue syndrome (PIFS), especially if fatigue persists after six months following COVID recovery. It is important for physicians, patients, and social systems to anticipate exercise intolerance lasting for weeks to months in patients with long COVID.

These findings underscore the importance of long-term management of patients with COVID and the need for ongoing research to identify effective treatments for exercise intolerance in this population. By recognizing and addressing exercise intolerance in patients with long COVID, clinicians can provide proper supportive interventions, such as exercise programs, physical therapy, and mental health counseling, to improve patient outcomes.

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications

Hawaii Medical Students Valuable Contribution to NIH NeuroCOVID Data/BioBank including data on Native Hawaiians & Pacific Islanders (NHPI)

National Institute of Neurological Disorders and Stroke

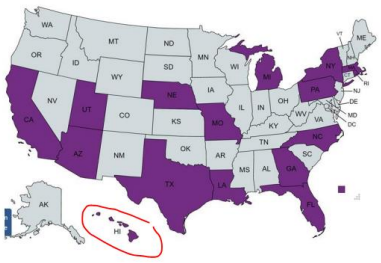
COVID-19 NEURO DATABANK/ BIOBANK

Hawaii NeuroCOVID Clinic & NeuroCOVID Research Lab is 1 of 17 US sites among Emory, Harvard/Mass Gen, NYU selected to participate in NIH funded [NeuoCOVID Project.](#)

NeuroCOVID: USA sites current status

- 17 sites in United States
- 2 sites on-boarding (AZ, CA)

- Brain & Spine*, AZ - Hemant Pandey
- Emory University School of Medicine, GA – Albert Anderson
- Hawaii Pacific Neuroscience, NeuroCOVID Clinic, HI - Kore Liow
- Madonna Rehabilitation Hospitals, NE – Judy Burnfield
- Massachusetts General Hospital, MA - Michael Levy
- New Orleans Children Hospital*, LA – Scott Schultz
- NYU Langone Health, NY – Jennifer Frontera
- Rhode Island Hospital, RI – Vincent LaBarbera
- South Shore Health, MA - Amy Trecartin
- Spectrum Health, MI – Muhib Khan
- University of Arizona, TX – Joyce Lee-Iannotti
- University of Massachusetts, MA - Nils Henninger
- University of North Carolina at Chapel Hill*, NC - Monica M. Diaz
- University of South Florida, FL – Keith Dombrowski
- University of Texas Health Science Center at Houston, TX - Rodrigo Hasbun
- University of Utah, UT - Adam DeHavenon
- Washington University School of Medicine, MO – Raj Dhar



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.

Characteristics

	Frequency	Percent
American Indian or Alaskan Native	6	<1%
Asian	35	4%
Black or African American	189	21%
Native Hawaiian or Pacific Islander	5	<1%
White	473	53%
More than 1 Race	8	<1%
Other	79	9%
Unknown	48	5%
Race Not Represented	45	5%
TOTAL	888	100%

The Hawaii's NeuroCOVID research team consisting of neurologists, researchers and medical students from the University of Hawaii John Burns School of Medicine.
As of April 2023, thanks to our medical students, Hawaii ranked #8 in data collected for NIH including valuable data on underrepresented minority groups like NHPI and Asian Americans.

HPN NeuroCOVID CLINIC NeuroCOVID RESEARCH

Principal Investigator, Kore Liow, MD, Neurologist & Director, [HawaiiNeuroCOVID Clinic,](#) Clinical Professor of Medicine (Neurology), Clinical & Translational Research
Medical students: Ward Weldon (lead), D-Dré Wright, Anita Cheung, Brandon Hong, Jonathan Carino, Cierra Nakamura, University of Hawai`i John Burns School of Medicine

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 and is funded by the NINDS, NIH through the NIH National Center for Advancing Translational Sciences through its Clinical and Translational Science Awards Program NIH, NINDS Grant 3UL1TR002541-01S1.

More Information: [NIH website](#), [NYU website, Hawaii Neuro COVID Clinic, Hawaii NeuroCOVID ResearchLab](#)

COMPREHENSIVE EPILEPSY CENTER

EPILEPSY RESEARCH UNIT


ABET
LAB
ACCREDITATION BOARD OF

Hawaii Comprehensive Epilepsy Center and Epilepsy Research Unit have a dedicated multidisciplinary team of epileptologist, neurologists, neurosurgeon neuropsychologists and research team whose sole purpose is to improve the quality of life of patients with epilepsy and seizure disorders from all Hawaiian Islands and the Pacific Rim. **Services available**

Honolulu, West Oahu & Neighbor Islands (808) 261-4476

We specialize in helping patients who were told by other doctors that there is nothing else could be done or where the diagnosis is not clear. Our professionals are experts in many diverse areas, from new medication development and state of the art diagnostic procedures including overnight Long Term Video-EEG Epilepsy Monitoring Unit (EMU) to improve the cognitive and behavioral functions in patients with epilepsy, implantation, and programming of innovative neuro device to cutting-edge groundbreaking research therapy.

Our specialists are bound laulima together by a deep, shared sense of teamwork and compassion including our tireless effort dedicated to advance the understanding of epilepsy and collaborating with other world-class leaders in the epilepsy field in developing better treatments for our patients. At the center, our philosophy isn't simply "no seizures, no side effects"; it is a balance that allows children and adults with epilepsy to lead full, high-quality lives as our Ohana.

Our Epilepsy Center is recognized nationally for its work not only in providing most advanced cutting edge treatments, but also work with other centers in US and global to offer groundbreaking Clinical Research at our Epilepsy Research nit.

Epilepsy Clinical Trials available at Epilepsy Research Unit

Publications by our specialists and researchers at the Comprehensive Epilepsy Center

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and have local resources available to you. Therefore, we work closely with and support Hawaii's local support group. Please visit their website. **Epilepsy Foundation Hawaii**

Kore Kai Liow, MD, FACP, FAAN
Director, Comprehensive Epilepsy Center
Principal Investigator, Epilepsy Research Unit
Hawaii Pacific Neuroscience
Clinical Professor of Medicine (Neurology), Graduate Faculty, Clinical & Translational Research, University of Hawaii John Burns School of Medicine
Fellowship: Clinical Neurophysiology, Epilepsy and Clinical Research, NINDS, NIH
Neurology Residency: University of Utah School of Medicine

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Identification of risk factors and distinguishing psychogenic nonepileptic seizures from epilepsy: A retrospective case-control study

Rachel Gorenflo [a], Richard Ho [a], Enrique Carrazana [a,b], Catherine Mitchell [b], Jason Viereck [a,b], Kore Kai Liow [a,b], Arash Ghaffari-Rafi [a,c,*,1]

a University of Hawaii John Burns School of Medicine, Honolulu, HI
b Hawaii Pacific Neuroscience, Comprehensive Epilepsy Center, Video-EEG Monitoring Unit, Honolulu, HI
c University of California, Davis, School of Medicine, Department of Neurological Surgery, Sacramento, CA

R. Gorenflo, R. Ho, J. Viereck, C. Mitchell, E. Carrazana, K. Liow, A. Ghaffari-Rafi
Brain Research, Innovation, Translation Labs (BRITL), Comprehensive Epilepsy Center & Video-EEG Epilepsy Monitoring Unit, University of Hawaii John Burns School of Medicine, HONOLULU, Hawaii

Introduction: Patients with psychogenic non-epileptic seizures (PNES) experience significant morbidity and early mortality, secondary to delayed diagnosis. Better characterizing risk factors and exploring how PNES differentially affects sex and racial strata may facilitate earlier diagnosis.

Methods: From a Hawai'i neuroscience institution, 101 PNES patients were investigated in relation to sociodemographic and medical comorbidities. Cases were compared to 202 sex-, age-, and race-matched controls—representing patients with neurological disorders (general controls)—, as well as 404 unmatched epilepsy controls.

Results: Relative to general controls, PNES patients had increased odds ($p < 0.05$) of being: female, younger age, Native Hawaiian or other Pacific Islander (NHPI), suburban origin, from the lowest income quartile, Medicaid, beneficiaries, homeless, current/former smoker, illicit drug users (marijuana, opioids/narcotics, polysubstance abuse), have anxiety, depression, post-traumatic stress disorder, bipolar disorder, traumatic history, World Health Organization obesity class 3, traumatic brain injury, epilepsy, and somatoform disorder. In relation to epilepsy controls, PNES patients exhibited increased odds of being: employed, having attention-deficit/hyperactivity disorder, asthma, migraines, and chronic pain. Relative to females, male PNES patients exhibited increased odds of military insurance, diabetes mellitus type 2, and hypertension. Relative to Whites, the NHPI and Asian PNES patients presented increased odds of asthma, migraines, chronic pain, gastroesophageal reflux disease, and thyroid disease. Per multivariable logistic regression, anxiety was the only consistent predictor of PNES across all sex and race strata.

Conclusion: Predictors of PNES's vary amongst the strata of race and sex. Lower socioeconomic status, along with several psychiatric and medical comorbidities, could increase a clinician's suspicion for earlier medical workup and diagnosis of PNES.

Congratulations to BRITL Scholars!

JABSOM Annual Biomedical Sciences & Health Disparities Symposium

2023 Outstanding Poster Award Medical Student

Investigating the Etiologies of Seizures in Patients Undergoing Video-EEG

Julia R Jahansooz, Anson Y Lee, Corey Nishimura, Uiyeol Yoon, Taylor Matsubara, Kyle Ishikawa, Connor Goo, Vimala Vajjala, Enrique Carrazana, Jason Viereck, Kore Kai Liow

Comprehensive Epilepsy Center and Epilepsy Research Unit, Hawaii Pacific Neuroscience, Honolulu, HI, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, Department of Quantitative Health Sciences, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI

Background
Video-EEG (vEEG) monitoring is classically used to confirm, diagnose, and classify epilepsy. Collecting data from a comprehensive epilepsy center will help to identify risk factors and guide diagnoses in underrepresented, diverse populations.

Methods
This retrospective cohort study analyzed patients from a comprehensive epilepsy center between 2015-2022. Two hundred forty-seven individuals ≥18 years old at the time of vEEG were included, totaling 294 vEEG reports. Data consisted of the presence of a vEEG abnormality, type of abnormality, the number of anti-epileptic drugs (AEDs) used, epilepsy risk factors, psychiatric comorbidities, and MRI structural abnormalities. Ethnicity and race data were collected from patient admission forms and hospital records. Characteristics of the vEEG reports were compared by Wilcoxon rank-sum tests for continuous variables and Fisher's exact test for categorical variables.

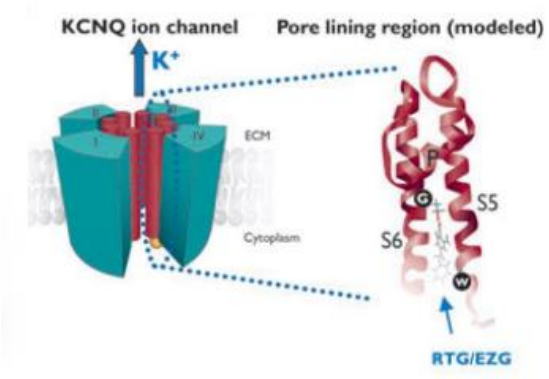
Results
Of the 294 vEEG reports, 209 (84.6%) were abnormal. Subjects with an abnormal vEEG were significantly more likely to have epilepsy ($p<0.001$) and be taking an AED ($p<0.001$). The 123 (58.9%) epileptic events were subcategorized into focal onset (69.1%), generalized onset (4.1%), and non-diagnostic (26.8%). These individuals were significantly more likely to have epilepsy ($p<0.001$) and be taking an AED ($p=0.002$). The 86 (41.1%) non-epileptic seizures were subclassified as psychogenic (7.0%), physiologic (13.0%), unspecified non-epileptic (68.6%), and non-diagnostic (12.7%). These non-epileptic seizure patients were significantly more likely to be Asian ($p=0.046$) or Other ($p=0.031$) race, have depression ($p=0.003$), and have anxiety ($p=0.035$).

Conclusions
These findings identified the breakdown of vEEG results of a racially diverse population seen at an epilepsy center. Asian populations were noted to have a higher incidence of non-epileptic seizures, depression, and anxiety as compared to other races like Native Hawaiians, Pacific Islanders, and Whites.

Comprehensive Epilepsy Center & Epilepsy Research Unit in Hawaii first in US to Investigate XEN1101 Differentiated Kv7 Potassium Channel Modulator in X-TOLE2 Phase 3 Focal Onset Epilepsy.

Honolulu, Hawaii November 2022

According to Xenon website, Epilepsy is a chronic neurologic disorder, the hallmark of which is recurrent, unprovoked and unpredictable seizures. Individuals are diagnosed with epilepsy if they have two unprovoked seizures. Focal seizures are the most common type of seizure experienced by people with epilepsy. Despite the availability of multiple treatment options, approximately 50% of patients are considered inadequately managed with initial lines of therapy warranting additional treatment options.



XEN1101, a differentiated Kv7 potassium channel opener, for the treatment of epilepsy, major depressive disorder (MDD), and potentially other neurological disorders. Xenon reported positive topline results from the Phase 2b X-TOLE clinical trial, which evaluated the clinical efficacy, safety, and tolerability of XEN1101 administered as adjunctive treatment in adult patients with focal epilepsy of which Hawaii's Comprehensive Epilepsy Center was part of.

(Pic: ASENT 2021 Xenon Presentation, Hawaii Epilepsy Research Team)

The phase 3 trial will recruit patients:

- 18 to 75 years of age
- Diagnosed with focal onset epilepsy

"Our neurologists, epileptologists & researchers at Hawaii's Comprehensive Epilepsy Center & Epilepsy Research Unit are honored to be first in US to contribute to this important study and making available this option to our local island populations who no longer has to travel to Mainland for research options"

Kore Kai Liow, MD, Neurologist & Principal Investigator.
Dedicated research hotline (808) 564-6141 or info@HawaiiNeuroscience.com

NEUROMUSCULAR REHABILITATION CENTER

NEUROMUSCULAR RESEARCH UNIT

Neuromuscular Rehabilitation Center & Neuromuscular Research Unit

Services available Honolulu, West Oahu and Neighbor Islands (808) 261-4476

Hawaii Pacific Neuroscience Neuromuscular Rehabilitation Center is a leader in providing the latest in neuromuscular evaluation and rehabilitation through an interdisciplinary approach with emphasis on quality of life and independent care. Neuromuscular conditions affect millions of Americans each year and can have a progressively debilitating course robbing an individual of their quality of life and independence.

Symptoms common to neuromuscular disorders include:
Muscle weakness, Muscle loss
Movement issues
Balance problems
Numbness, tingling or painful sensations
Droopy eyelids
Double vision
Trouble swallowing
Trouble breathing

Neuromuscular disorders include:
Amyotrophic lateral sclerosis (ALS)
Charcot-Marie-Tooth disease
Muscular dystrophy
Myasthenia gravis
Myopathy
Myositis, including polymyositis and dermatomyositis
Peripheral neuropathy
Spinal muscular atrophy

Through a collaborative team of neurologist, physical medicine and rehabilitation, internist, physiatrist, we will utilize the latest in diagnostic and therapeutic interventions to preserve and improve your quality of life.

Your team of experts will manage you from inpatient to outpatient and includes the latest in EMG/electrodiagnostic evaluations, therapy, medications, Botox, Neuromodulation and other interventional care. Our Neuromuscular Rehabilitation Center has been selected as a national MGFA (Myasthenia Gravis Foundation of America) Partner.

Clinical Trials available at Neuromuscular Research Unit

Publications by our specialists and researchers at the Neuromuscular Center

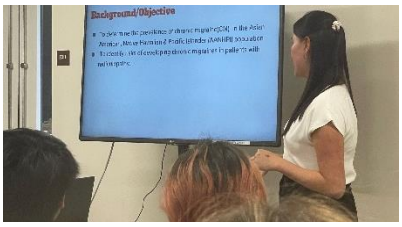
Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and encourage you to contact local resources available to you.

Jason Chang, MD
Director, EMG & Neuromuscular Rehabilitation Center
Sub investigator, Neuromuscular Research Unit
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine, University of Hawaii John Burns School of Medicine
PM & R Residency: University of California School of Medicine, Irvine

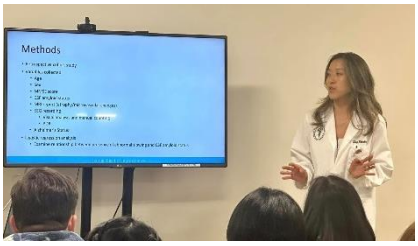
Hawaii Promoting Myasthenia Gravis Awareness, Education & Neuroscience Research

June 17th, 2023

More than 50 neurologists, physicians, students attended the 2023 Inaugural Hawaii MG Symposium sponsored by the Center for Rare Neurological Diseases and the Myasthenia Gravis Foundation of America addressing unmet MG especially for underrepresented minority groups in Hawaii & Pacific Islands.



We cannot be more proud of the University of Hawaii John Burns School of Medicine medical students who presented their research work at the scientific session of 2023 Hawaii Spring Neuroscience Research Competition & congratulations to 1st Prize winner medical students Anita Cheung and Runner up Shay Nakahira for their outstanding research projects.



Mahalo to plenary session keynote speaker Richard Nowak, MD, Director, Myasthenia Gravis Clinic, Assistant Professor of Neurology, Yale University School of Medicine & Chief Medical Advisor, Myasthenia Gravis Foundation of America for 2023 MG keynote lecture: Advances in MG Treatments & Research and Meridith O'Connor, Assistant Vice President, Patient Engagement, Advocacy & Policy, Myasthenia Gravis Foundation of America. The conference would not have been possible without the support of many including our sponsors, Samantha Masterson, President and CEO of Myasthenia Gravis Foundation of America. We are very grateful to Janette Abramowitz, MD for the lectures on Psychiatric Issues in MG care and How We can Improve MG Care in Hawaii. Events photos available on: https://www.facebook.com/HIPacNeuro

Spine & Pain Management Center

Pain Research Unit

Spine and Pain Management Center

Spine injuries and chronic pain are leading causes of disability in America. Our team of experienced specialists in neurology, physical medicine and neurorehabilitation are experts in developing interdisciplinary service lines to create customized, patient centered treatment plans for patients with an emphasis on compassionate care and functional independence to improve quality of life.

It is our goal to create the most comprehensive spine and pain center in Hawaii, where patients can receive all aspects of their care under one roof and from time of initial consultation to the resolution of symptoms. To be a leader in conservative pain management as well as interventional care. Where a multitude of specialists and staff can come to the patient and provide all aspects of care.

We use a multimodal approach to pain management with expertise in: physical therapy, occupational therapy, speech therapy, neuropsychology, vocational training, acupuncture, chiropractic care, behavioral modifications/wellness, oral/topical and injectable medications, botox, neuromodulation, and minimally invasive surgical techniques. Each patient will have a comprehensive physical and functional evaluation with access to ultrasound, xrays, CT scans, MRI's, and electrodiagnostic testing.

PT/OT/ST, vocational training, work hardening
Neuropsychology, Behavioral health
Wellness center, Acupuncture, Chiropractic
Interventional procedure: botox, spasticity management, epidural, facet, trigger point, neuromodulation, minimally invasive neurosurgery
Headache management
Research Therapies for the right candidate

American Chronic Pain Association

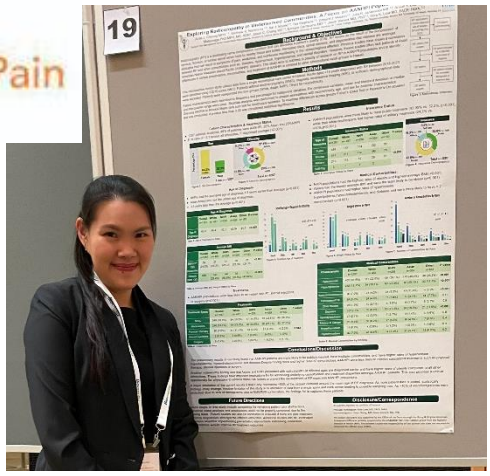
Clinical Trials available at Spine & Pain Research Unit

Publications by our specialists and researchers at the Spine Center

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and have local resources available to you. Therefore, we work closely with and support Hawaii's local support group.

Jason Chang, MD
Director, Spine and Pain Management Center
Sub investigator, Spine and Pain Research Unit
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine,
University of Hawaii John Burns School of Medicine
PM & R Residency: University of California School of Medicine, Irvine

Neuropathic-Pain 2023
The 3rd International Conference on Controversies in Neuropathic Pain
20-21 November 2023, Brussels, Belgium



Exploring Radiculopathy in Underserved Communities: A Focus on AANHPI Populations

Anita J. Cheung MPH [1,2], Matthew K. Nishimura[1,3], Kai J. Miyaki[1,4], Tea A. Stephens[1,5], Edward J. Weldon[1,2], Julia R. Jahansooz MS [1,2], Anson Y. Lee[1,2], Masako Matsunaga PhD, MPH, MS, RDN[2], Jason C. Chang MD[1,2], Enrique Carrazana MD[1,2], Jason Viereck MD, PhD[1,2], Kore K. Liow MD, FACP, FAAN1,[1,2]

1. *Spine & Pain Management Center, Hawaii Pacific Neuroscience*
2. *John A. Burns School of Medicine, University of Hawaii, Honolulu, HI,*
3. *Pitzer College, Claremont, CA*
4. *Boston University, Boston, MA*
5. *University of Hawaii, Honolulu, HI*

Background/ Objectives: *Radiculopathy (RP) is a debilitating nerve compression condition. This study aims to address the paucity of research on RP in Asian American, Native Hawaiian and other Pacific Islanders (AANHPI) populations and to identify differences in clinical presentation, comorbidities, and treatment of AANHPI in contrast to other ethnocultural racial groups in Hawaii.*

Methods*:This retrospective cohort study utilizes data from a single neurological care center in Hawaii. Adults aged ≥18 years diagnosed with RP between 2016-2023 were identified using ICD10 codes. Patients without electromyography (EMG), magnetic renaissance imaging (MRI), or sufficient demographical data were excluded. Statistical analysis was completed on R, with $p<0.05$ considered statistically significant.*

Results: *Data from 1287 out of 1,640 patients are included in the analysis, with 353 excluded. The cohort consisted of 28% Asians and 20% NHPIs. NHPIs had the youngest age of diagnosis, while Asians had the highest age of diagnosis ($p<0.001$). AANHPI populations were likelier to have public insurance ($p<0.001$). NHPIs had the highest rates of obesity ($p<0.001$ while Asians had the lowest ($p<0.001$). AANHPIs were more likely to have more than two medical comorbidities ($p<0.001$) and higher rates of hypertension ($p<0.001$), hyperlipidemia ($p<0.001$), hypercholesterolemia ($p<0.001$), and diabetes ($p<0.001$). AANHPIs were mainly treated with medications and were less likely to have received physical therapy, steroid injections, or surgery ($p=0.042$)*

Conclusion: *AANHPI patients are more likely to be publicly insured, have multiple comorbidities, and are less likely to receive specialized treatments. NHPI are diagnosed earlier and have higher rates of obesity. These findings are important for addressing underlying comorbidities and treatment disparities amongst AANHPI patients*

Association of Academic Physiatrists
February 1 – 5, 2022, New Orleans, Louisiana

Sociodemographic Disparities of Patients with Lumbar Radiculopathy: A Single-Centered Retrospective Study

Ilana Buffenstein, BA[1,2]; Frances Morden, BS[1,2]; Charissa Tan, BS[1,2]; Johanna Linna, BA[1,3]; Alexandra Masca, BS[1,4]; Raksana Kayumova, BS[1,5]; Jonathan Ragheb, BA[1,6]; Rachel Gorenflo, BA[1,2]; Enrique Carrazana, MD[1,2]; Jason Viereck, MD, PhD[1,2]; Kore Kai Liow, MD, FACP, FAAN[1,2]; Jason Chang, MD[1]

[1]Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu HI, [2]John A. Burns School of Medicine, University of Hawaii Honolulu, HI, [3]Princeton University, Princeton, New Jersey, [4]University of Notre Dame, Notre Dame, Indiana, [5]University of Hawai'i at Mānoa, Honolulu, Hawaii, [6]Harvard University, Cambridge, Massachusetts

Objectives

Investigate sociodemographic disparities and differences in pain reporting amongst patients with chronic pain due to lumbar radiculopathy (LR) in a diverse minority-majority state.

Design

A single-centered, retrospective study was conducted to identify patients with LR who underwent both electromyography (EMG) to confirm LR and lumbar magnetic resonance imaging (MRI); had a chief complaint of low back pain (LBP), numbness, tingling, or weakness; and received the ICD-10 code for LR. We identified 108 patients who met inclusion criteria. Nonparametric bivariate analyses with an alpha < 0.05 were utilized.

Results

Asian LR patients were 8.00 years older than other LR patients (p=0.017). LR patients of other underrepresented minorities (OUM; including Black, Hispanic, and Native American) were 23.00 years younger than other LR patients (p=0.0012). Native Hawaiian and other Pacific Islander (NHPI) LR patients were 3.85 times more likely to be employed (95%CI: 1.13-15.50; p=0.030), while Asians were 4.36 times more likely to be retired (95%CI: 1.43-13.92; p=0.0066). OUM LR patients were at increased odds of reporting pain consistent with the severity of neuroforaminal stenosis identified on MRI (OR=14.59; 95%CI: 1.30-768.33; p=0.012). Both OUM (OR=7.42; 95%CI: 1.12-83.13; p=0.017) and Medicaid LR patients (OR=3.98; 95%CI: 1.40-11.66; p=0.0063) had increased odds of having no findings on MRI or EMG. Medicare LR patients were 3.73 times more likely to have moderate stenosis on MRI (95%CI: 1.31-10.85; p=0.0094).

Conclusions

The results suggest that Asian LR patients were significantly older and more likely to be retired. Conversely, NHPI LR patients were at increased odds of being employed and OUM LR patients were younger at diagnosis, suggesting that these minority groups tended to present at working age. Additionally, OUM were more likely to accurately endorse lumbar pain of the same severity as reported in imaging. Overall, minority LR patients have diverse experiences of pain and require a biopsychosocial approach to pain management.

TBI CONCUSSION CENTER

CONCUSSION RESEARCH UNIT

TBI & Concussion Center & Concussion Research Unit

Services available Honolulu, West Oahu & Neighbor Islands (808) 261-4476

A concussion or other types of traumatic brain injury can affect everyone differently. Common symptoms include headaches, dizziness, imbalance, falls, mood disturbances and memory problems. Most improve within a week or two, but some symptoms last longer and can affect daily life. Hawaii Traumatic Brain Injury (TBI) and Concussion Center at Hawaii Pacific Neuroscience is dedicated to provide comprehensive care that includes clinical evaluation, treatment and rehabilitation for those with concussion or severe traumatic brain injuries.

After a comprehensive evaluation, an individualized treatment plan customized for individual needs will be tailored. Our multidisciplinary team at the Concussion Center.

Our experienced physiatrists including a board certified Brain Injury Medicine physician can provide rehabilitative treatment options for severe traumatic brain or spinal cord injuries. Our neurologists are skilled at treating not only posttraumatic seizures and epilepsy but also posttraumatic headaches, which are very common after any concussion.

Clinical Trials available at TBI Research Unit

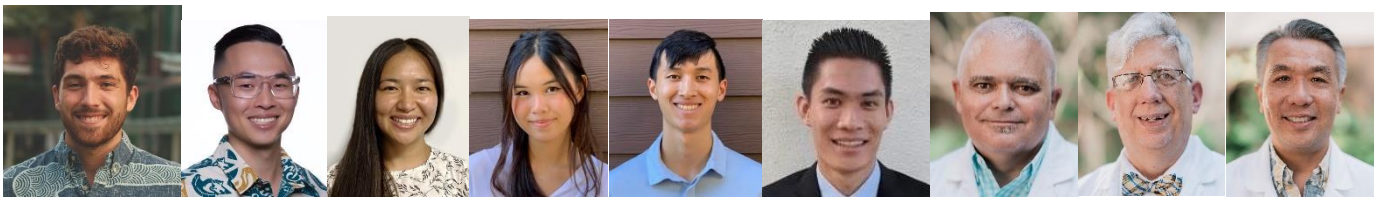
Publications by our specialists and researchers at the Concussion Research Unit

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and have local resources available to you. Therefore, we work closely with and support Hawaii's local support group. Please visit their website.

Interdisciplinary Specialists & Services

Neurologist – Specializes in concentration, attention, and cognitive symptoms, headache, facial & neck pain
Neurorehabilitation – specializes in pain, muscle weakness and cognitive evaluation rehabilitation
Neurorehabilitation – specializes in rehabilitation to minimize on-going damage and restore neuro functions
Sleep specialist – specializes in evaluating insomnia", restless leg, sleep disorders associated with TBI
Wellness Physician - board certified in lifestyle medicine specializing in brain health

American Academy of Neurology (AAN)
2023 Annual Meeting, April 2023, Boston, MA



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

Edward Weldon[1], Ryan Nakamura[1], Tracy Van[2], Ana Nakamura[3], Chancen Law[4], Connor Goo[1], Meliza Roman[1], Enrique Carrazana[5], Jason Viereck[5], Kore Liow[1,5]

[1]University of Hawaii, John A. Burns School of Medicine [2]University of Colorado, Aurora [3]University of California, Santa Barbara [4]Kamehameha Schools Kapālama High School [5]Concussion & TBI Center, Brain Research, Innovation, Translation Labs (BRITL), Hawaii Pacific Neuroscience

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

Background:
Recommendations on return-to-exercise post-traumatic brain injury (TBI) remain controversial. This study surveyed Hawaii's diverse population to identify trends in exercise and recovery for TBI patients to shape recommendations on return-to-exercise. This study also aimed to identify health inequities and factors contributing to different outcomes, allowing inequities to be addressed.

Design/Methods:
Retrospective review of 100 patients diagnosed with TBI between January 2020 and January 2022 was performed. Variables collected include demographics, etiologies, and symptoms at diagnosis. Self-generated phone surveys were completed to evaluate exercise patterns post-TBI and barriers to recovery. Statistical analysis was performed using RStudio.

Results:
Patients who recovered within two years displayed similar exercise patterns to patients who took longer than two years. Exercise frequency, intensity, and duration did not differ significantly ($p=0.75$, $p=0.51$, $p=0.80$, respectively). Hiking/walking for exercise was more common in the long recovery group ($p=0.018$), likely reflecting advanced age compared to the short recovery group (50 vs. 39 years old, $p=0.003$). Otherwise, exercise modalities did not differ significantly. Additionally, no correlation exists between exercise intensity and symptom change ($p=0.920$), suggesting patients exhibit exercise patterns suitable for their specific condition. Finally, when comparing TBI recovery resources accessed across races or insurance types, Caucasian patients and individuals with private insurance utilized the most resources ($p=0.032$).

Conclusions:
Return-to-exercise does not appear to be a predictor for TBI recovery. If encouraged to exercise post-TBI, patients will self-regulate a regimen not likely exacerbating their symptoms or recovery time, thus it may be suitable to recommend return-to-exercise as tolerated. The study also found worrying inequitable trends in TBI recovery resources accessed, and these disparities should be further investigated to rectify this issue.

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications

Impact of Mild Cognitive Impairment on One's Fall Risk and Risk for More Frequent and Severe Traumatic Brain Injuries

Chloe D. Delos Reyes, Ryan Nakamura, Anson Y. Lee, Edward J. Weldon, Julia R. Jahansooz, Kyle M. Ishikawa, Enrique Carrazana, Jason Viereck, Kore K. Liow

Introduction
Assessing fall risks in older adults is crucial as falls may lead to traumatic brain injuries (TBI) resulting in high morbidity and mortality. Yet, there is sparse research on whether mild cognitive impairment (MCI) may be associated with more frequent TBIs due to falls. As such, this project investigated the relationship between MCI and both increasing fall risk and incidence of mild-to-moderate TBIs.

Methods
Retrospective chart review was completed for all TBI patients at a single outpatient neurology clinic between 2020-2022. Patients included in the study were those with a new diagnosis of MCI. Collected variables included demographics, mini-mental state examination (MMSE) scores, fall risk evaluation, number of falls within three years following diagnosis, and number of TBIs three years following diagnosis.

Results
Overall, 13 patients were included with a mean age at MCI diagnosis of 64 years and mean MMSE score of 25.6. Approximately 53.8% of patients were classified in the no fall risk category and 46.2% of patients were in the moderate risk category. Three patients (23.0%) reported TBIs following their MCI diagnosis of which two were male (66.7%), two (66.7%) were at risk for major depressive disorder, and all were in the moderate risk category.

Conclusions
While a diagnosis of MCI did not seem to increase the risk for falls, those that had MCI and were at moderate risk for falls appeared more likely to suffer a TBI. Further investigation may ascertain whether improving fall risk assessments may further decrease TBI risk in MCI patients.

American Academy of Neurology (AAN)
2022 Annual Meeting
Neuro Trauma Poster Presentation
April 2022, Seattle, WA, USA

Influence of Ethnoracial and Sociodemographic Variables on Incidence and Management of Traumatic Brain Injury Patients in Hawaii

Kayti Luu[1,2], Michelle Pang[1,2], Rachel Gorenflo[1,2], Frances Morden[1,2], Ariel Ma[2,3], Nicholas Sims[2,4], Lauren Fujii[2,5], Kent Yamamoto[2], Enrique Carrazana[1,2], Jason Viereck[1,2], Kore Liow[1,2]

[1]John A. Burns School of Medicine, University of Hawai'i at Manoa, [2]Concussion and Traumatic Brain Injury Center, Hawaii Pacific Neuroscience, [3]Rice University, [4]University of California, Berkeley, [5]Santa Clara University

Objective:

Investigate potential sociodemographic disparities and medical comorbidities associated with the diagnosis and management of traumatic brain injury (TBI) in a minority-majority state.

Background:

Previous studies have identified a relationship between TBI and sociodemographic variables, such as race and insurance status. However, few studies have investigated these variables in a minority-majority population in the United States.

Design/Methods:

A retrospective case-control study was conducted on TBI patients seen at a traumatic brain injury center within the last 2 years. We identified 412 patients with TBI. 412 unmatched controls were randomly selected from the institution's patient pool. Injury characteristics, sociodemographic information, and psychological and biological variables were collected.

Results:

Patients diagnosed with TBI had higher odds of being younger ($p<0.0001$), male ($p<0.0001$), Native Hawaiian or other Pacific Islander (NHPI; $p=0.049$), and having a lower median household income ($p=0.032$). NHPI patients with TBI were 2.87 times more likely to have Medicaid insurance (95% CI: 1.70-4.85; $p<0.0001$). Asian patients with TBI were 6.36 times (95% CI: 3.22-13.17; $p<0.0001$) less likely to have depression at diagnosis compared to other races. In contrast, other underrepresented minorities (OUM) reported depression 6.62 times more (95% CI: 1.18-16.89; $p=0.022$). Hispanics reported sleep disturbance 18.23 times more (95% CI: 1.76-909.14; $p=0.0049$). Caucasian patients with TBI underwent diagnostic imaging 1.99 times more than other races (95% CI: 1.23-3.23; $p=0.0042$).

Conclusions:

Patients with TBI were more likely to be young, male, NHPI, and have a lower median income, which suggests a potential socioeconomic disparity. In addition, differing rates of Medicaid insurance, sleep disturbances, depression, and diagnostic imaging amongst ethnoracial groups indicates the need for a biopsychosocial approach to management.

Association of Academic Physiatrists
February 1 – 5, 2022, New Orleans, Louisiana

Sociodemographic and Biological Differences Between Traumatic Brain Injury Patients Of Different Ethnoracial Groups

Michelle Pang[1,2], Kayti Luu[1,2], Rachel Gorenflo[1,2], Frances Morden[1,2], Ariel Ma[1,3], Nicholas Sims[1,4], Lauren Fujii[1,5], Kent Yamamoto, MD[1], Enrique Carrazana, MD[1,2], 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]Rice University, Houston, TX, [4]University of California, Berkeley, Berkeley, CA,[5]Santa Clara University, Santa Clara, CA.

Introduction

Traumatic Brain Injury (TBI) is a significant public health concern. This study aimed to examine the intersection of race, sex, socioeconomic, psychiatric, and biological variables for TBI patients in a diverse minority-majority state.

Methods

Retrospective chart review was conducted on TBI patients seen at a multidisciplinary neurological institution from 1/1/19 to 6/23/21. Patients were excluded for insufficient information in the electronic health record. 412 unmatched controls were randomly selected from the institution's patient pool. Variables collected include sociodemographic information, characteristics of the injury, in addition to psychological and biological variables.

Results

Of the 412 patients included, 56% were male and 44% were female (p=0.00013). 32.0% of patients were white, 23.3% were Native Hawaiian or Other Pacific Islander (NHPI), 20.9% were Asian, 3.6% were Hispanic, 3.6% were other underrepresented minorities (OUM; included Black and Native American/Alaska Native), and 16.5% did not report their race. Caucasian patients with TBI underwent diagnostic imaging 1.99 times more than other races (95% CI 1.23-3.23; p=0.0042). Asian patients had an odds of 2.17 (95% CI 1.26-3.77; p=0.0041) for being employed and 2.32 (95% CI 1.36-4.02; p=0.0015) for having private insurance. NHPI had an odds of 0.53 (95% CI 0.32-0.88; p=0.014) for having private insurance and an odds of 4.22 (95% CI 1.18-16.89; p=0.019) for exhibiting Class III obesity. Hispanics reported sleep disturbance 18.23 times more (95% CI 1.76-909.14; p=0.0049) and OUM reported depression 6.62 times (95% CI 1.18-16.89; p=0.022) when compared to other races.

Conclusion

These results suggest that Caucasian patients with TBI were more likely to undergo imaging studies. Asians were at an increased odds of having private insurance, while NHPI were at decreased odds, suggesting a potential disparity in diagnosing TBI. Hispanics had significantly higher rates of sleep disturbances, while OUM had higher rates of depression, which indicate the need for a biopsychosocial approach to TBI management.

Headache & Facial Pain Center

Headache Research Unit

Headache & Facial Pain Center & Headache Research Unit

Services Available Honolulu, West Oahu & Neighbor Islands (808) 261-4476

The Hawaii Headache Center is dedicated to relieving the pain and suffering of headache patients and improving their quality of life. Our physicians specialize in the treatment of patients with different headache types. The treatment effectively integrates medical and non-medical therapies, such as alternative medicine, Botox injections, physical therapy, and supportive counseling.

This is an exciting time in headache management with the recent advancements such as anti-Calcitonin Gene Related Peptide (CGRP) therapies and neuromodulation. Anti CGRP therapies are migraine-specific medications targeting the inflammatory mediator involved in generating migraines, and available as both preventive and abortive treatments. Neuromodulation devices are advanced medical tools effective in treating migraines and cluster headaches and can be considered in patients who cannot take medications.

Our Headache Center is recognized nationally for its work not only in providing most advanced cutting edge treatments, but also work with other centers in US and global to offer groundbreaking Clinical Research.

Headache Clinical Trials available at Headache Research Unit

Publications by our specialists and researchers at the Headache Center & Research Unit

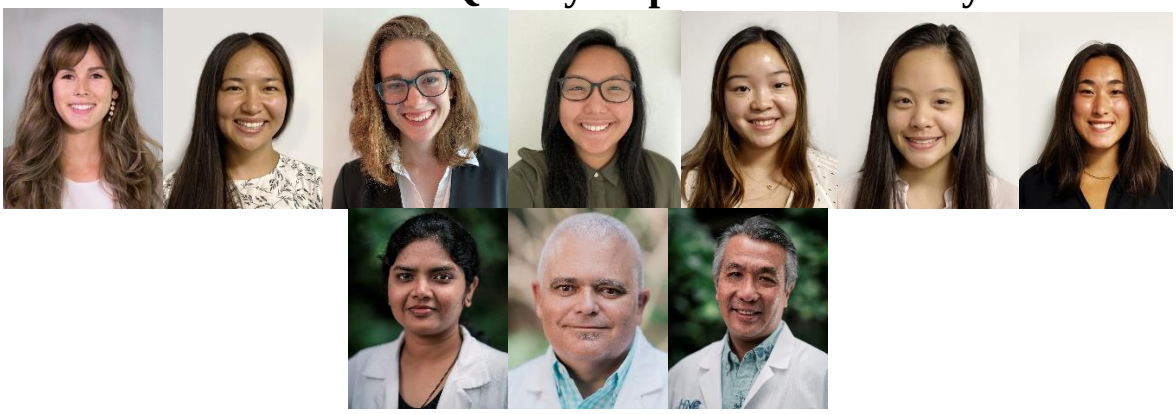
Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and want to be sure you do not feel alone in this journey and have local resources available to you.

Interdisciplinary Specialists & Services

Neurologist – Specializes in diagnosis of complex headache, facial & neck pain
Neurorehabilitation – Specializes in neck and upper back pain, and rehabilitation
Neurorehabilitation – Specializes in minimizing on-going damage and restore neuro functions
Sleep specialist – Specializes in evaluating insomnia", & other sleep disorders associated with Headaches
Wellness Physician - Certified in lifestyle medicine specializing in promoting wellness in headaches conditions

American Academy of Neurology (AAN)
2022 Annual Meeting
April 2022, Seattle, WA, USA

Employability, Work Difficulties and Factors Impacting Chronic Migraine Patients of Hawaii: Results of a Quality Improvement Survey



Michelle Stafford, Tracy Van, Rachel Gorenflo, Frances Morden, Kara Ushijima, Ashley Ung, Emma Inouye, Uiyeol Yoon, Dr. Vimala Vajjala, Dr. Enrique Carrazana, Dr. Kore Liow

Chronic intractable migraines have a significant impact on patients' daily lives. Many tools measure migraine impact on daily functioning, but triggers and work-related difficulties are often inadequately addressed. The Headache Impact Test (HIT-6) and HEADWORK questionnaire capture a variety of difficulties and factors that may impact patients with migraine at work and home.

Objective: Investigate the relationship between work-related difficulties and key factors that negatively impact employability and quality of life (QoL) for patients with intractable vs. non-intractable chronic migraines.

Methods: A single-centered, retrospective chart review was conducted to identify patients diagnosed with migraine and seen in the clinic between April 2021 through June 2021. Patient demographics, past medical history, and medication trials for abortive and preventative migraine treatments were collected. Phone surveys were performed using the HIT-6 and HEADWORK questionnaire. Employed patients were categorized using the Standard Occupational Classification system for statistical analysis. Nonparametric bivariate analyses with an alpha < 0.05 were utilized.

Results: Of 654 patients recruited for phone calls, 182 (28%) completed the survey and were further analyzed. 64.8% were diagnosed with intractable migraines and 35.2% with non-intractable migraines. Using non-intractable migraine patients as the reference group, patients with intractable migraines had an odds ratio of 0.51 for being employed and were 3.70 times as likely to encounter difficulties dealing with work problems. There was no statistically significant difference in other work-related difficulties, such as paying attention to tasks, solving organizational problems, and reading and writing. Patients with intractable migraines also had one more factor affecting work (e.g., noise, smell, brightness, extended working hours, negative attitudes of colleagues, air conditioning) than their counterparts.

56.3% of patients have tried five or more medications to control their migraines with 37.5% of these patients having a positive HIT6 score and 70% having intractable migraines.

Conclusions: The findings suggest that intractable migraine patients are less likely to be employed, but when they are, there are greater challenges faced during work, highlighting the incapacitating nature of this condition. Higher HIT-6 scores and evidence of polypharmacy in intractable migraine patients is another measure corresponding to decreased QoL. The multifactorial management of these patients with potentially debilitating migraines may necessitate a biopsychosocial approach for improved quality of care and life.

Chronic Migraine and Comorbidity Characterization: A Focus on Native Hawaiians and Other Pacific Islanders

Anita Cheung MPH [1,2], Michelle Lu [1,2], Anson Y. Lee[1,2], Julia R. Jahansooz MS [1,2], Edward J. Weldon[1,2], Meliza Roman MS[3], Enrique Carrazana MD[1,2], Jason Viereck MD, PhD[1,2], Kore Kai. Liow MD, FACP, FAAN1,[1,2]

1. *Headache & Facial Pain Center, Hawaii Pacific Neuroscience*
2. *John A. Burns School of Medicine, University of Hawaii, Honolulu, HI,*
3. *Department of Quantitative Health Sciences, John A Burns School of Medicine, University of Hawaii, Honolulu, HI*

Objectives:
Migraines are the second leading cause of disability worldwide. However, there is a paucity of research focused on the clinical presentation of chronic migraines (CM) in Native Hawaiian and other Pacific Islanders (NHOPI). This study aims to identify possible differences in the clinical presentation of CM in NHOPI in contrast to other Ethnocultural racial groups in Hawaii.

Methods:
A retrospective case-control study was conducted to examine the relationship between demographics, comorbidities, and chronic migraines. Data from a single neurological care center in Hawaii were used to identify adults aged ≥18 years diagnosed with CM between 2018-2023. Adults with CM were matched for age and sex to 3 controls (patients with radiculopathy who did not present with CM).

Results:
Overall, 309 CM patients and 964 matched controls were identified for analysis. NHOPI populations accounted for 24.9% of CM and 25% of radiculopathy patients. NHOPIs, on average, were diagnosed with CM or radiculopathy 2-3 years earlier ($p=0.07$) and had a higher average BMI than their White counterparts ($p<0.01$). Among NHOPIs, CM cases were more likely to have public insurance coverage ($p=0.04$), hyperlipidemia ($p<0.01$), diabetes ($p=0.02$), and insomnia ($p=0.01$). They were also more likely to be on more medications than White patients ($p<0.001$).

Conclusion:
NHOPI CM patients were more likely to be diagnosed earlier than White patients and had higher BMIs, as well as higher rates of hyperlipidemia, insomnia, diabetes, and polypharmacy. These findings have important implications for understanding underlying comorbidities among NHOPI CM patients and developing targeted interventions.

Comprehensive MS Center

MS Research Unit

COMPREHENSIVE MS CENTER & MS RESEARCH UNIT

Services Available Honolulu, West Oahu & Neighbor Islands
(808) 261-4476

The Hawaii Comprehensive MS Center at Hawaii Pacific Neuroscience cares for more MS patients than any other centers in Hawaii. The center leverages a multidisciplinary approach of neurologists, rehabilitation specialists, lifestyle wellness physicians to ensure that MS patients get the benefit of a comprehensive holistic approach including:

Comprehensive Holistic Neurologic, Medical and Lifestyle Care includes:
Addressing pain
Restore function and quality of life
Addressing other symptoms such as fatigue, incontinence
Access to nutrition counseling and general wellness
Ongoing Neurorehabilitation efforts with PT, OT, Speech
Cognitive assessments
Comprehensive Neurological evaluation
Onsite Diagnostic services including onsite 3T MRI, Labs, Floro Xray for Spinal Tap
Disease-modifying therapy
Infusion unit for IV Therapies
Research Options

Clinical Trials available at Hawaii MS Research Unit

Publications by our specialists and researchers at the Hawaii MS Research Unit

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and encourage our patients to seek out credible resources with local and national support groups. Please click on their website.

National Multiple Sclerosis Society

Jason Viereck, MD, PhD
Director, Comprehensive MS Center
Sub investigator, MS Research Unit
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine, Graduate Faculty, Clinical & Translational Research, University of Hawaii John Burns School of Medicine
Neurology Residency: Boston University Medical School, Boston

Hawaii Promoting MS Awareness, Education & Neuroscience Diversity

January 14th, 2023

More than 50 neurologists, physicians, medical students, MS advocates and sponsors attended the 2023 Hawaii MS Symposium sponsored by the Center for Neuroscience Diversity and the National MS Society.

We cannot be more proud of the University of Hawaii John Burns School of Medicine medical students who presented their research work at the symposium including poster of the year by med student Shin Chang on "Psychiatric Disorders Associated with Comorbid Autoimmune Diseases in Multiple Sclerosis".

Mahalo to Dr. Russell Woo, JABSOM Associate Chair of Research, Dr. Jason Viereck and Dr. Enrique Carrazana for their mentorship of these students from the Brain Research Innovation and Translation Lab.

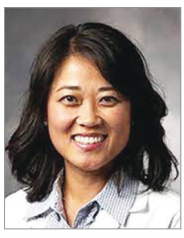
The conference would not have been possible without the support of many including our sponsors, Alisa Schwaneberg of National MS Society and our amazing hard working staff Kimberly Ko and Danrie Miral. We are very grateful to Dr. Alexander Galati, Dr. Paul Smith and Dr. Janette Abramowitz for the lectures on the state of MS care and How We can Improve MS Care in Hawaii. Pictures of events available on: https://www.facebook.com/HIPacNeuro

A SUPPLEMENT TO
NEUROLOGY REVIEWS
MAY 2022

MS in Asian, Native Hawaiian, and Pacific Islander Populations:

ADDRESSING UNMET NEEDS

Lily Jung Henson, MD



Jong-Mi Lee, NP

Kore Kai Liow, MD

Introduction

Multiple sclerosis (MS) is a presumed autoimmune disorder of the central nervous system (CNS) characterized by inflammatory demyelination and neurodegeneration. It affects approximately 1 million people across the United States and an estimated 2.8 million people worldwide.[1] Symptoms of MS, a disease typically diagnosed between ages 20 and 50 years, vary tremendously and may comprise diffuse symptoms such as depression, pain, cognitive difficulties, and fatigue, as well as focal symptoms such as motor and sensory deficits, visual disorders, spasticity, bladder and bowel dysfunction, and dysphagia. Diagnosis at a young age makes MS a long-term disease that impacts patients, the health care system, and society for decades. Patients diagnosed at a younger age hit disability milestones earlier and therefore could be considered to have a poorer prognosis.

Although the cause of MS is unknown, it is a heterogeneous disease thought to result from complex interactions among genetic predisposition, sex, and the environment. Race is another important factor, but due to the complexity of the disease and its overlap with some of the aforementioned characteristics, there is uncertainty around the role of race in MS. What is clear is that around the world, the variability in the prevalence of MS, and the differences in presentation, depict MS as a complicated disease that requires inclusion of diverse groups in study populations in clinical trials. For example, Balo's disease, a rare and progressive variant of MS, has a greater prevalence in the Philippines than in other Asian regions.[2] In many Asian countries, and China, corticospinal involvement is the predominant presentation.

A complex task is to ensure that when marginalized groups are included, they represent the full spectrum of the population targeted to receive the therapy. The ultimate goal of this process is to learn how to prescribe drug therapies safely for the patient groups who will be receiving them.

MS has been reported in most ethnic/racial groups, but it tends to be more common in Whites of northern European ancestry. Minority populations in the United States, such as Asian Americans and Hispanic Americans, have a higher incidence of MS compared with their ancestral countries of origin. However, minority populations are often underrepresented in clinical trials not only in the United States, but worldwide.[3-5] It is therefore difficult to assess treatment response in minority populations, even in subgroup analyses, because of the small numbers of patients.

The growing arsenal of disease-modifying therapies (DMTs) offers opportunities to reduce disability and extend survival for persons with MS. Thus, there is a continued, compelling need for high-quality epidemiologic data worldwide to improve our understanding of disease risk, support health policies aimed at meeting the diverse needs of people with MS, and encourage advocacy efforts.

This supplement is developed under the direction and sponsorship of Biogen.
Biogen-158359

High-quality epidemiologic data has the potential to improve personalized medicine. This occurs through earlier diagnosis, more effective prevention programs, and a higher precision in the treatment of disease in diverse populations.[6] An epidemiologic perspective applies principles of population screening to preventive medicine and uses evidence-based practices to personalize medicine.

Update: Worldwide Trends in MS Prevalence

The estimated prevalence of MS has increased worldwide, with the number of affected patients rising from 2.1 million in 2008[7] to 2.8 million in 2020 (**Figure**).[1] The 2020 global prevalence is 35.9 (95% CI, 35.87, 35.95) per 100,000 people, compared with a global prevalence of 29.26 (29.21, 29.30) per 100,000 in 2013.[1]

However, the increase has not been uniform around the globe. Although Asia was considered a low-risk zone for MS in the past, the epidemiologic status of MS in Asia has changed in recent decades, with studies showing an increased prevalence in many countries in Asia.[8-10] It is important to note that within Asia, where half of the world's population resides, there is vast geographic, ethnic, and cultural diversity; therefore, the Asian population cannot be grouped into one large ethnicity.[10]

Racial-ethnic differences in MS underscore the complex interaction between genetic, biologic, and environmental factors in the etiology of this disease. More studies are needed to understand differences in MS prevalence among diverse racial-ethnic groups across geographic regions and within populations residing in the same geographic region.

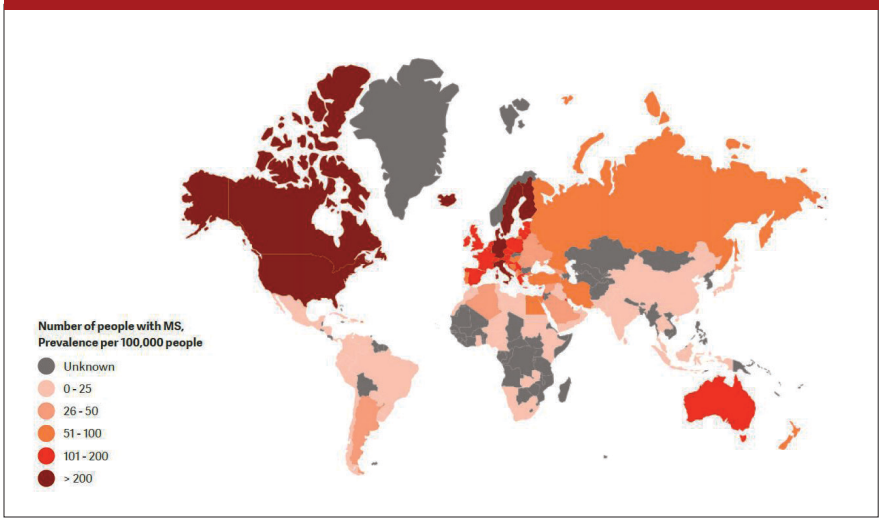
How MS Differs in Asian Populations

The presentation and progression of MS in the Asia-Pacific region may differ from presentation and progression in Europe and North America. Unfortunately, data collection systems and registries for neurologic diseases that are necessary for understanding the burden of the disease (eg, accumulation of disability, impact of DMTs, safety risks, financial impact, effects on quality of life) are limited in the region.[10] Nationalized health care systems in some Asian countries are able to track disease prevalence[11]; some report into networks like MSBase. However, it may be the access to health care within the country that limits accurate data collection. Furthermore, because the Asian population covers a vast geography, and there is substantial diversity as a result of the numerous countries of origin, collection of data from one region within Asia may not be reflective of other regions. However, even with recognizing this, some similarities and commonalities across Asian regions may exist.

Differences in Presentation

In studies of Asian populations, many differences in presentation have been reported versus MS in White populations.[10-15] In general, MS in Asians is characterized by a more rapid progression, limited familial occurrence, more frequent attacks, more severe involvement of the visual system at onset as well as during the entire clinical course, and more common opticospinal

Distribution of MS Cases Around the World



Atlas of MS, 3rd ed.[30] *Reprinted with permission of MSIF (Multiple Sclerosis International Foundation)*

AFFILIATIONS AND DISCLOSURES:

KORE KAI LIOW, MD
Neurologist, Comprehensive MS Center
Principal Investigator, MS Research Unit
Neuroscience Chair, Hawaii Pacific Neuroscience
Clinical Professor, Dept. of Medicine (Neurology)
Graduate Faculty, Clinical & Translational Research, University of Hawaii
John Burns School of Medicine

Research Funding received from: NIH, NINDS, CDC, T3D, Athira, Takeda, UCB, NovoNordisk, Ipsen, Avanir, Ra Pharma, Sanofi, Novartis, Praxis, Annovis, Merck, NeuroDerm, Cerevel, Acadia, Biogen, Idorsia, Eisai, Xenon, SK Life Science, Axsome, Engage, Livanova, Neurelis, Longboard, Sage, Jazz, NLS, Cyclerion, Takeda

JONG-MI LEE, NP
Jong-Mi Lee is a consultant for Biogen, Horizon, Sanofi-Genzyme, and Alexion.

LILY JUNG HENSON, MD
CEO, Piedmont Henry Hospital

Dr. Henson serves on the National Board of Directors of the National MS Society and the Board of Directors of the American Academy of Neurology, Piedmont Healthcare Foundation, Piedmont Healthcare/Encompass Health Joint Venture and Gordon State University Foundation. Also serves on the Georgia Board of Healthcare Workforce.

involvement (**Table**). This opticospinal involvement is sometimes misdiagnosed as neuromyelitis optica (NMO),[12] which is more common in Japanese and Chinese populations.[16]

Cerebrospinal Fluid (CSF) Findings

The hallmark of MS-specific changes in CSF is the detection of oligoclonal bands, which are seen in the vast majority of Western MS patients (at least 90%). In contrast, the frequency of oligoclonal bands in Japanese patients with MS is reported to be much lower (~50%).[17] These findings have been documented in a few other Asian populations,[18-20] but more data is needed in this large and diverse region.

MRI Findings

In Asian patients with "Western-type" MS, MRI findings are largely similar to those of Western patients in terms of lesion distribution and appearance; however, there are significant differences in patients with opticospinal MS. These patients have fewer lesions on brain MRI. The spinal MRI shows larger and more extensive spinal cord lesions.[12,21]

Genetic Differences

Changes in the *HLA-DRB1* gene and the *IL-7R* gene are the strongest genetic risk factors for developing MS. "Western-type" MS is associated with HLA-DRB1*1501, whereas opticospinal MS is associated with HLA-DPB1*0501.

However, variations in dozens of other genes are thought to be involved in MS risk. It is extremely difficult to compare genetic characteristics of MS in Western and Asian populations since the Asian subcontinent comprises such racially and geographically diverse populations.[15] Recent studies call into question the strength of the genetic component as a differentiating factor between MS in Western populations and that in Asian populations. For example, Pandit and colleagues[22] suggest that many, if not all, of the MS risk variants identified in populations of European ancestry are likely also risk variants in the Indian population.

Impact of Environment

Geographic gradient. MS is known to occur more frequently in areas that are farther from the equator; some of the highest prevalence rates are in Canada, the United States, and the Scandinavian countries (**Figure**). Epidemiologists continue to examine variations in geography, demographics (age, gender, and ethnic background), genetics, infectious causes, and migration patterns in an effort to understand why.

Migrant studies support the important influence of environmental factors in the risk of MS. In a systematic review of such studies, two consistent patterns were apparent: migrants moving from a region of high MS risk to one of lower risk had a lower-than-expected MS prevalence, particularly when migration occurred before age 15 years; and migrants moving from an area of lower risk to one of higher risk tended to retain the lower MS risk of their country of origin, with no clear age-at-migration effect.[23]

In Asian populations, MS is more often characterized by[14]:

- Selective clinical involvement of both the optic nerve and the spinal cord
- A higher cell count and total protein concentration in the CSF
- A higher frequency of gadolinium-enhanced lesions on spinal cord MRIs
- Fewer lesions on the T2-weighted as well as gadolinium-enhanced TI-weighted brain MRIs

A Call to Action

Despite mandates from the National Institute of Minority Health and Health Disparities (within the National Institutes of Health [NIH]) to include more minorities in clinical trials, the participation of members of minority populations, especially Asian, Native Hawaiian, and Pacific Islander populations is disproportionately low in clinical trials funded by the NIH.[24] This underrepresentation hinders the ability to identify differences in treatment response and supports the need for epidemiologic studies to incorporate cultural, environmental, or physiologic factors unique to that population.

Because MS differs both in incidence and clinical expression, prospective cohort studies that incorporate race/ethnicity need to be conducted if we are to better understand MS and establish the best standard of care specific to each

Is it MS or NMO?

While MS is a demyelinating disease of the CNS, NMO is an inflammatory disease of the CNS that selectively affects the optic nerves and spinal cord. MS in Asian populations is often characterized by the selective and severe involvement of the optic nerves and spinal cord. This form, termed 'opticospinal MS', has features similar to those of the relapsing form of NMO in Western populations.

A summary of differential diagnosis is[29]:

- On spinal MRI, NMO is strongly suggested by acute continuous longitudinal lesions covering three or more vertebral levels, while MS is suggested by patchy lesions that are rarely continuous over more than one vertebral segment
- In NMO, spinal cord lesions tend to be centrally located, rarely extending to the surface of the cord; whereas in MS, such lesions are usually located peripherally
- Chronic cord lesions in NMO often change over time, becoming patchier in appearance, making these distinguishing criteria less applicable to older lesions

The 2017 McDonald Criteria for Diagnosis of MS: Need for Validation in Diverse Groups

MS can be difficult to diagnose because there is no single test that can determine the presence of the condition. The process of diagnosis involves obtaining evidence from a clinical examination, medical history, lab tests, and MRI imaging of the brain and, sometimes, the spinal cord. These tests are intended to rule out other possible causes of a person's neurologic symptoms and to gather data consistent with MS. A key principle for diagnosing MS has been to uncover evidence that demonstrates lesions in the CNS showing "dissemination in space" (suggestions of damage in more than one place in the CNS) and "dissemination in time" (suggestions that damage has occurred more than once).

The 2017 revision of the McDonald criteria for diagnosing MS was designed, in part, to allow earlier diagnosis of MS.[27] As such, it allowed an alternative to dissemination in time. In patients who present with a typical clinically isolated syndrome and clinical or MRI demonstration of dissemination in space, the presence of CSF-specific oligoclonal bands confirms a diagnosis of MS.[27]

However, 40% to 55% of Asian persons with MS are negative for oligoclonal bands.[17,28] The 2017 criteria are derived mainly from Western European/White populations. The authors note that the criteria require validation in diverse populations, in this case, persons of Asian ethnicity.[27]

patient's needs. The increased recruitment and inclusion of ethnic minority patients in MS research are essential.[25]

Robers and colleagues[26] conducted a systematic literature review of studies of DMTs for people with MS of varied racial and ethnic backgrounds published as of December 2019. Of 275 search results, 32 articles met the inclusion criteria; only 4 were randomized controlled trials (RCTs). Among studies that included Asian patients, the investigators found studies supporting the efficacy of interferons, fingolimod, teriflunomide, dimethyl fumarate, natalizumab, and alemtuzumab in Asian populations. Additionally, studies evaluating efficacy in Asian versus White patients have revealed no differences, suggesting that DMT choice need not differ in Asian patients. However, the studies included in this literature review were small[26]; more larger studies are needed. Future RCTs should strive to increase minority representation and planned analyses that incorporate race and ethnicity.

REFERENCES

1. Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: insights from the atlas of MS, third ed. *Mult Scler.* 2020;26(14) :1816-1821.
2. National organization for Rare Diseases. *Balo disease.* Accessed March 22, 2022. https://rarediseases.org/rare-diseases/balo-disease/
3. Ma GX, Seals B, Tan Y, Wang SY, Lee R, Fang CY. Increasing Asian American participation in clinical trials by addressing community concerns. *Clin Trials.* 2014;11(3):328-335.
4. National Institute on Minority Health and Health Disparities. Investigator-initiated research on minority health and health disparities program. Accessed January 20, 2022. https://www.nimhd.nih.gov/programs/extramural/investigator-initiated-research/investigator-Initiated.html
5. Knepper TC, McLeod HL. When will clinical trials finally reflect diversity? *Nature.* 2018;557(7704):157-159.
6. Patel K, Patel M, Mukhi H. Despite advances in precision medicine, disparities persist. *Targeted Therapies in Oncology.* 2020;9(16). Accessed January 20, 2022. https://www.targetedonc.com/view/despite-advances-in-precision-medicine-disparities-persist
7. Kingwell E, Marriott JJ, Jette N, et al. Incidence and prevalence of multiple sclerosis in Europe: a systematic review. *BMC Neurol.* 2013;13:128.
8. Eskandarieh S, Sahraian MA. Epidemiological evidence of the recent surge in MS in Asia and Australia: a systematic review. *J Kermanshah Univ Med Sci.* 2021;25(2):e111028.
9. GBD 2016 Multiple Sclerosis Collaborators. Global, regional, and national burden of multiple sclerosis 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(5):269-285.
10. Cheong WL. Mohan D, Warren N, Reidpath DD. Multiple sclerosis in the Asia Pacific region: a systematic review of a neglected neurological disease. *Front Neurol.* 2018;9:432.
11. Eskandarieh S, Heydarpour P, Minagar A, Pourmand S, Sahraian MA. Multiple sclerosis epidemiology in East Asia, South East Asia and South Asia: a systematic review. *Neuroepidemiology.* 2016;46(3):209-221.
12. Chong HT. Multiple sclerosis in South East Asia and diagnostic criteria for Asians. *Neurol Asia.* 2008;13(2):145-146.
13. Chong HT, Tan CT. A review of multiple sclerosis with Asian perspective. *Med J Malaysia.* 2008;63(5):356-361.
14. Kira J, Kanai T, Nishimura Y, et al. Western versus Asian types of multiple sclerosis: Immunogenetically and clinically distinct disorders. *Ann Neurol.* 1996;40(4):569-574.
15. Wasay M, Khatri IA, Khealani B, Sheerani M. MS in Asian countries. *Int MS J.* 2006;13(2):58-65.
16. Hor JY, Lim TT, Chia YK, et al. Prevalence of neuromyelitis optica spectrum disorder in the multi-ethnic Penang Island, Malaysia, and a review of worldwide prevalence. *Mult Scler Relat Disord.* 2018;19:20-24.
17. Nakashima I, Fujihara K, Misu T, et al. A comparative study of Japanese multiple sclerosis patients with and without oligoclonal IgG bands. *Mult Scler.* 2002;8(6):459-462.
18. Li T, Xiao H, Li S, Du X, Zhou J. Multiple sclerosis: clinical features and MRI findings in Northern China. *Eur J Med Res.* 2014;19:20. Accessed January 21, 2022. http://www.eurjmedres.com/content/19/1/20
19. Viswanathan S, Rose N, Masita A, et al. Multiple sclerosis in Malaysia: demographics, clinical features, and neuroimaging characteristics. *Mult Scler Int.* 2013;2013:614716. doi: 10.1155/2013/614716. Accessed January 21, 2022. http://dx.doi.org/10.1155/2013/614716
20. Jugkarin L, Sasitorn S, Naraporn P. Cerebrospinal fluid analyses in Thai multiple sclerosis patients. *Neurol Asia.* 2009;14(2):141-147.
21. Matsuoka T, Matsushita T, Osoegawa M, et al. Association of the HLA-DRB1 alleles with characteristic MRI features of Asian multiple sclerosis. *Mult Scler.* 2008;14(9):1181-1190.
22. Pandit L, Ban M, Beecham AH, et al. European multiple sclerosis risk variants in the south Asian population. *Mult Scleros J.* 2016;22(12):1536-1540.
23. O'Gorman C, Lucas R, Taylor B. Environmental risk factors for multiple sclerosis: a review with a focus on molecular mechanisms. *Int J Mol Sci.* 2012; 13(9):11718-11752.
24. Doan LN, Takata Y, Takuma K-LK, Irvin VL. Trends in clinical research including Asian American, Native Hawaiian, and Pacific Islander participants funded by the US National Institutes of Health, 1992 to 2018. *JAMA Network Open.* 2019;2(7):e197432.
25. Khan O, Williams MJ, Amezcua L, Javed A, Larsen KE, Smrtka JM. Multiple sclerosis in US minority populations. Clinical practice insights. *Neurol Clin Pract.* 2015;5(2):132-142.
26. Robers MV, Soneji D, Amerzcua L. Multiple sclerosis treatment in racial and ethnic minorities. *Pract Neurol.* 2020:49-54.
27. Thompson AJ, Banwell BL, Barkof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol.* 2018;17(2):162-173.
28. Zhao L, Abrigo J, Chen O, et al. Advanced MRI features in relapsing multiple sclerosis patients with and without CSF oligoclonal IgG bands. *Sci Rep.* 2020;10(1):13703.
29. Lalan S, Khan M, Schlakman B, Penman A, Gatlin J, Herndon R. Differentiation of neuromyelitis optica from multiple sclerosis on spinal magnetic resonance imaging. *Int J MS Care.* 2012;14(4):209-214.
30. Multiple Sclerosis International Foundation. Atlas of MS, 3rd ed. September 2020. Accessed January 25, 2022. https://www.msif.org/wp-content/uploads/2020/10/Atlas-3rd-Edition-Epidemiology-report-EN-updated-30-9-20.pdf

PARKINSON'S DISEASE CENTER

PARKINSON'S RESEARCH UNIT

Hawaii Parkinson's Disease and Movement Disorders Center provides comprehensive, compassionate and timely treatment to patients with Parkinson's disease, ataxia, dystonia, essential and other tremors, Lewy body dementia, Frontotemporal dementia, Huntington's Chorea, motor stereotypies and other movement and imbalance disorders. **Services available Honolulu, West Oahu & Neighbor Islands (808) 261-4476**

Our goal is to offer knowledge and symptom control to help patients feel empowered and overcome barriers to living life to the fullest. Our multidisciplinary team of specialists includes neurologists, neurosurgeons and rehabilitation doctors, lifestyle wellness physicians, and other areas work together to determine the most appropriate treatment for your condition. You may work with rehabilitation specialists to manage problems with walking, speaking, swallowing and other aspects of daily life. Your treatment team also includes social workers, physical, occupational and recreational therapists to help you manage Parkinson's disease.

Our Parkinson's Disease and Movement Disorders Center is recognized national for our work in Parkinson's and Movement Research Unit and is offer our patients groundbreaking research.

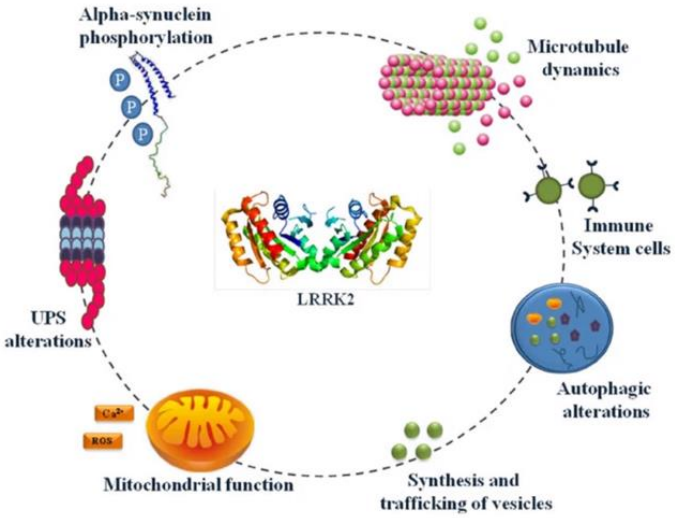
Clinical Trials available at Hawaii PD and Movement Research Unit

Publications by our specialists and researchers at the PD & Movement Disorders Center

Our specialists and staff are passionate about making a difference not just for our patients but for their precious families and caregivers. We understand the challenges of facing these issues and encourage our patients to seek out credible resources with local and national support groups. Please visit their websites.

Jason Viereck, MD, PhD
Director, Parkinson's Disease and Movement Disorders Center
Sub investigator, Parkinson's Research Unit
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine, Graduate Faculty, Clinical & Translational Research, University of Hawaii John Burns School of Medicine
Neurology Residency: Boston University Medical School, Boston

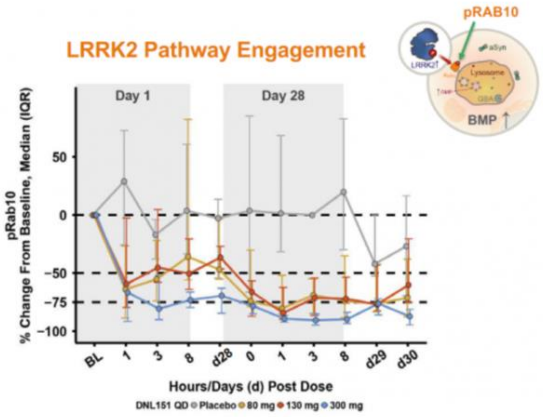
Hawaii's Team first in the World in Phase 2B Study investigating BIIB122 Leveraging Transport Vehicle (TV) Platform Technology to cross BBB (Blood Brain Barrier) delivering BIIB122 to block LRRK2 (*Leucine-rich repeat kinase 2) Restoring Lysosomal Activities to Slow Parkinson's Progression***



The many jobs of LRRK2. Source: Researchgate

According to Parkinson's News Today, Parkinson's does not have a clear genetic cause, but research suggests that mutations in the gene that codes for the protein leucine-rich repeat kinase 2 (LRRK2), also known as dardarin, may increase a person's disease risk. Mutations in the LRRK2 gene, which broadly cause an overactivation of LRRK2, are associated with both familial and sporadic Parkinson's disease, but patients without these mutations also show higher levels of active LRRK2 protein.

While the role of LRRK2 is not fully clear, a body of research suggests that its aberrant activation affects transit within cells, particularly the activity of lysosomes, subcellular compartments responsible for breaking down and recycling excess material and damaged cell parts. Abnormalities in lysosome activity may contribute to neurodegeneration. *Photos credit: https://scienceofparkinsons.com/2022/01/24/lrrk2-2/*



BIIB122/DNL151, co-developed by Denali and Biogen, is a selective small molecule designed to cross the blood-brain barrier and block LRRK2 activity, specifically in the nervous system. The companies believe that doing so could restore lysosomal function and potentially slow Parkinson's progression.

Phase 1 trial noted dose-dependent reduction of at least 50% in active LRRK2 was observed in the blood of healthy volunteers at doses higher than 70 mg, the release reported, and in Parkinson's patients at all dose levels: 80 mg, 130 mg, and 300 mg once daily. A reduction of at least 80% in the levels of active LRRK2 were also observed at doses of 225 mg or higher in both studies. A dose-dependent reduction in the levels of phosphorylated Rab10 was observed in healthy volunteers, and that of at least 50% at all dose levels in Parkinson's patients.

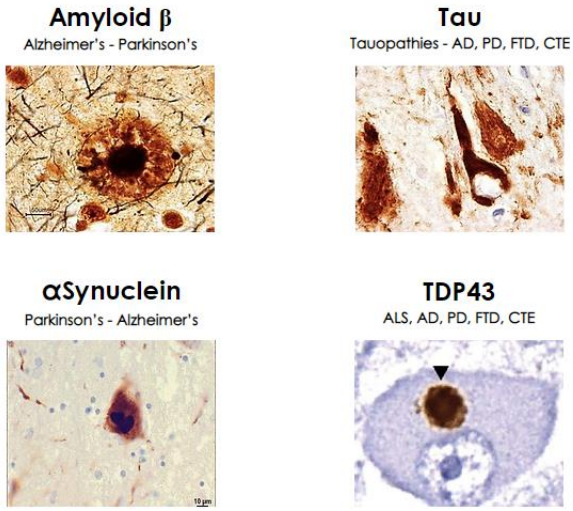
Phase 2b LUMA study — will evaluate BIIB122/DNL151 in patients with and without LRRK2 mutations. Hawaii **Parkinson's & Movement Disorders Center** and **Parkinson's Research Unit** working with Queens Imaging Center along with other top Parkinson's dis centers will recruit about 640 patients without LRRK2 mutations for 48 weeks.

"Our team of neurologists, neuroscience specialists and researchers in Hawaii cannot be more proud to be part of this ground breaking research to develop a drug to potentially slow Parkinson's disease progression" says Kore Liow, MD, Principal Investigator, Neurologist & Neuroscience Chair at Hawaii Pacific Neuroscience & Clinical Professor of Medicine (Neurology).

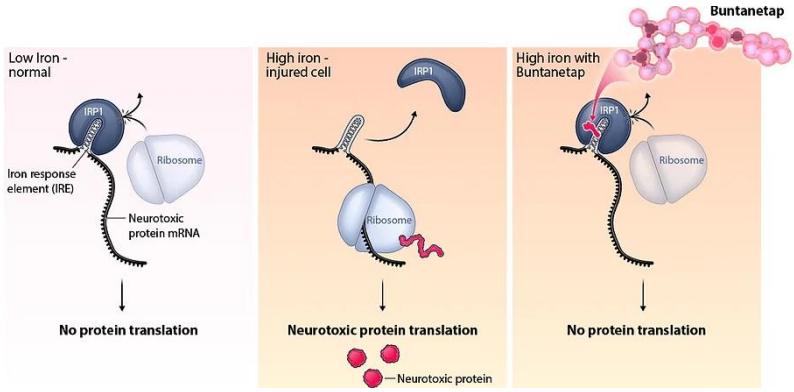
Interested patient or referring physicians to contact Parkinson's Research Unit Hotline (808) 564-6141 info@HawaiiNeuroscience.com

Hawaii Alzheimer's & Parkinson's Researchers and Doctors investigates Buntanetap, reducing APP, tau and αSYN levels, Improving Axonal Transport and Impedes the Toxic Cascade Leading to Neurodegeneration.

According to Annovis Website, Buntanetap is a translational inhibitor of neurotoxic aggregating proteins (TINAPs). Different from monoclonal antibody therapies, buntanetap is an orally available small molecule, and its unique mechanism of action allows it to inhibit multiple neurotoxic proteins at once. Recent research has shown that multiple neurotoxic proteins are at play in all neurodegenerative diseases. Buntanetap is the only drug to attack multiple neurotoxic proteins simultaneously.



Buntanetap has shown to reduce inflammation and preserve axonal integrity and synaptic functions as well as neurotoxic proteins in previous Phase 2a studies. In this study we plan to measure plasma GFAP, NFL and potentially TDP43. (Photo credits: www.annovisbio.com)



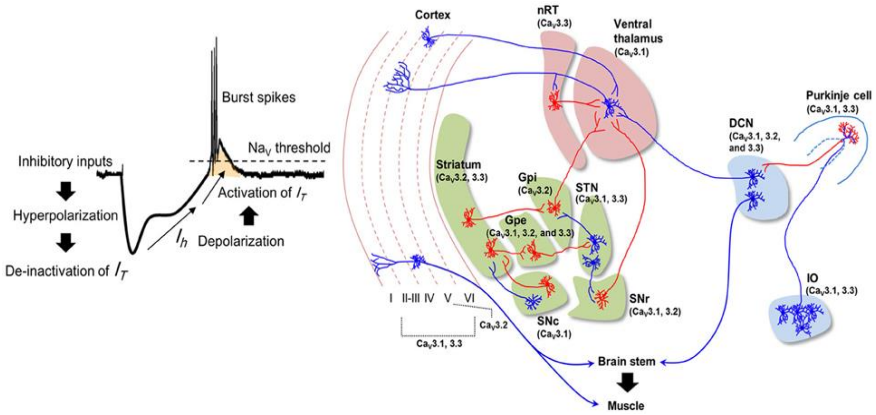
Buntanetap inhibits the translation of neurotoxic proteins by increasing the binding of a special mRNA sequence that is preserved among neurotoxic aggregating proteins and its binding protein that keeps it from going to the ribosome and being translated.

Buntanetap-treated AD patients showed a statistically significant cognitive improvement of 30% as measured by ADAS-Cog11 and in the WAIS Coding Scale, when compared with baseline results. Buntanetap is the only drug so far to show improvement in cognition in AD patients and motor function in PD patients.

See Website to see Who is Eligible for Study

"Our team of neurologists, neuroscience specialists and researchers in Hawaii cannot be more proud of our Hawaii Patients who have contributed to and many who will contribute to this important research study" says Kore Liow, MD, Principal Investigator, Neurologist & Neuroscience Chair at Hawaii Pacific Neuroscience & Clinical Professor of Medicine (Neurology), University Hawaii JABSOM

Hawaii Parkinson's & Movement Disorders Center and Parkinson's & Movement Research Unit 1 of 20 sites in US Selected to Investigate Suvecaltamide, Selective T-Type Calcium Channel Modulator for Parkinson's Tremor.



According to Parkinson's Foundation website, Tremor is often the first motor symptom of Parkinson's disease (PD). About 70-90% of people with PD experience a tremor at some point in their lives. Levodopa is the first-line therapeutic option. The addition of dopamine agonists or anticholinergics can lead to further tremor reduction. For pharmacological-resistant tremor, Botulinum toxin injection and Deep brain stimulation are other options. However, even with these options, many patients' tremor remains uncontrolled. (*Photo credit: Frontiers Neural Circuits, 28 October 2013)*

According to Practical Neurology, Suvecaltimide is a highly selective T-type calcium channels modulator. Suvecaltimide is being investigated for Essential Tremor in once-daily oral dose of 10, 20, or 30 mg suvecaltimide or placebo for 12 weeks. Improvement in ET will be assessed with the combined Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) outcome score, which incorporates the Activities of Daily Living and Performance subscales to enroll 400 adults, age 18 to 80 years, who are diagnosed with moderate-to-severe ET associated with moderate-to-severe disability of which Hawaii Parkinson's & Movement Disorders Center is one of the site. Current study for Parkinson's Tremor is a 17-week double-blind, placebo-controlled, randomized, flexible-dosing, parallel-group, multicenter study.

Eligible Patients:

(i) 40-80 years old (ii) Parkinson's diagnosed within past 5 years

(iii) Must have moderate to severe Parkinson's tremor that is not adequately controlled by medications and interferes with their activities of daily living (ADL).

"Our team of neurologists, neuroscience specialists and researchers in Hawaii cannot be more proud to be selected to contribute to this important research study" says Kore Liow, MD, Principal Investigator, Neurologist & Neuroscience Chair at Hawaii Pacific Neuroscience & Clinical Professor of Medicine (Neurology), University Hawaii JABSOM

For more information, Parkinson's Research Hotline (808) 564-6141 (NCT05642442) Hawaii Parkinson's Disease Center & Hawaii Parkinson's Research Unit or 2230 Liliha Street #104, HONOLULU, HI 96817,

Center for Neuromodulation

Neuromodulation Research Unit

Hawaii Center for NEUROMODULATION

Services available Honolulu, West Oahu & neighbor Islands (808) 261-4476

Neuromodulation is technology that acts directly upon nerves. It is altering or modulating nerve activity by delivering electrical impulses directly to a target area. Neuromodulation can be life changing and enhance the quality of life in individuals who suffer severe chronic neurological conditions such as persistent pain; spinal injury; spasticity; movement disorders; epilepsy; Parkinson's disease, tremors and stroke.

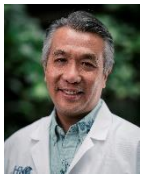
Neuromodulations Therapies offered in Hawaii:

Vagal Nerve Stimulation (VNS) – Epilepsy, Stroke Recovery
Deep Brain Stimulation (DBS) – Parkinson's disease & Epilepsy
Hypoglossal Nerve Stimulator (HNS) - Obstructive Sleep Apnea
Spinal Cord Stimulation (SCS) – Failed Back Surgery, MS, Complex Regional Pain Syndrome, Chronic Painful Neuropathy or Plexopathy
Cala Trio – Essential Tremor

Neuromodulation Research Modalities in Hawaii

Brain Computer Interface (BCI) & Neural Network Research Lab.
Neurotechnology & AI (Artificial Intelligence) Research Lab.

Hawaii Center for Neuromodulation at Hawaii Pacific Neuroscience in collaboration other neuromodulations centers in US as well as experts in neurology, neurosurgery, biomedical engineering, neuroradiology, international partners work together to provide cutting edge neuromodulation therapies to patients in Hawaii who could benefit from them and also conduct active research to advance understanding of how neuromodulation can drive "bench to bedside" translational science to benefit patients in Hawaii and worldwide suffering from chronic refractory neurological conditions.



Hawaii Center for Neuromodulation is directed by Kore Kai Liow, MD, Neurologist and Clinical Professor of Medicine (Neurology), University of Hawaii John Burns School of Medicine who has successfully implanted over 300 patients with neuromodulation devices over the last 25 years and have seen how they positively changed their lives. He works and collaborates with a team of neuroscience specialists including neurologists, pain specialists, neurosurgeons, neurorehabilitation specialists to choose the right treatment plan, which may include medications and counselling, based on individual patient's needs and medical situation.

Hawaii Center for Neuromodulation at Hawaii Pacific Neuroscience

Call or text (808) 261-4476, Research (808) 564-6141


HPN
INFUSION CENTER

Since 2017, Our experienced team of neurologists and infusion care team has been safely providing IV infusions to Hawaii's patients with neurological conditions at the state's first & only Infusion Center specifically dedicated & designed to optimally care for patients with neurological conditions.

Our onsite specialists are nationally recognized experts in neuroscience field and a pioneering leader & often FIRST in state & Pacific region to provide cutting edge research as well as FDA approved medications such as *Aducanumab & Lecanemab*.

Why getting Infusions at an Infusion Center which specializes in neurological condition is important? How is it different from getting them at other settings? What can you expect?

Benefits to Patients:

-Convenience of an outpatient setting in easy to get to central location in Honolulu (15 min from airport)
-Easy parking and access to Infusion Center
-Relaxed, comfortable outpatient setting : Reclining chair, TV (Netflix), Wi-Fi, snacks, privacy
-On site experienced neurologists and IV care team to closely assess drug side-effect surveillance like *ARIA* and monitor long term clinical outcome for efficacy
-On site specialized facilities including 3T MRI, CT, EEG, EMG for easy access for timely testing if needed
-On site convenient labs and pharmacy
-Concierge personalized patient care coordinator walking you through the process & financial counselor to look at ways to minimize out of pocket costs

Benefits to Referring Providers:

Click here to download - Infusion Order Form
-Specialized drug & patient education provided by experienced neuroscience team in office.
-Handle every aspect of Infusion including Prior authorization, cost, patient education, adherence
-Experienced infusion team to optimize follow up care, education and support for patients & families.

Benefits & Sustainability to our Community:

-Significant cost savings compared to hospital or home based infusion
-Benefits of experienced onsite specialized neuro & infusion care team while reducing burden of care & unnecessary cost at acute care facilities

Mahalo for trusting us since 2017 to provide optimal care model for neurological patients needing infusion in the setting of an integrated quality clinical care aligned with specialized infusion services. The outpatient ambulatory setting within a neuro-centric clinical care model improves patient care, as well as streamlining the process and making it much easier to respond to infusion reactions and to monitor and manage long-term side effect surveillance by a team of experienced neuroscience specialists.

Kore Kai Liow, MD, FACP, FAAN
Director, Infusion Center for Neurological Conditions,
Hawaii Pacific Neuroscience
Clinical Professor of Medicine (Neurology),
Graduate Faculty, Clinical & Translational Research,
University of Hawaii John Burns School of Medicine

Member

INFUSION CTR

NATIONAL INFUSION CENTER ASSOCIATION

INSOMNIA
AND SLEEP CENTER

SLEEP RESEARCH UNIT

ACCREDITED

Facility Member™

HPN SLEEP DISORDERS CENTER
SLEEP RESEARCH UNIT

Sleep and Insomnia Center is the only sleep center in Hawaii to offer clinical as well as groundbreaking research therapies for sleep disorders.

The Sleep and Insomnia Center is dedicated to the comprehensive clinical evaluation and laboratory evaluation for patients with all types of sleep disorders including sleep apnea (obstructive, mixed, and central), insomnia, restless leg syndrome, parasomnias, delayed and advanced sleep phase, and general pediatric sleep disorders.

Our goal is to help improve quality of life by assisting patients to achieve high-quality sleep to take a well-rounded and comprehensive approach that is patient-centered. We believe that high-quality sleep should be considered a priority in maintaining a healthy lifestyle and helping to improve other chronic diseases.

Nicholas Anderson, M.D.
Director, Sleep & Insomnia Center & AASM Accredited Sleep Laboratory
Sub-investigator, Sleep Research Unit

SLEEP CENTER

REFERRAL FORM

Fellowship: Sleep Medicine, University of Utah School of Medicine
Residency: Family Medicine, University of Hawaii John Burns School of Medicine
Medical School: University of Colorado School of Medicine

Hawaii Pacific Neuroscience - **HONOLULU**, 2230 Liliha Street #104, Honolulu, HI 96817 (St Francis Liliha)
Hawaii Pacific Neuroscience – **WEST OAHU**, 94898 Lumiaina St. #203, Waipahu, HI 96797 (Waikele Prof. Bldg.)
Call or Text (808) 261-4476 or Fax Referral Form to (808) 263-4476

Hawaii Center for NEUROMODULATION

Services available Honolulu, West Oahu & neighbor Islands (808) 261-4476

Neuromodulation is technology that acts directly upon nerves. It is altering or modulating nerve activity by delivering electrical impulses directly to a target area. Neuromodulation can be life changing and enhance the quality of life in individuals who suffer severe chronic neurological conditions such as persistent pain; spinal injury; spasticity; movement disorders; epilepsy; Parkinson's disease, tremors and stroke.

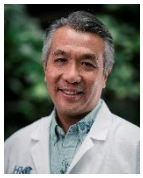
Neuromodulations Therapies offered in Hawaii:

Vagal Nerve Stimulation (VNS) – Epilepsy, Stroke Recovery
Deep Brain Stimulation (DBS) – Parkinson's disease & Epilepsy
Hypoglossal Nerve Stimulator (HNS) - Obstructive Sleep Apnea
Spinal Cord Stimulation (SCS) – Failed Back Surgery, MS, Complex Regional Pain Syndrome, Chronic Painful Neuropathy or Plexopathy
Cala Trio – Essential Tremor

Neuromodulation Research Modalities in Hawaii

Brain Computer Interface (BCI) & Neural Network Research Lab.
Neurotechnology & AI (Artificial Intelligence) Research Lab.

Hawaii Center for Neuromodulation at Hawaii Pacific Neuroscience in collaboration other neuromodulations centers in US as well as experts in neurology, neurosurgery, biomedical engineering, neuroradiology, international partners work together to provide cutting edge neuromodulation therapies to patients in Hawaii who could benefit from them and also conduct active research to advance understanding of how neuromodulation can drive "bench to bedside" translational science to benefit patients in Hawaii and worldwide suffering from chronic refractory neurological conditions.



Hawaii Center for Neuromodulation is directed by Kore Kai Liow, MD, Neurologist and Clinical Professor of Medicine (Neurology), University of Hawaii John Burns School of Medicine who has successfully implanted over 300 patients with neuromodulation devices over the last 25 years and have seen how they positively changed their lives. He works and collaborates with a team of neuroscience specialists including neurologists, pain specialists, neurosurgeons, neurorehabilitation specialists to choose the right treatment plan, which may include medications and counselling, based on individual patient's needs and medical situation.

Hawaii Center for Neuromodulation at Hawaii Pacific Neuroscience

Call or text (808) 261-4476, Research (808) 564-6141

Self-Care & Wellness Center & Wellness Research Unit

Services available Honolulu, West Oahu & Neighbor Islands (808) 261-4476

The Self-Care & Wellness Center at Hawaii Pacific Neuroscience promotes lifestyle choices as life skills in self-care. The choices we make in what we eat, when we eat, how active we are, our sleep habits, stress management, use of alcohol, tobacco and risky substances, and our social connections/relationships with others have a profound impact on our health and well-being.

■ Each of us makes choices every day that affect our health. With the myriad of health information resources available that sometimes provide conflicting information; it can be intimidating to know what constitutes the "healthy choice."

■ Through the Self-Care and Wellness Center you will learn the Six Pillars of Lifestyle Medicine

- Nutrition,
- Physical Activity,
- Sleep Hygiene,
- Stress Management,
- Social Connectedness
- Avoidance of Risky Substances

■ Lifestyle Medicine is an evidenced-based practice of helping individuals and families adopt and sustain healthy behaviors that affect health and well-being. It effectively promotes "lifestyle as medicine."

Brain health can be improved by changing our lifestyle behaviors, including the right nutrients in our daily diet and regular physical activity. To build a personalized wellness road map begins with assessing your health risks and your readiness to change unhealthy behaviors.

Clinical Trials available at Hawaii Stroke Research Unit

Publications by our specialists and researchers at the Hawaii Stroke Restoration Research Unit

Paul Smith, MD, MPH
Director, Self-Care & Wellness Center
Sub-investigator, Clinical Research Center
Hawaii Pacific Neuroscience
Clinical Assistant Professor of Medicine (Neurology),
University of Hawai`i John A. Burns School of Medicine
Residency: Occupational and Environmental Medicine, Preventive Medicine
MPH: University of Hawaii
Medical School: University of Hawaii, John A Burns School of Medicine