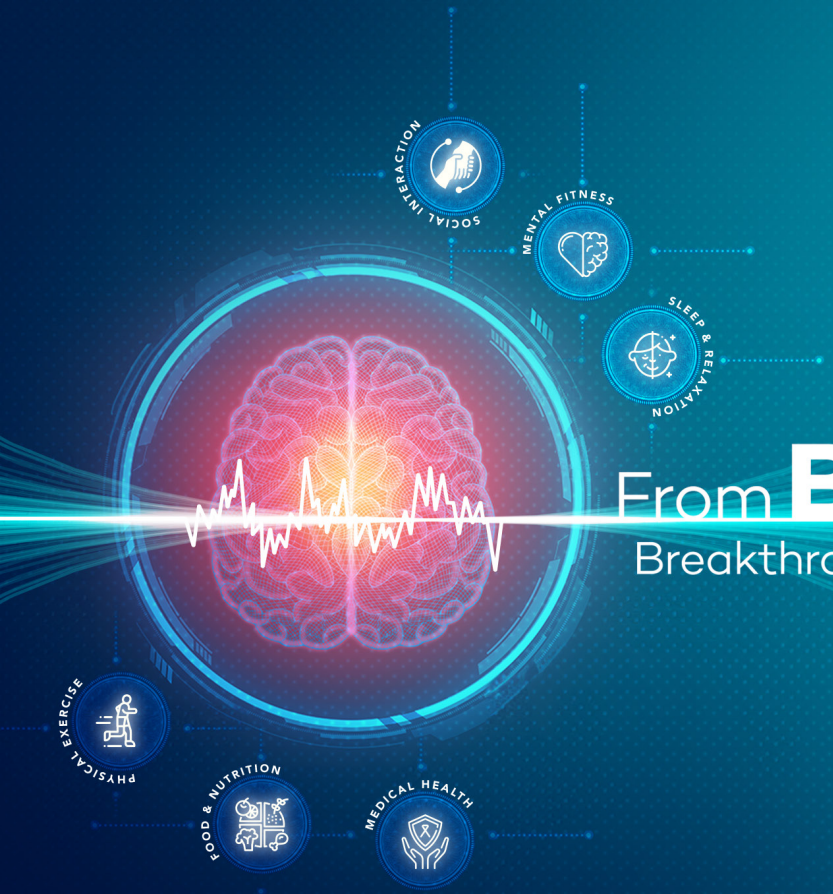

From Brainwaves to Breakthroughs Neuroscience

15TH ANNIVERSARY

HPNS HAWAII PACIFIC NEUROSCIENCE Symposium

Conference info

October 19th Saturday
7:00 AM - 4:00 PM

Ko'Olau Ballrooms & Conference Center
45-550 Kionaole, Kaneohe, Hi 96744

TABLE OF CONTENT

Aloha,

It is with great honor and pleasure that we invite you to be part of our 15th Anniversary to celebrate the privilege and honor of serving the people of Hawaii since 2009.

John Wooden once said “it isn’t about what you do, but how you do it” and that has been so true for us for the past 15 years. Anyone can treat patients, do research and teach but it is “how” and “why” that made us who we are today. Our compassion for people, especially for the underserved compelled us to forsake our retirement and invest in training like-minded individuals who sacrificially come alongside us to serve. The “why” then drives the “how” to ensure these people have the absolute best care and services including world class research options without having to travel far away from their ohana here in Hawaii to find hope. Click for history by KITV News.

We are honored to have Hawaii Governor Joshua Green, MD, who shares the same heart and compassion for the underserved in our community to celebrate with us.

It is with great pleasure we invite you to join Hawaii Governor Green and us to celebrate and honor these amazing physicians, scientists, researchers, staff and aspiring students who have worked tirelessly to advance neuroscience care for the future of Hawaii since 2009 and will continue to do so for generations to come!

Aloha,

Kore Kai Liow, MD
Neuroscience Chair & Founder
Hawaii Pacific Neuroscience
Clinical Professor, Dept. Medicine (Neurology) Graduate Faculty, Clinical and Translational Research
University Hawaii John Burns School of Medicine

Michelle Liow
Healthcare Administrator & Co-Founder
Hawaii Pacific Neuroscience

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HDRS
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Agenda

Timeline for the event

7:30am	8:15am	**Doors Open / Registration**
7:30am	9:30am	**Continental Breakfast**
8:00am	9:30am	**Scientific Session / Exhibit Hall**
9:45am	9:55am	**Opening Remarks** ***Kore Kai Liow, M.D., F.A.A.C.P*** Neuroscience Chair & Clinical Professor of Medicine (Neurology) University of Hawaii John Burns School of Medicine
10:00am	10:25am	**Culturally Responsive Strategies to Reduce the Risk for Neurodegenerative Diseases in Native Hawaiians and Pacific Islanders** ***Keawe Kaholokula, Ph.D.*** Professor & Chair, Department of Native Hawaiian Health University of Hawaii John A. Burns School of Medicine
10:30am	10:55am	**Leveraging Neuroimmunology Targeting Precise Mechanistic Targets** ***Natalia Gonzalez-Caldito, M.D.*** Director, MS & Neuroimmunology Center Director, ALS & Neuromuscular Center Hawaii Pacific Neuroscience
11:00am	11:25am	**Mapping the Last Frontier – The Human Brain** ***Darren DuGas, M.D.*** Director, Video-EEG Epilepsy Monitoring Unit Co-Director, Comprehensive Epilepsy Center Hawaii Pacific Neuroscience
11:30am	11:55am	**Restful Sleep - Essential for a Sound Mind** ***Nicholas Anderson, M.D.*** Director, Sleep Insomnia Center Hawaii Pacific Neuroscience
12:00pm	1:00pm	**Lunch**
01:00pm	1:40pm	**Augmented Reality-The AI Explosion / Applying for a Residency- Be Successful and Remain Sane** ***David Baskin, M.D.*** Kenneth R. Peak Presidential Distinguished Chair Residency Program Director, Department of Neurosurgery Houston Methodist Hospital Weill Cornell Medical College
01:30pm	02:00pm	***Joshua Green, M.D.*** Honorable Governor State of Hawaii
02:00pm	02:45pm	**Awards / Photos**

03:00pm	03:30pm	**Frontiers in Neuroscience - Bench to Bedside Translational Discovery for GBM** ***Michael Lim, M.D.*** Professor & Chair, Department of Neurosurgery Stanford University School of Medicine
03:30pm	04:00pm	**Dawn of a New Therapeutic Era for Alzheimer's & Parkinson's Disease** ***Kore Kai Liow, M.D. F.A.A.C.P*** Neuroscience Chair & Clinical Professor of Medicine (Neurology) University of Hawaii John Burns School of Medicine ***Michael Sonson, M.D.*** Cognitive Neurology Fellow Cedar Sinai UCLA ***Bryce Kalei Chang, M.D.*** Neurology Instructor Mayo Clinic College of Medicine and Science
04:00pm	05:00pm	**Exhibition / Posters/Break**
06:00pm	06:00pm	**Welcome HPN Dinner Celebration**

Speakers

Symposium Speakers

Welcome: Compassion, Excellence & Innovation – Synapsing Together in Hawaii

Kore Kai Liow, M.D. F.A.A.C.P

Neuroscience Chair & Clinical Professor of Medicine (Neurology)
University of Hawaii John Burns School of Medicine

Clinical Focus

- Research
- Neurodegenerative Diseases
- Cortical Physiology
- AI Applications in Neuroscience

Education

- Fellowship: Clinical Neurophysiology, NINDS, Bethesda MD
- Clinical Research, FAES School of Biomedical Research, NIH, Bethesda, MD
- Residency: Neurology, University of Utah School of Medicine, Salt Lake City, UT
- Medical School: St George's University School of Medicine, West Indies

Biography

Kore Liow, MD, FACP, FAAN is Founder & CEO; Neuroscience Chair of Hawaii Pacific Neuroscience. He is Clinical Professor of Medicine (Neurology), Graduate Faculty in Clinical & Translational Research at the University of Hawaii John A. Burns School of Medicine in Honolulu, Hawaii.

Having trained as a research neurologist at NINDS, NIH, he has devoted his life and spends majority of his time in neuroscience research where he has served as principal investigator (PI) for over 180 phase 0-IV clinical trials sponsored by the NIH, CDC and the industries. He continues to serve NIH on its Review Study Section, Scientific Merit Review committees and advisory panel for CDC, AMA, AAN etc. He has published over 85 peer reviewed PubMed publications.

He has worked with sponsors/CROs on trial conception, design, development in submission to FDA IND application, FDA trial approval, and submission of CSR (Clinical Study Report) to FDA. Liow and his neuroscience faculty currently mentors over 20 medical students at the BRITL (Brain Research, Innovation & Translation Labs).

Fun Fact

Dr. Liow believes every challenge presents an opportunity and credits this mindset as a key to his success.

Synopsis

Dr. Liow will discuss the importance of compassion, excellence, and innovation in healthcare, highlighting the collaborative efforts at HPN and the impact of cutting-edge neuroscience research on patient care in Hawaii.

Culturally Responsive Strategies to Reduce the Risk for Neurodegenerative Diseases in Native Hawaiians and Pacific Islanders

Keawe Kaholokula, PhD

Professor & Chair, Department of Native Hawaiian Health
University of Hawaii John A. Burns School of Medicine

Clinical Focus:

- Health Disparities
- Cardiometabolic Health
- Culturally Responsive Healthcare

Education:

PhD, MA, Clinical Psychology, University of Hawai'i at Mānoa
Postdoctoral Fellowship in Clinical Health Psychology

Biography:

Dr. Keawe Kaholokula is a leading expert in Native Hawaiian and Pacific Islander health, with extensive experience in community-engaged research. His work has led to the development of culturally responsive health programs aimed at reducing health disparities. As the Principal Investigator for the Center of Pacific Innovations, Knowledge, and Opportunities (PIKO), Dr. Kaholokula is dedicated to improving the health of Indigenous Pacific People through innovative research and community collaboration.

Fun Fact:

Dr. Kaholokula was a member of the King's Guards of Hawai'i, a trick rifle exhibition group.

Synopsis:

Dr. Kaholokula will present strategies for reducing the risk of neurodegenerative diseases in Native Hawaiians and Pacific Islanders, emphasizing the role of cultural assets in healthcare.

Leveraging Neuroimmunology Targeting Precise Mechanistic Targets

Natalia Gonzalez Caldito, M.D

Director, MS & Neuroimmunology Center
Director, ALS & Neuromuscular Center
Hawaii Pacific Neuroscience

Clinical Focus:

- Neuromuscular Disorders
- Electromyography (EMG)
- MS & Neuroimmunology

Education:

- Fellowship: Neuromuscular, University of California, Irvine
- Fellowship: MS & Neuroimmunology, Northwestern University
- Residency: Neurology, University of Texas Southwestern, Dallas, TX
- Medical Degree: University of Oviedo, Spain

Biography:

Dr. Gonzalez, originally from Asturias, Spain, is a specialist in neuroimmunology and neuromuscular diseases. With dual fellowship training, she is pioneering the first MS and Neuroimmunology program in Hawaii. Her work focuses on developing and implementing advanced therapies for complex neurological conditions, ensuring that patients in Hawaii have access to the latest treatments and clinical trials.

Fun Fact:

Dr. Gonzalez has an identical twin sister who specializes in dermatology. The sisters share a passion for both medicine and the great outdoors, and Dr. Gonzalez is particularly excited to hone her surfing skills while in Hawaii.

Synopsis:

Dr. Gonzalez will explore the advancements in neuroimmunology, focusing on targeted therapies for autoimmune neurological diseases such as Multiple Sclerosis, Neuromyelitis Optica, and Myasthenia Gravis.

Mapping the Last Frontier – The Human Brain

Darren DuGas, M.D

Director, Video-EEG Epilepsy Monitoring Unit
Co-Director, Comprehensive Epilepsy Center
Hawaii Pacific Neuroscience

Clinical Focus:

- Epilepsy
- Seizure Disorders
- Headache
- General Neurology

Education:

- Epilepsy EEG Fellowship: Yale University
- Neurology Residency: Medical College of Wisconsin, Milwaukee

Biography:

Dr. Darren DuGas, a native of Vancouver, Canada, transitioned from a career in pharmacy to neurology, driven by a passion for understanding the brain's complexities. He now leads the Video-EEG Epilepsy Monitoring Unit at Hawaii Pacific Neuroscience, where he is dedicated to providing the highest quality care for patients with seizure disorders and advancing epilepsy research in Hawaii.

Fun Fact:

Before Medical School Dr. DuGas completed all three levels of the Chartered Financial Analyst exams.

Synopsis:

Dr. DuGas will discuss the latest advancements in epilepsy research and treatment, emphasizing the importance of evidence-based practices and innovative care in improving patient outcomes.

Restful Sleep – Essential for a Sound Mind

Nicholas Anderson, M.D

Director, Sleep Insomnia Center
Hawaii Pacific Neuroscience

Clinical Focus:

- Sleep Disorders
- Insomnia
- Pediatric Sleep Disorders

Education:

- Fellowship: Sleep Disorders, University of Utah
- Residency: Family Medicine, University of Hawaii
- Medical School: University of Colorado School of Medicine
- Undergraduate: BYU, BS in Exercise Science

Biography:

Dr. Nicholas Anderson specializes in the treatment of sleep disorders. Originally from Colorado, he completed his medical training in Hawaii and Utah. Dr. Anderson is passionate about helping patients achieve high-quality sleep, which he believes is essential for overall health and well-being. He also advocates for increased awareness of sleep disorders within the medical community and among the general public.

Fun Fact:

Dr. Anderson is an avid Denver sports fan and enjoys basketball and tennis.

Synopsis:

This presentation will cover the science of restful sleep and practical tips for enhancing sleep quality. Topics include sleep patterns, recommendations for sleep duration by age group, common sleep disorders, and the role of wearable technology.

Augmented Reality – The AI Explosion: Applying for a Residency – Be Successful and Remain Sane

David Baskin, M.D

Kenneth R. Peak Presidential Distinguished Chair
Residency Program Director, Department of Neurosurgery
Houston Methodist Hospital Weill Cornell Medical College

Clinical Focus:

- Neurosurgery

Education:

Residency, University of California
Internship, University of California
MD, Mount Sinai School of Medicine of New York City

Biography:

Dr. Baskin began his research career while still a resident at the University of California San Francisco (UCSF). In 1982, he spent a year as a Research Associate at the University of Capetown Medical School and Groote Schuur Hospital in Capetown, South Africa. The following year, Dr. Baskin returned to UCSF and served as a Research Associate in the Hormone Research Laboratory. After completing his residency, Dr. Baskin was appointed as Assistant Professor of Neurological Surgery and Assistant Professor of the Center for Biotechnology at Baylor College of Medicine, with a joint appointment as Chief of Neurological Surgery at the VA Hospital. In 1994 he was promoted to Professor at Baylor College of Medicine in the departments of Neurosurgery and Anesthesiology, positions he held until 2005 when his academic career transitioned to Methodist.

Dr. Baskin has received many national and international honors and awards. He has served as principal investigator on numerous research projects funded by private, state and federal sources, resulting in multiple patents and patent applications. He has also chaired or served on review panels and advisory councils for private, state and federal agencies. Dr. Baskin has published over 100 scientific manuscripts and book chapters and currently serves as Program Director in Houston Methodist Neurological Institute, as well as Professor of Neurosurgery at Weill Cornell Medical College, and Research Professor at the University of Houston in both the Cullen College of Engineering's Department of Electrical and Computer Engineering and the School of Pharmacy.

Fun Fact:

Dr. Baskin has been coming to Hawaii for 40 years, ever since beginning his residency at the University of California in San Francisco. His favorite activities are snorkeling and diving, watching monk seals on the beach in Kauai, campfires on the beach at night, hiking on the many wonderful mountain trails in the state, and eating Shave ice at the many Stands in Honolulu and Kauai.

Synopsis:

Augmented Reality in Medicine

Augmented reality (AR) has evolved significantly from its origins in gaming, exemplified by Pokémon Go, to becoming a valuable tool in medicine. Advances in technology now allow AR to assist in the operating room, enhancing preoperative patient education and resident training. Using devices like the Oculus Rift, surgeons can explore the brain in a virtual environment, providing a detailed view of its structures. For instance, if a tumor surrounds blood vessels, surgeons can visualize the pathways of the vessels by viewing the tumor from different angles. This immersive technology has improved understanding of complex anatomical relationships.

Having operated on over 1,000 patients with AR, the author attests to its positive impact on patient satisfaction, resident education, and surgical outcomes through enhanced anatomical visualization. Specific examples and live demonstrations of AR in the operating room will be shared.

Bonus Discussion: Applying for a Neurosurgical Residency

Neurosurgery is a challenging and rewarding field, and competition for residency positions is escalating. At Houston Methodist Hospital, over 300 applicants vied for just two spots. Previously, more than 70 applicants had USMLE scores in the 95th percentile, with around 50 being part of the Alpha Omega Alpha (AOA) honor society.

This presentation will detail the application process and the key factors influencing success, including signaling, sub-internships, research opportunities, GPA, honor society membership, and publications. Tailored strategies for applicants will be discussed, with examples provided. Attendees will also have the chance to consult with Dr. Baskin to aid in their application efforts.

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reunion NEUROSCIENCE

Honored Guest

Award Presentation

2024 Hawaii Neuroscience Research Award Presentation

Joshua Green, M.D

Honorable Governor, State of Hawaii

Education:

- Undergraduate: Swarthmore College, Biology & Anthropology
- Medical School & Residency: Penn State Milton S. Hershey Medical Center, Pennsylvania State University
  (Family & ER Practice)

Biography:

Governor Josh Green, a physician and politician, has spent two decades caring for families in Hawaii. His legislative efforts have focused on healthcare, housing, and public health, including spearheading Hawaii's COVID-19 response. Governor Green is committed to improving the health and well-being of Hawaii's residents through innovative policies and community initiatives.

Fun Fact:

In 2019, during the measles epidemic, Gov. Green led a medical mission to Western Samoa, successfully vaccinating 37,000 people.

Sessions

Symposium Speakers

3:00 – 3:30 PM

Frontiers in Neuroscience – Bench to Bedside Translational Discovery for GBM

Michael Lim, M.D

Professor & Chair, Department of Neurosurgery
Stanford University School of Medicine

Clinical Focus:

- Brain Tumors (Gliomas, Meningioma, Pituitary Tumors)
- Skull Base Tumors
- Immunotherapy for Brain Tumors

Education:

- Chair of Neurosurgery: Stanford University Hospital
- Residency: Neurosurgery, Stanford University Hospital
- Medical Degree: Johns Hopkins University School of Medicine

Biography:

Dr. Michael Lim specializes in neurosurgery with a focus on brain tumors. His research is centered on developing immune-based therapies for brain tumors, aiming to translate findings from his laboratory into clinical applications. Dr. Lim has led numerous immunotherapy clinical trials and is a recognized leader in the field of neuro-oncology.

Fun Fact:

Dr. Lim used to work at McDonald's and still loves Big Macs.

Synopsis:

Dr. Lim will discuss the challenges and opportunities in developing new therapies for glioblastoma, focusing on the lessons learned from recent immunotherapy trials and the unique immunosuppressive hurdles in treating this aggressive cancer.

3:00 – 3:30 PM

Dawn of a New Therapeutic Era for Alzheimer's & Parkinson's Disease

Michael Sonson, M.D

Cognitive Neurology Fellow,
Cedar Sinai UCLA

Clinical Focus:

- Neurocognition
- Alzheimer's
- Memory Disorders

Education:

- Fellowship: Neuro Behavioral, Cedars Sinai Hospital
- Residency: Neurology, NYU School of Medicine
- Undergrad: Biola University Medical School: NYU School of Medicine
- Certification: Behavioral Neurology
- BRITL Intern 2016

BIO:

Dr. Michael Sonson grew up in Waipahu Hawaii, attended Hanalani Schools and Biola University, is a graduate of the NYU School of Medicine and Neurology Residency program, and is now training as a Fellow at the Cedars Sinai Medical Center to pursue certification in Behavioral Neurology. His areas of interest include the underlying mechanisms of memory and personality and the processes which slow them down or are protective.

Fun Fact:

During the pandemic Dr. Sonson adopted a puppy and picked up skateboarding to keep up with her on his morning runs.

3:00 – 3:30 PM

Dawn of a New Therapeutic Era for Alzheimer's & Parkinson's Disease

Bryce Kalei Chang, M.D

Neurology Instructor: Mayo Clinic College of Medicine and Science

Clinical Focus:

- Neurology
- Neuromuscular

Education:

- Faculty: Mayo Clinic College of Medicine and Science
- Fellowship: Neuromuscular, Mayo Clinic, Rochester Minnesota
- Residency: Neurology, Mayo Clinic, Rochester Minnesota
- BRITL Intern 2016

BIO:

Dr. Bryce Kalei Chang is a resident in neurology with a focus on neuromuscular medicine. His research and publications delve into the intricate relationships between the peripheral nervous system, behavior, and neurological autoimmunity. As a dedicated clinician educator, Dr. Chang has completed the Stanford Faculty Development Center's Course in Clinical Teaching. He has been recognized by the American Academy of Neurology with a resident scholarship for his work on enhancing evidence-based learner self-assessment tools and developing a mobile application to aid in peripheral nervous system localization and electromyography. In the upcoming academic year, Dr. Chang will join the Mayo Clinic College of Medicine and Science as an Instructor in Neurology, where he will contribute to the pre-clerkship neuroscience curriculum. Additionally, he actively participates in the departmental family workgroup, focusing on addressing the unique challenges faced by residents with families, including issues related to parental leave and work shift scheduling.

Fun Fact:

I enjoy nature walks, traveling, musical theatre, gardening, and doing home improvement projects with my wife, Jana–a fellow in hematology and oncology–and our 2-year-old daughter, Ellie. Dr. Liow was my first mentor in neurology, and he inspired me to be a neurologist.

Synopsis:

This lecture explores the latest advancements in Alzheimer's disease treatment, marking a significant shift from symptomatic management to targeted therapeutic approaches. The session will begin by delving into the emerging role of monoclonal antibodies, such as donanemab and lecanemab, which are designed to target amyloid plaques—one of the hallmark pathologies of Alzheimer's. We will examine the mechanisms of action, clinical trial outcomes, and potential benefits and challenges of these therapies.
Beyond monoclonal antibodies, the lecture will highlight innovative approaches on the horizon for early diagnosis and treatment personalization. Attendees will gain insights into the evolving landscape of Alzheimer's disease treatment, the implications for clinical practice, and the future direction of research that aims to modify disease progression and improve patient outcomes.

Judges

Panel of Judges

Panel of Judges

Kore Liow, MD
Neurology

David Baskin, MD
Houston Methodist Neurological Institute

Janette Abramowitz, MD
Queens Neuropsychiatry

Keawe Kaholokula, PhD
Native Hawaiian Health in John A. Burns School of Medicine

Dominic Chow, MD
Queens Medical Group

Samia Valeria, PhD, RN
University of Hawaii

Michael Lui, MD
Hawaii Pacific Health

Karen DaSilva, MD
Queens Medical Center

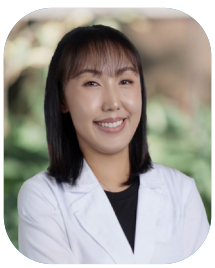
VD Patel, MD
Queens Medical Center

Michael Jaffe, DO
Hawaii Brain & Spine

Monique Canonico, DO
Kaiser Permanente Medical Center

Chathura Siriwardhana, PhD
John A. Burns School of Medicine

Nicholas Anderson, MD
Hawaii Pacific Neuroscience



Qi Zhi, DNP, MPH, FNP-BC
Hawaii Pacific Neuroscience

Qing Li, PhD
University of Hawaii at Manoa

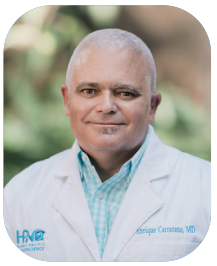
Katy Tarrit, PhD
University of Hawaii at Manoa

Darren Dugas, MD
Hawaii Pacific Neuroscience

Natalia Gonzales, MD
Hawaii Pacific Neuroscience

Michael Sonson, MD
Cedars Sinai

Bryce Kalei Chang, MD
John A. Burns School of Medicine



Enrique Carrazana, MD
Neurelis

Abstract

Research Symposium

- The 10-Year Decreasing Trend of Youth Soccer Head Injuries and Concussions Presenting to U.S. Emergency Departments
- Development and Validation of a Syncope Algorithm to Reduce Unnecessary Echocardiograms: A Single Center Retrospective Quality Improvement Project
- Characterizing Epilepsy in Asian American and Native Hawaiian/Pacific Islander Populations
- Analyzing the Relationship Between Patient Ethnicity and Differences in Treatment for Chronic Migraines
- Lack of Differentiating Demographics and Comorbidities in Episodic vs. Chronic Migraine Patients Presenting with Cervicalgia or Radiculopathy
- Intraoperative Assessment of Brain Lesions Using Combined Frozen Section, Squash (Crush), and Touch Preparation Cytology at the Queens Medical Center: A 7-Year Retrospective Analysis
- Leading Risk Factors for White Matter Hyperintensity in Alzheimer Disease Among Native Hawaiians/Pacific Islanders, Asians, and Whites
- Racial disparities in cardiometabolic disorders among alzheimer disease patients: a focus on native hawaiians and pacific islanders
- Intraventricular metastasis: A systematic review of patient demographics, clinical characteristics, and outcomes
- Native Hawaiian and Pacific Islander Participation in Alzheimer's Disease Clinical Trials: Exploration of ZIP Code Based Heat Map Patterns
- Trends in Antidepressant use among Ethnic-Racial Groups in Hawai'i: focus on Native Hawaiian and other Pacific Islanders.
- Chemogenetic Activation of Hypothalamic Oxytocin Neurons is Cardioprotective in Pre-diabetes
- Evaluating Fall Risk Factors and Comorbidities in Patients with Mild Cognitive Impairment: Insights from a Diverse Population in Hawaii
- Indigenous Participants' Preliminary Measurements of Tau, Amyloid, and Amyloid Onset Age from the Wisconsin Alzheimer's Disease Research Center Studies
- Anterior Cingulate Cortex Activation in Cutaneous Itch and Inflammatory Pain: Role of IL-31 and IL-1
- Efficacy and safety of donanemab, a novel amyloid-targeting therapy
- A comparison of EEG Biomarkers in Alzheimer's and Mild Cognitive Impairment With and Without Comorbid Major Depressive Disorder using BEAM AI Technology
- Utility of EEG biomarkers in the early identification of Alzheimer's Disease: A systematic review
- Comparative Efficacy of BEAM EEG and MMSE in Early Detection of Mild Cognitive Impairment: A Pilot Study
- Deaths from Severe Serious Adverse Events Following SARS-CoV-2 Vaccination: Focusing on Neurological Aspects

- A Retrospective Analysis of Multiple Sclerosis Patients in Hawaii: How Do Caucasians Compare with Other Ethnocultural Groups?
- A Multiple Sclerosis Pilot Study: Are There Differences in Spinal Cord Involvement Among the Ethnocultural Groups of Hawaii?
- Effect of Brimonidine on Retinal Ganglion Cell Function by in vivo Calcium Imaging of Optic Nerve Crush in Mice
- Correlation of Serum Neurofilament Light Chain and Glial Fibrillary Acidic Protein with 2-Year Disease Outcome in Anti-NMDA Receptor Encephalitis
- Development of Metrics for Assessing Impact of COVID-19 Vaccine-Related Adverse Effects and Long COVID-19
- U.T.E.R.U.S: Utilization of a Three-D Model for Education and Research in Uterine Simulation
- Five years of Ublituximab in relapsing multiple sclerosis: additional results from open-label extension of ULTIMATE I and II studies
- Identifying Racial Differences in Clinical Presentation of Obstructive Sleep Apnea in Native Hawaiian and Pacific Islander Patients
- Exploring Carpal Tunnel Syndrome in Underserved Communities: A Focus on AANHPI Populations and Risk Factors
- Long-term Efficacy and Safety of Ravulizumab, a Long-acting Terminal Complement Inhibitor, in Adults with Anti-acetylcholine Receptor Antibody-positive Generalized Myasthenia Gravis: Final Results from the Phase 3 CHAMPION MG Open-label Extension
- Alignment Outcomes Following Total Knee Arthroplasty Using Handheld Navigation Versus Conventional Instruments
- BMI and Associated Health Disparities in Parkinson’s Disease Risk and Progression
- CPAP Therapy Compliance in Obstructive Sleep Apnea Patients in Hawai'i
- Prevalence and Correlates of Obstructive Sleep Apnea in Parkinson’s Disease: A Logistic Regression Analysis
- The Implications of Perioperative Halo Traction for Adult Patients with Severe Spinal Scoliosis- A Systematic Review and Meta Analysis
- Evaluating Risk Factors for Back Pain in Native Hawaiian and Other Pacific Islanders
- Retrospective Comparison of Long versus Short Ultrasound Guided Peripheral Catheters on Extravasation Outcome in Hospitalized Pediatric Patients
- Examining Cerebral Small Vessel Disease (CSVD) in Native Hawaiian/Pacific Islander (NHPI) Stroke Patients: A Pilot Study
- A Clever Stroke Mimic: Thrombotic Thrombocytopenic Purpura Without Schistocytes
- BEAMTM: A point-of-care EEG and ERP neurocognitive assessment platform: Report of a successful implementation at Hawaii Pacific Neuroscience

Concussion, TBI

The 10-Year Decreasing Trend of Youth Soccer Head Injuries and Concussions Presenting to U.S. Emergency Departments

Alex G. Chun[1], Eli M. Snyder[1], Kyle K. Obana[2], Beth G. Ashinsky[2], Robert L. Parisien[3], Thomas S. Bottiglieri[2], Christopher S. Ahmad[2], David P Trofa[2]

[1]John A. Burns School of Medicine University of Hawai'i, [2]Columbia University Irving Medical Center, [3]Mount Sinai Hospital

Objectives : Nearly 3 million children participate in youth soccer annually in the United States. Popularity of youth soccer within recent years has prompted investigation describing youth-soccer concussion trends presenting to United States emergency departments (EDs).

Methods : Data from National Electronic Injury Surveillance System were analyzed for soccer players 2 to 18 years old sustaining concussions from January 2013 to December 2022. Patient data included age, sex, mechanism of injury, setting (practice vs. game), diagnosis, loss of consciousness, and disposition. Raw data were used to calculate national estimates based on assigned statistical sample weight of each hospital.

Results: A total of 80,582 youth soccer concussions were diagnosed in US EDs (51.0% female, 49.0% male). The most common mechanism of injury was head to ball (31.0%). On average, overall concussions decreased by 572 per year ($p=0.02$). Head to body concussions decreased by 169 per year ($p<0.01$) and head to ground concussions decreased by 155 per year ($p<0.01$). No changes per year in concussion trends for head to ball, head to head, not specified, and other mechanisms. Exclusion of years 2020 and 2021 (COVID), demonstrated decreases in concussions for head to body by 125 ($p=0.01$) and head to ground mechanisms by 135 per year ($p=0.01$).

Conclusion: There is a decreasing trend in youth soccer head injuries and concussions presenting to US emergency departments from 2013 to 2022. The trends from this study indicate that heading may be the most important aspect of soccer-related concussions presenting to US emergency departments. This study contributes to the growing literature regarding concussions in youth soccer athletes.

Epilepsy, Syncope, Other Seizures

Development and Validation of a Syncope Algorithm to Reduce Unnecessary Echocardiograms: A Single Center Retrospective Quality Improvement Project

Kevin Benavente, Bradley Fujiiuchi, Samantha Wong, Sean Choi, Benita Tjoe, Michael Tanoue

While still the second most common cause of syncope, cardiac etiologies only account for roughly 18% of all cases. Of these cases, only 22% of cardiac causes are due to structural abnormalities that might be detected via echocardiography. The diagnostic yield of echocardiography has been demonstrated to be as low as 1% in the evaluation of syncope. Despite current guidelines from the American College of Cardiology which recommend the selective use of cardiac ultrasound guided first by a complete history, physical exam, and electrocardiogram, the prevalence of ordering regular echocardiograms still occurs.

In this quality improvement project, our team conducted an extensive literature review to identify tools (such as the San Francisco Syncope Rule, Romeo Criteria) and key patient risk factors correlated with structural cardiac pathology (history of cardiomyopathy/arrhythmias, abnormal ECG characteristics) that would increase the yield of echocardiograms ordered for the indication of syncope. Our team then designed an algorithm to help guide physician decision making, providing a clear list of history, physical, ECG, and laboratory findings that would provide an indication for an echocardiogram. Patient's not meeting any of these criteria do not have a clear indication for an echocardiogram, and thus should not be ordered. The goal of this algorithm was to ultimately reduce the number of extraneous echocardiograms being ordered.

The algorithm was then retrospectively implemented amongst all patient cases of syncope for which an echocardiogram was ordered during the month of April 2024 at the largest tertiary referral hospital in Honolulu, Hawaii. Syncope cases were assessed via detailed manual chart review. The most common causes of syncope were idiopathic or orthostatic (20.8% respectively). A large proportion of echocardiograms were ordered inappropriately for nonsyncopal complaints, such as dizziness or near-syncope (15.3%). Our analysis demonstrated that echocardiography was non-contributory to the patient's workup in 90.3% of cases, with structural-cardiac related etiologies found by echocardiography being a relatively rare occurrence. Hospitalists had the highest percentage of echocardiograms ordered without a clear syncope indication based on our algorithm, while resident trainees had the lowest percentage of unindicated echocardiograms (32% vs 18% respectively).

Application of the syncope algorithm reduced unnecessary orders by 27.8%. In 100% of these cases, the patient's ultrasound was safely found to be non-contributory to the ultimate diagnosis of their syncope. In addition, amongst patients admitted under observation level of care, half of patients were discharged within 24 hours of the echocardiogram result being published, with a mean time from echocardiogram completion to hospital discharge of 4.3 hours. This likely indicates a significant proportion of patients whose discharge is being delayed by the result of an echocardiogram, even though the underlying indication for these echocardiograms may not be appropriate. Applying our results to the total number of echocardiograms ordered for syncope at our hospital in 2023, a cost-savings analysis demonstrated a $365,810 annual cost savings, with a reduction of more than 294 unnecessary ultrasounds, as well as up to 3900 cumulative hours spent per year awaiting echocardiogram results that could have been avoided using this algorithm. This preliminary data demonstrates an important area of improvement that can be addressed using an evidence-based algorithm to cut unnecessary testing in the evaluation of syncope, reduce cost, and potentially decrease patient length of stay. Plans to implement, distribute and monitor the effects of our algorithm prospectively are underway, with hopes of reducing unnecessary testing, reducing healthcare costs, and improving patient experience.

Epilepsy, Syncope, Other Seizures

Characterizing Epilepsy in Asian American and Native Hawaiian/ Pacific Islander Populations

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Background: Epilepsy is a neurological disorder affecting around 50 million people globally, but there is limited research focusing on Native Hawaiian/Pacific Islander (NHPI) and Asian American individuals with epilepsy. This project aims to expand on the current literature by comparing the clinical presentations of epilepsy in both Asian Americans and NHPIs with those of other race groups.

Methods: A retrospective chart review was conducted on patients diagnosed with epilepsy seen at Hawaii Pacific Neuroscience (HPN) between 1/1/2023 and 12/31/2023. Demographics, epilepsy characteristics (clinical presentation, etiologies, severity, and treatment), and comorbidities were collected. Significant differences were derived between each racial group through the use of statistical tests: Kruskal-Wallis rank sum test, Pearson's Chi-squared test, and Fisher's Exact Test for Count Data with simulated p-value.

Results: Of the 474 patients included for analysis, 155 were Caucasian, 116 were Asian, 113 were Native Hawaiian, 31 were Other Pacific Islanders, and 59 were Other Race. Native Hawaiians had a higher proportion of public insurance (83%) compared to Caucasians (63%; $p < 0.001$)and Asians (66%; $p = 0.010$). Asians were older at age of onset (median age: 36) than Other Races (median age: 20). Native Hawaiians had a higher use of rescue medications (21%) than Asians (7.8%). Native Hawaiians and Pacific Islanders had higher BMIs (29 and 32, respectively) than Caucasians (26; $p = 0.012$ and $p = 0.002$, respectively) and Asians (25; $p < 0.001$ and $p < 0.001$, respectively).
Conclusions: To our knowledge, this research study is the first to compare the Asian American and Native Hawaiian populations, both to one another and to other racial groups. Prevalent use of rescue medication amongst Native Hawaiians may potentially signify higher severity of epilepsy, which may have a correlation to higher BMIs observed in this population. However, further investigations must be conducted to better understand these findings.

Headache

Analyzing the Relationship Between Patient Ethnicity and Differences in Treatment for Chronic Migraines

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Background: Standard treatments for chronic migraine (CM) are classified as abortive (acute) or preventative (prophylactic) drugs. This study aims to determine if a correlation exists between certain ethnicities or comorbidities and medications prescribed for patients with chronic migraines among the Native Hawaiian and Pacific Islander (NHPI) population in Hawaii.

Methods: A retrospective chart review was conducted using adult patients diagnosed with CM at Hawaii Pacific Neuroscience from 2021 to 2024. Patients were identified using ICD-10 codes. Patient charts were reviewed for socio-demographics, lifestyle factors, psychiatric and medical comorbidities, clinical presentation, and medication. Statistical analyses were performed on R, with $p<0.05$ considered statistically significant.

Results: The data included 340 CM patients. NHPI (51%, $p<0.001$) were publicly insured. Preventative medications were more commonly prescribed to White (71%) and NHPI (75%, $p<0.01$). Among the comorbidities analyzed, increased BMI (31.1, $p<0.001$) , obesity (15%, $p<0.001$) and type 2 diabetes (6.3%, $p=0.042$) were significantly more common in the NHPI population than non-NHPI. NHPI also reported higher rates of pain scale ($p=0.017$) with an average rating of 7 ($p=0.001$).

Discussion: This study highlights key differences in CM treatment, particularly among NHPI. NHPI and Asians had higher rates of public and private insurance, suggesting insurance status may contribute to the type of medications prescribed. NHPI patients exhibited higher pain scales and higher rates of prescribed preventative medications, suggesting a racial disparity in treatment options for NHPI compared to non-NHPI.

Headache

Lack of Differentiating Demographics and Comorbidities in Episodic vs. Chronic Migraine Patients Presenting with Cervicalgia or Radiculopathy

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Background: Previous literature has reported neck and back pain as comorbidities of chronic migraines. This study aims to corroborate this observation and uncover any differences in demographic features or comorbidities between patients with episodic versus chronic migraines.

Methods: A retrospective chart review of 459 chronic migraine patients (ICD10 codes G43.711, G43.719, G43.701, G43.709, G43.E11) seen at Hawaii Pacific Neuroscience from June 2021 - June 2024 was conducted. Patients without migraine frequency data were excluded. Chronic and episodic migraines were defined per the International Classification of Headache Disorder, 3rd edition. Wilcoxon rank sum tests, Fisher's Exact Tests, and Pearson's Chi-squared statistical tests were performed.

Results: Chronic migraines were associated with radiculopathy (p=0.004), cervicalgia (p=0.006), and chronic pain syndrome approached significance (p=0.053) compared to their episodic migraine counterparts. Tricyclic antidepressants were more commonly prescribed to chronic migraineurs (p=0.035). There were no significant differences in migraine frequency between ethnocultural-racial groups, depression, insurance, associated migraine symptoms, length of migraine diagnosis, general health comorbidities, psychological comorbidities, other neurological comorbidities, smoking, alcohol, and substance abuse.

Conclusions: Our study did not identify particular demographics or comorbidities that are associated with the expected higher prevalence of cervicalgia and radiculopathy in chronic migraine patients. We speculate that higher use of tricyclic antidepressants was due to the intractability of chronic migraines and use of end-of-line medications. The study design was limited by a retrospective chart review, single-center study, and location in the unique minority-majority state of Hawaii. Larger multi-center studies are suggested.

Leading Risk Factors for White Matter Hyperintensity in Alzheimer Disease Among Native Hawaiians/Pacific Islanders, Asians, and Whites

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Background: Vascular comorbidities contribute to brain structural changes like white matter hyperintensities (WMHs), which appear on MRI scans as early markers of cognitive impairment and neurodegeneration. Our previous research found that Asians had a later onset of Alzheimer disease (AD) than Whites and Native Hawaiians/Pacific Islanders (NHPIs), with NHPIs having higher rates of vascular comorbidities and Whites having more alcohol use. However, research on WMH severity in Asians and NHPIs with AD is limited.

Objective: This study aims to identify risk factors associated with extensive WMHs (Fazekas ≥ 2) in AD patients from different ethnic-racial groups—Asians, Whites, and NHPIs—in Hawaii.
Method: A retrospective review of AD patient records from a single center in Hawaii (June 2018–June 2024) was conducted. Variables assessed included age at diagnosis, sex, race, marital status, alcohol use, vascular comorbidities, and Fazekas scores from MRI reports. Statistical comparisons were made across groups.

Results: Among 411 patients (187 Asians, 76 NHPIs, 137 Whites, 11 Others), Asians had the highest rate of extensive WMHs at 28.9% ($P = 0.037$), followed by NHPIs (21%) and Whites (13.8%). Significant risk factors for extensive WMHs included age over 80 years ($P < 0.001$), being single (25.2%, $P < 0.001$), prediabetes (55.9%, $P < 0.001$), type I or II diabetes (29.3%, $P < 0.001$), hyperlipidemia (26.2%, $P = 0.028$), hypercholesterolemia (26%, $P = 0.009$), and stroke/transient ischemic attack (40.5%, $P = 0.040$). Alcohol use was associated with lower rates of extensive WMHs compared to non-drinkers (17.1% vs. 23.2%, $P = 0.035$).

Conclusion: Asians and NHPI AD patients in Hawaii show a higher prevalence of extensive WMHs compared to Whites, suggesting more severe AD progression. Older age of AD onset in Asians and higher rates of vascular comorbidities in NHPIs likely contributes to more severe WMHs, while moderate alcohol use may have a neuroprotective effect in Whites.

Memory Disorders

Native Hawaiian and Pacific Islander Participation in Alzheimer's Disease Clinical Trials: Exploration of ZIP Code Based Heat Map Patterns

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Objectives: Alzheimer's Disease (AD) is the most common neurodegenerative disorder in the United States, and it disproportionately burdens minority populations. Previous research demonstrated that Asian and Native Hawaiian patients were less likely than White patients to participate in AD clinical trials. Native Hawaiians and Pacific Islanders (NHPI) make up 27% of the population in Hawaii and 0.5% of the United States population. The goal of this study was to determine what percentage of AD clinical trial participants were NHPI, as well as patterns in their demographics.

Methods: A retrospective chart review of AD patients (ICD G31.84) who participated in AD clinical trials at two outpatient neurological clinics between the year 2020 and 2024 was conducted. One-way ANOVA or Kruskal-Wallis rank sum test for continuous variables and Fisher's Exact Test or Pearson's Chi-squared test for categorical variables were used to examine differences across racial groups. ZIP code heat maps were used to depict participation of various ethnocultural racial groups.

Results: Total of 244 patients participated in AD clinical trials. Overall, White patients had the highest percentage of participation (31%), followed by Asians (24%), and NHPI (10%) patients. Based on ZIP code heat maps the three ethnocultural racial groups had different patterns of referral to AD clinical trials. NHPI patients represented, on average, the youngest group diagnosed with AD at 71 years old (p=0.01).

Conclusion: In a majority minority state like Hawaii, NHPI population makes up 20% of the population in this memory clinic, however, they are under-represented in participation in AD clinical trials (10%). ZIP code-based heat maps can provide insights into the pattern of referrals and clinical trial participation for NHPI as well as to their counterparts.

Memory Disorders

Trends in Antidepressant use among Ethnic-Racial Groups in Hawai'i: focus on Native Hawaiian and other Pacific Islanders.

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Keywords: Alzheimer's Disease, Antidepressants, Cognitive Impairment, Racial Groups, SSRIs, MMSE, Comorbidities, NHPI

Objectives: In Hawaii, approximately 31,000 individuals aged 65 and older are affected by Alzheimer's disease (AD). Racial disparities exist in AD diagnosis and treatment of AD, but there is limited data on Native Hawaii and Pacific Islander (NHPI) populations. This study explores patterns of antidepressant use among NHPI AD patients compared to other ethnic-racial groups.

Methods: A retrospective chart review was conducted on 243 patients diagnosed with AD at Hawaii Pacific Neuroscience, using patient data collected from 5/1/2015 to 5/1/2023. Data collection included demographics, relevant comorbidities, Mini-Mental State Evaluation (MMSE) scores, and antidepressant medications, across ethnic-racial groups. Statistical analysis included Fisher's Exact Test and Kruskal-Walli's rank sum test.

Results: The study analyzed patients averaging 77.6 years old (80 males and 163 females). Antidepressant use was more common among Asian (N = 89) and White (N = 56) patients, primarily selective serotonin reuptake inhibitors (SSRI), while NHPI patients had lower antidepressant use (33/46). Patients with moderate cognitive impairment) had the highest usage of antidepressants, followed by those with mild impairment. Hypertension was the most common comorbidity (57/84) among those on antidepressants. Significant differences in MMSE scores ($p<0.001$) were found across racial groups, with moderate impairment most common among Asian (20/39) and NHPI patients (16/39). NHPI patients exhibited lower rates of anxiety despite the moderate degree of cognitive impairment.

Conclusion: Antidepressant use was found higher among Asian and White ethnic-racial groups, particularly SSRIs, and lowest among NHPI. While acknowledging the limitations associated with a retrospective study based in a single center, these are interesting findings on the NHPI population afflicted with AD with merit further exploration.

Evaluating Fall Risk Factors and Comorbidities in Patients with Mild Cognitive Impairment: Insights from a Diverse Population in Hawaii

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Objective: This study aims to identify risk factors and comorbidities associated with a higher fall risk in patients with mild cognitive impairment (MCI) in a single-center, ethnically diverse population.

Introduction: Fall prevention guidelines for patients with mild cognitive impairment (MCI) have not been universally established because many clinical practice recommendations are based on trials which, either systematically or unintentionally, excluded adults with cognitive impairment. Thus, there is a potential need to further understand these risk factors to make a consensus recommendation for fall screening and assessment in patients with MCI.

Methods: A retrospective chart review of 274 patients diagnosed with MCI using 2011 NIA-AA diagnostic criteria between 11/1/2022-11/1/2023 was conducted. Demographics, mini mental status examination (MMSE) scores, number of falls one year after MCI diagnosis, comorbid conditions, and medications at time of MCI diagnosis were collected. Wilcoxon rank sum tests, Fisher's Exact Tests, and Pearson's Chi-squared tests were performed.

Results: The mean age of the study population was 73 years and the mean MMSE score was 24.32. There was no significant correlation between MMSE score and total number of falls (Spearman's Rho=0.053). Univariate analysis revealed that older age (p=0.008) and older age at diagnosis (p=0.006) were associated with an increased number of falls. Use of anticholinergics (p=0.039) and antihypertensives (p=0.027) were also associated with increased falls.

Conclusion: Characterizing fall risk in patients with MCI is complex and multifactorial. This study suggests that older age at diagnosis and use of anticholinergics and antihypertensives are negatively associated with future fall risk. Although a subset of antihypertensives are included on Beer's criteria for medications to avoid in the elderly, many patients require strict blood pressure management. This finding suggests that patients taking antihypertensives should be carefully monitored and educated on fall prevention strategies. These findings should help contribute to fall screening and prevention suggestions for patients with MCI.

RACIAL DISPARITIES IN CARDIOMETABOLIC DISORDERS AMONG ALZHEIMER DISEASE PATIENTS: A FOCUS ON NATIVE HAWAIIANS AND PACIFIC ISLANDERS

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Aims: Cardiometabolic disorders may accelerate the progression of Alzheimer Disease (AD), potentially impacting ethnic-racial groups with a higher prevalence of diabetes, obesity, and cardiovascular disease, though limited data exists on Native Hawaiians and Pacific Islanders (NHPI) populations. This study aims to examine the prevalence of diabetes and associated comorbidities among AD patients from different ethnic-racial groups—Asians, Whites, and NHPIs—in Hawaii, with a focus on identifying risk factors linked to AD.

Methods: A retrospective review was conducted on AD patient records from a single center in Hawaii, spanning June 2018 to June 2024. Variables assessed included age at diagnosis, sex, race, insurance type, alcohol use, comorbidities, and Mini-Mental State Examination (MMSE) scores. Statistical comparisons were conducted to identify group differences.

Results: Among 540 patients (286 Asians, 89 NHPIs, 182 Whites, and 13 Others), NHPIs exhibited the highest rates of hypertension (66.3%), diabetes (31.5%), obesity (23.6%), congestive heart failure (13.5%), and coronary artery disease (6.7%). Whites exhibited a higher prevalence of anxiety (18.1%), cardiac arrhythmia (15.4%), and alcohol use (37.4%) compared to Asians and NHPIs. Females had lower mean MMSE scores compared to males (18.3 ± 7.4 vs 21.0 ± 6.2, respectively), along with higher rates of anxiety (16.3%), hypertension (62.2%), hyperlipidemia (47.4%), and underweight body mass index (10.8%).

Conclusions: NHPI AD patients in Hawaii face a higher prevalence of diabetes and a greater burden of cardiometabolic disorders compared to other racial groups. White AD patients show higher rates of anxiety, alcohol consumption, and cardiac arrhythmia compared to Asians and NHPIs. Females with AD exhibited worse cognitive function and more vascular comorbidities compared to males.

Indigenous Participants' Preliminary Measurements of Tau, Amyloid, and Amyloid Onset Age from the Wisconsin Alzheimer's Disease Research Center Studies

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The amyloid cascade hypothesis of Alzheimer's disease (AD) centers the brain's accumulation of pathological amyloid and accumulation of tau neurofibrillary tangles eventually leading to cognitive decline. Identifying the age of onset of amyloid accumulation may aide in optimizing AD interventions. Recent advances have enabled measurement of amyloid burden – e.g., through positron emission tomography imaging (PET) of Pittsburgh compound B (PiB) or blood plasma phosphorylated tau 217 measurement (pTau217). The utility of these biomarkers to capture preclinical amyloid onset is unknown for Indigenous (self-identifying American Indian, Alaska Native, Native Hawaiian) participants in AD research. Here we describe preliminary analyses of plasma pTau217 concentrations (n=49), amyloid PET PiB positivity (n=32), and estimated amyloid onset ages for Indigenous participants at the Wisconsin Alzheimer's Disease Research Center (WADRC).

Forty-nine Indigenous participants had a plasma pTau217 measurement (~53% had >1 sample; 81% female; mean±SD age was 68.6±9.9). At baseline, mean±SD pTau217 was 0.428±0.330 pg/mL; 63.3%, 22.5%, and 14.3% were in the presumed PiB negative, intermediate/indeterminate, and PET PiB positive range respectively, per previously published cut-offs (Ashton et al., 2024). Median(Q1-Q3) plasma-based, sampled iterative local approximation(SILA)-estimated amyloid onset in the latter two categories was 68(54-77) years old.

Ten of 28(35.7%) Indigenous participants who had a PET scan were PiB+ using a previously published threshold (95% CI:18.6%-55.9%). In the non-Indigenous participants, 234/852(27.5%) were PiB+ (95% CI:24.5%-30.6%). More sampling is required to understand if this trend of higher PiB+ in Indigenous populations is widespread. Median(Q1-Q3) PiB-based, SILA-estimated amyloid onset for those with PiB distribution volume ratios greater than 1.13 was 62(56-69) years old. Mixed models examining amyloid burden's associations with longitudinal cognition were inconsistent and a larger sample is needed. These preliminary findings support investigation of pTau217, PiB positivity, and estimations of amyloid onset age for non-invasively measuring time to implement AD therapeutic medications for Indigenous populations.

Lay Summary: Providing interventions for Alzheimer's disease prior to symptom onset, such as drugs that slow the onset of symptoms, is critical to improving the lives of Indigenous communities who are at high risk for developing the disease. We preliminarily report on a blood test and brain scans that predict the age of onset of biological processes involved in development of Alzheimer's disease in Indigenous participants. These preliminary findings support an opportunity to predict Alzheimer's disease prior to symptom onset in an Indigenous community setting through a blood draw.

Efficacy and safety of donanemab, a novel amyloid-targeting therapy

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Background: The safety and efficacy of donanemab has been evaluated in early Alzheimer's disease in TRAILBLAZER-ALZ and TRAILBLAZER-ALZ 2.

Objective: To characterize the efficacy and safety associated with donanemab, a novel amyloid-targeting therapy (ATT).

Methods: TRAILBLAZER-ALZ (phase 2) and TRAILBLAZER-ALZ 2 (phase 3) were multicenter, randomized, double-blind, placebo-controlled, 18-month trials that assessed the safety and efficacy of donanemab in patients with early Alzheimer's disease. The primary outcome in both studies was change from baseline on the Integrated Alzheimer's Disease Rating Scale (iADRS). Secondary outcomes included change from baseline on CDR-SB, ADAS-Cog13, ADCS-iADL, and MMSE. Amyloid-related imaging abnormalities of edema/effusion (ARIA-E), amyloid-related imaging abnormalities of microhemorrhages and hemosiderin deposits (ARIA-H), and infusion-related reactions were adverse events of special interest.

Results: TRAILBLAZER-ALZ 2 demonstrated a slowing of clinical progression at 76 weeks and had a safety profile consistent with TRAILBLAZER-ALZ. In the low/medium-tau population in TRAILBLAZER-ALZ 2, change in iADRS score demonstrated a 35% slowing of disease progression (difference, 3.25; 95% CI, 1.88 to 4.62; P<0.001), and change in CDR-SB demonstrated a 36% slowing (difference, -0.67; 95% CI -0.95 to -0.40; P<0.001). Participants with low/medium-tau who received donanemab experienced a 39% lower risk of progressing to the next disease stage versus placebo over 76w (CDR-Global score, Hazard Ratio=0.61; P<0.001). Significant, positive results across all clinical endpoints were also observed in the combined (low/medium and high tau) population. Adverse events with donanemab in TRAILBLAZER-ALZ 2 included ARIA-E (24.0%, 6.1% symptomatic); ARIA-H (31.4%); and infusion-related reactions (8.7%).

Conclusions: TRAILBLAZER-ALZ and TRAILBLAZER-ALZ 2 trials demonstrated that donanemab significantly slowed cognitive and functional decline in amyloid-positive early symptomatic AD participants and lowered their risk of disease progression while adverse events were consistent with donanemab's well-characterized safety profile and known class risks.

Memory Disorders

A comparison of EEG Biomarkers in Alzheimer's and Mild Cognitive Impairment With and Without Comorbid Major Depressive Disorder using BEAM AI Technology

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Introduction: Understanding the differences in EEG biomarkers among patients with Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI), both with and without comorbid Major Depressive Disorder (MDD), is crucial for advancing diagnostic and therapeutic strategies. This study investigates comorbid depressive disorders associated with distinct EEG biomarker profiles (N1 Peak Latency and P300), providing insights into the neurobiological interplay of their impact on cognitive impairment.

Objective: To determine significant differences in various EEG biomarkers, known to be associated with cognitive impairment, among individuals with AD, MCI, and comorbid conditions such as MDD.

Methods: In the preliminary phase of this study, data was collected from the HPN EHR database focusing on neurological diagnoses of AD, MCI, and comorbid psychiatric condition (MDD). EEG biomarkers were extracted using the BEAM method. For the current analysis, a total of 104 participants were divided into four groups: AD, MCI, AD + MDD, and MCI + MDD. We chose to investigate two biomarkers commonly associated with Alzheimer's, N1 Peak Latency and P300. N1 Peak Latency is a measurement associated with the N1 event-related potential related to slowing of oscillatory brain activity and reduced synchronization and P300 is another (ERP) associated with decision making. Both are commonly increased in AD. Given the numerical nature of the data, a one-way ANOVA was performed to identify significant differences among the groups, followed by post hoc testing using Tukey's method to pinpoint specific group differences. We chose to set our significance level at p=0.05.

Results: The analysis revealed that the null hypothesis was not rejected for N1 Peak Latency nor the P300 Max Latency biomarkers, indicating no significant differences between the four groups (AD, MCI, AD + MDD, MCI + MDD) in either of these biomarkers. Post hoc testing was not conducted as a result.

Conclusions: While we did not find significant differences in this analysis, it is worth noting our sample size is quite small (n=104) and not evenly distributed with a majority of our participants in the MCI group (n=70), which could explain why we found no significant difference between our AD and MCI groups, which would've been expected and consistent with the current literature. Yet given our limitations, it seems the next step would be to expand our sample size, and wait before drawing any broad conclusions. It is also worth noting that mild cognitive impairment and AD are not independent diagnoses, therefore depending on the timing of the administration of the EEG we could expect to see differences even within the MCI group, but that is for a future study.

Luckily at Hawaii Pacific Neuroscience research is ongoing and as more patients are seen we seek to continue investigating not only these biomarkers, but other biomarkers associated with AD and MCI, as well as other potential comorbidities that those with MCI or AD may suffer from such as anxiety and sleep among other disorders. We hope that this research merely serves as a stepping stone to improving patient care, and together with the rest of BRITL, the BEAM team in California, and all of those in ANNE to continue to investigate Alzheimer's and its associated conditions.

Utility of EEG biomarkers in the early identification of Alzheimer's Disease: A systematic review

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Introduction: Alzheimer's disease (AD) is a progressive, chronic, neurodegenerative disease and the leading cause of dementia worldwide. With no cure, an early diagnostic tool that can identify mild cognitive impairment (MCI) in AD is critical. Electroencephalogram (EEG) biomarkers have been proposed to be a noninvasive tool in identifying and managing AD.

Methods: Databases used included PubMed with a search term of "Alzheimer's disease p300". Inclusion criteria included articles that were found in PubMed, peer-reviewed, and a minimum sample size of 20 participants. Studies included either discussing auditory oddball tasks, ERP, or neuropsychological battery exams. Exclusion criteria included studies not published within the last 12 years, not published in English, and did not only use human subjects.

Results: The keyword search yielded 308 articles. After filtering by the exclusion criteria, 108 articles remained. 36 articles were selected based on their relevance to the P300 biomarker and its association with AD/MCI. The studies consistently found that AD patients exhibited reduced P300 amplitudes and prolonged P300 latencies compared to healthy controls at the Pz electrode site. P300 has also been used to evaluate cognition in other pathologies and measure clinical efficacy of pharmacologic treatments for AD/MCI.

Conclusion: The review suggests that P300 can be used as a biomarker to detect AD. These findings highlight the need for standardized protocols and further validation to establish the clinical utility of P300 in AD. The varying ways in which studies use the P300 biomarker highlights the utility of the it and other EEG biomarkers not limited to P300.

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Comparative Efficacy of BEAM EEG and MMSE in Early Detection of Mild Cognitive Impairment: A Pilot Study

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by cognitive decline. Screening for AD and its precursor state, mild cognitive impairment (MCI), is often achieved using the Mini-Mental State Examination (MMSE). However, its efficacy at identifying early stages of MCI is inconsistent. BEAM (Biomarker-based Electrophysiology for Advanced Brain Monitoring) is a novel diagnostic tool which utilizes AI technology to evaluate electroencephalograms (EEG) administered under neurocognitive testing conditions to identify event-related potentials (ERPs) that are early biomarkers of MCI.

Objective: To evaluate the effectiveness and accuracy of BEAM in predicting MCI by analyzing the correlation between BEAM biomarkers and age, compared to MMSE scores and expected values for MCI patients.

Methods: A retrospective chart review was conducted at Hawaii Pacific Neuroscience for patients who were candidates for BEAM testing from March to June 2024. We identified 104 patients diagnosed with AD or MCI based on current MMSE scores and who successfully completed EEG testing under resting state (eyes-open and eyes-closed, 5-minutes each) and three neurocognitive testing scenarios: Auditory Oddball (AO), 3-Choice Vigilance (3CVT), and Standard Image Recognition (SIR). Data collected also included demographic information and comorbidities.

Results: The cohort had a mean MMSE score of 24.47. Resting state EEG peak alpha scores displayed a weak indirect correlation with age ($r = -0.20$, $p < 0.05$). MMSE scores demonstrated a moderate indirect correlation with age ($r = -0.31$, $p < 0.01$). Conversely, AO N1 peak latency exhibited a strong direct correlation with age ($r = 0.34$, $p < 0.001$). AO P300 max latency was weakly directly correlated with age ($r = 0.23$, $p < 0.05$). Accuracy was indirectly correlated with age for sustained attention tasks in both 3CVT ($r = -0.24$, $p < 0.05$) and SIR ($r = -0.33$, $p < 0.05$) scenarios. P2 peak latency during 3CVT was moderately positively correlated with age ($r = 0.40$, $p < 0.01$).

Conclusion: There exists a need for development of early diagnostic tools that can accurately detect MCI without the need for costly, invasive, and time-intensive procedures. BEAM parameters, particularly AO N1 peak latency and 3CVT P2 peak latency, have proved to be useful biomarkers for cognitive decline. The significant correlations between BEAM biomarkers and age further highlight its potential in clinical settings for diagnosing MCI.

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A Retrospective Analysis of Multiple Sclerosis Patients in Hawaii: How Do Caucasians Compare with Other Ethnocultural Groups?

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Background: Historically, Multiple Sclerosis (MS) has largely been considered a disease disproportionately affecting Caucasians. However, current literature points to an increasing burden of MS in certain minority groups, namely African Americans and Hispanics. As Hawaii is a majority-minority state with a diverse population, it is a prime location for the analysis of MS burden among ethnocultural groups.

Objectives: To uncover similarities and differences in clinical presentation and initial imaging between the Caucasian MS patient population and MS patients of other ethnocultural groups (OEG) in Hawaii.

Methods: This is a single center retrospective pilot study of patients ages 18+ years with a diagnosis of MS (ICD-10 G35) between 2008-2023. Demographics, comorbidities, and presenting Expanded Disability Status Scale (EDSS) scores were collected for all patients. Initial spine and brain magnetic resonance imaging (MRI) reports and EDSS scores at time of imaging were recorded as available, with particular attention to lesion location and number. Patients with unknown racial status or yet to be seen in the office were excluded.

Results: Of the 128 patients analyzed, 85 were Caucasian (C) and 43 were confirmed members of Other Ethnocultural Groups (OEG) which included 12 Hispanics, 10 Asians, 9 African-Americans, 6 Native Hawaiian and Other Pacific Islanders, and 6 who identified as Other. There were no significant differences in sex, home zip code, insurance status, or family history of MS. Caucasians had a lower prevalence of hypercholesterolemia (p=0.021) and slightly lower EDSS scores at time of presentation (p=0.047; C: median of 3.50, interquartile range [IQR] of 3.00-4.50; OEG: median of 4.00, IQR 3.25-5.00). While there was no difference in age at time of initial presentation, Caucasians were older at the time of their spine MRI compared to OEG (p=0.017; C: median=43, IQR 35-58; OEG: median=37, IQR 28-44). No significant differences were found for either spine or brain MRI lesion burden or lesion location.

Conclusions: The key findings are that OEG presented with worse initial EDSS scores and Caucasians were older in age at the time of initial spinal cord MRI. Whether these differences should be attributed to biological influence, socioeconomic factors, and/or other phenomena is unclear at this time. Further investigation is required for confirmation as the limitations of this study include its single center nature, small sample size, and varying detail of records.

A Multiple Sclerosis Pilot Study: Are There Differences in Spinal Cord Involvement Among the Ethnocultural Groups of Hawaii?

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Objective: To detect differences in lesion burden, clinical presentation, and disability severity among newly diagnosed Multiple Sclerosis (MS) patients in Hawaii as stratified by ethnocultural background.

Background: In their 2013 paper, Amezcua suggests that spinal cord lesion burden on initial presentation may correlate with disability level in Hispanic MS patients, and posits that spinal magnetic resonance imaging (MRI) may be helpful in predicting long-term outcomes for MS patients. Similar studies have not yet been conducted to analyze potential associations within the richly diverse population of Hawaii.

Methods: This is a single center retrospective study of patients ages ≥18 with an MS diagnosis (ICD-10 G35) between 2008-2023. Demographics, comorbidities, and presenting Expanded Disability Status Scale (EDSS) scores were collected. Initial spine and brain MRI reports and EDSS scores at imaging were recorded as available.

Results: The ethnocultural breakdown of the 128 patients gathered: 85 White, 12 Hispanic, 10 Asian, 9 Black, 6 Native Hawaiian and Other Pacific Islander (NHOPI), and 6 Other. There were no significant differences in demographics or comorbid conditions. Caucasians presented at a significantly older age as compared to Hispanics (p=0.0015). NHOPI had significantly higher EDSS scores at presentation compared to Hispanics (p=0.036). No significant differences were found for either spine MRI lesion burden or location (n=62), or brain MRI lesion burden or location (n=67). Multiple lesions on spine MRI correlated significantly with higher EDSS scores than those with 1 lesion on spine MRI (p=0.0067), but this relationship did not hold when compared to those with no lesions (p=0.58).

Conclusions: There was no difference in the burden or location of spinal/brain MRI lesions at time of diagnosis. Interestingly, NHOPI had higher EDSS scores at presentation when compared to Hispanics. While the data hint at positive correlation between number of spine lesions on MRI and EDSS scores, larger sample sizes are needed to confirm.

Correlation of Serum Neurofilament Light Chain and Glial Fibrillary Acidic Protein with 2-Year Disease Outcome in Anti-NMDA Receptor Encephalitis

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Background: Anti-NMDA receptor encephalitis is a rare autoimmune disease that affects approximately 1.5 per million people worldwide each year. The disease occurs when autoantibodies target N-methyl-D- aspartate receptors (NMDAr), causing brain inflammation and neurological damage. Diagnosis includes clinical evaluations and neuronal antibody testing in both cerebrospinal fluid (CSF) and serum. However, there are no well-established biomarkers regarding patient prognosis. Therefore, we evaluated the feasibility of neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) indicative of axonal and astrocyte degradation as biomarkers of disease outcome in anti-NMDA encephalitis.

Objective/Hypothesis: Our aim was to investigate serum NfL and GFAP levels and correlate them with disease outcome in anti-NMDA receptor encephalitis (anti-NMDARE) over a 2-year period. We hypothesize that increases or decreases in serum NfL and GFAP will correlate with 2-year disease outcome.

Materials and Methods: An individual diagnosed with anti-NMDA receptor encephalitis (AIE) was admitted to King Chulalongkorn Memorial Hospital. Following admission, patients undergo neurocognitive testing. Blood (5 mL) is collected from each patient; serum NfL and GFAP are measured using a Simoa SR-X Analyzer at baseline (0 month), 12 and 24 months.
Results: Patients with anti-NMDAr encephalitis have the highest serum NfL and GFAP levels at diagnosis and decrease when patients receive treatment. Serum NfL and GFAP levels are also higher than in healthy individuals.

Conclusions: Serum NfL and GFAP are consistent with patient symptoms, MRI and EEG. They can be used as prognostic markers for anti-NMDAr encephalitis. Although currently expensive, this test could become more affordable if it becomes widely available.

MS & Neuroimmunology

Development of Metrics for Assessing Impact of COVID-19 Vaccine-Related Adverse Effects and Long COVID-19

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Background:
Elucidate the hypercytokinemia state and neurological effects of Long COVID to facilitate treatment.

Methods:
Quantify interferon, interleukin blood biomarkers in Long COVID and Vaccinated patients in Thailand

Results:
IFN-γ, IL-12p70, and IL-33 were elevated in both vaccinated and unvaccinated patients (n = 168).

Conclusion:
Investigate additional biomarkers, continue surveillance of Long COVID patients, expand sample size.

Neuromuscular

Exploring Carpal Tunnel Syndrome in Underserved Communities: A Focus on AANHPI Populations and Risk Factors

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Background/ Objectives: Carpal tunnel syndrome (CTS) is a debilitating nerve condition caused by compression of the median nerve in the carpal tunnel. This study aims to address the paucity of research on CTS 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 CTS between 2019-2023 were identified using ICD10 codes. Patients without confirmation of diagnosis via electromyography (EMG), clinical presentation, or sufficient demographical data were excluded. Statistical analysis was completed on R, with $p<0.05$ considered statistically significant.

Results: Data from 404 patients are included in the analysis. The cohort consisted of 35% NHPIs and 33% Asians. AANHPI had the highest rates of public insurance usage ($p<0.001$). NHPI had the highest rates of obesity ($p<0.001$) while Asians had the lowest rate of obesity ($p<0.001$). Native Hawaiians and Asians had higher rates of hypertension ($p=0.022$, $p=0.002$), hyperlipidemia ($p=0.042$, $p=0.020$), and diabetes ($p=0.008$, $p=0.021$) compared to Whites. Native Hawaiians had the highest rates of active or former smokers ($p=0.003$). Asians had a lower proportion of treatment with opioid agonists compared to others (AIAN, Blacks, Hispanics) ($p=0.033$).

Conclusion: AANHPI patients presenting with CTS are more likely to have public insurance, and present with hypertension, hyperlipidemia, and diabetes. Native Hawaiian patients specifically were also more likely to be obese and be current/former smokers. Asians were diagnosed later and were least likely to be treated with opioids compared to other racial groups. These findings are vital for addressing the underlying comorbidities seen in CTS to reduce treatment disparities among AANHPI patients.

Long-term Efficacy and Safety of Ravulizumab, a Long-acting Terminal Complement Inhibitor, in Adults with Anti-acetylcholine Receptor Antibody-positive Generalized Myasthenia Gravis: Final Results from the Phase 3 CHAMPION MG Open-label Extension

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Objective: To evaluate the long-term efficacy and safety of ravulizumab in adults with anti-acetylcholine receptor antibody-positive (AChRAb+) generalized myasthenia gravis (gMG).

Background: The 26-week, double-blind, randomized, placebo-controlled period (RCP) of the CHAMPION MG study demonstrated the efficacy and favorable safety profile of ravulizumab in adults with AChRAb+ gMG. Participants who completed the RCP could receive ravulizumab in the open-label extension (OLE; NCT03920293).

Methods: In the OLE, patients could receive intravenous ravulizumab (blind induction or bridging dose at Week 26 [OLE start] for those previously receiving placebo or ravulizumab, respectively, then 3000–3600 mg according to body weight at Week 28 and every 8 weeks thereafter) for up to 4 years at database lock. Assessments included Myasthenia Gravis-Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) total scores, and safety evaluations.

Results: The final analysis included data from 161 patients (78 received ravulizumab, 83 received placebo in the RCP) who entered the OLE and received ravulizumab for up to 164 weeks. Mean duration of ravulizumab treatment was ~2 years. Improvements in MG-ADL total score seen in ravulizumab-treated patients in the RCP were maintained: least-squares mean change from RCP baseline at Week 164 was -4.0 (95% confidence interval [CI] -5.3, -2.8; p<0.0001). Patients who switched from placebo in the RCP to ravulizumab in the OLE showed rapid improvements in MG-ADL score, which were maintained through 138 weeks (least-squares mean change from OLE baseline at Week 164: -2.1 [95% CI -3.3, -0.9]; p<0.0005). QMG total score improvements were also maintained in patients continuing ravulizumab in the OLE and scores improved from OLE baseline in patients switching from placebo to ravulizumab. Ravulizumab was well tolerated; no meningococcal infections were reported.

Conclusions: Ravulizumab, administered every 8 weeks, demonstrated clinically meaningful sustained improvements in MG symptoms and was well tolerated for up to 164 weeks in adults with AChRAb+ gMG.

Intraoperative Assessment of Brain Lesions Using Combined Frozen Section, Squash (Crush), and Touch Preparation Cytology at the Queens Medical Center: A 7-Year Retrospective Analysis

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Objective: Squash/crush (SP) and touch preparations (TP) are rapid techniques employed in intraoperative assessment of brain lesions. Given the major updates to the 2016 WHO brain tumor classification affecting histologic and molecular diagnoses, we aimed to assess the continued efficacy of combined intraoperative frozen section/SP/TP, and to examine factors affecting the sensitivity and specificity of our methods.

Study Design: Our database was searched for all brain lesions examined intraoperatively at the Queens Medical Center from January 2017 to December 2023.

Results: During our 7-year study period, 588 brain lesions were assessed intraoperatively. 528 (89.8%) and 60 (10.2%) were neoplastic and nonneoplastic lesions, respectively. The most common neoplasms were meningioma (171, 29.1%), metastatic cancer (92, 15.7%), glioblastoma (88, 15.0%), astrocytoma (35, 6.0%), lymphoma (33, 5.6%) and oligodendroglioma (19, 3.2%). 28 (4.8%) intraoperative assessments were deemed indeterminate and deferred to permanent sections. There was discordance between intraoperative and histological diagnoses in 25 (4.5%) of the remaining 560 cases, including 13 sampling and 12 interpretation errors. The latter included 3 false positive cases misdiagnosed as lymphoma and 4 false negative gliomas. There were also 5 misclassifications of tumor subtype, including 4 cases involving meningiomas.

Conclusion: Intraoperative brain assessment with combined frozen section/SP/TP demonstrated high sensitivity (96.8%), specificity (94.6%), and overall diagnostic accuracy (91.0%), which is comparable to published accuracy rates. The efficacy of our intraoperative brain assessments was affected by glial tumor classification updates, as well as diagnostic challenges related to meningioma.

Chemogenetic Activation of Hypothalamic Oxytocin Neurons is Cardioprotective in Pre-diabetes

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Autonomic nervous system imbalance manifesting as cardiac autonomic neuropathy (CAN) is a common but poorly understood complication of diabetes, detectable even at the pre-diabetic stage. Clinical indications range from resting tachycardia and exercise intolerance to myocardial infarction, fatal arrhythmias and sudden death. Although CAN is a strong predictor of mortality in the diabetic population, current strategies for addressing the decreased parasympathetic activity are limited and lack cardiac specificity. Recent work has indicated that activation of hypothalamic paraventricular nucleus (PVN) oxytocin neurons excites cardiac vagal neurons (CVNs), which originate in the brainstem and synapse directly on the heart, increasing cardiac parasympathetic stimulation by an unknown mechanism. To investigate this, pre-diabetes (PD) was induced in rats by 10 months of high-fat high-fructose feeding. Compared to Control, PD animals had reduced left ventricular ejection fraction and elevated fasting glucose, insulin and triglyceride levels. In a Treatment group of PD, the PVN of neonatal rats was transfected with vectors to express designer receptors exclusively activated by designer drugs (DREADDs) in PVN oxytocin neurons, chronically activated with the designer drug clozapine-n-oxide (CNO). After 4 weeks of CNO, Treatment animals had improved left ventricular function compared to non-treated PD animals, yet fasting glucose, insulin and triglycerides remained unchanged. Preliminary transcriptional analysis of left ventricle tissue suggests preservation of key pathways involved in redox regulation (Msra, Txnrd1) and ion channel function (Sln, Atp1b2, Kcnk2) in the Treatment animals compared to PD. These data highlight potential cardiac and central nervous system pathways that are altered in PD yet rescued with PVN OXT treatment. Therefore, PVN OXT neurons may be promising therapeutic targets to activate beneficial parasympathetic-mediated cellular pathways within the heart during diabetic CAN.

Other

Intraventricular metastasis: A systematic review of patient demographics, clinical characteristics, and outcomes

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Background: Intraventricular metastases (IVM) are rare occurrences of brain metastases that arise within the brain's ventricles from primary tumors elsewhere in the body. While brain metastases are common, IVM account for only 1-2% of such cases and present unique treatment challenges due to their deep-seated location.

Objective: This systematic review aims to comprehensively analyze patient demographics, clinical characteristics, treatment approaches, and outcomes for individuals diagnosed with IVM.
Methods: A systematic search of online journals was performed to identify and include studies regarding metastases within the brain's ventricles from non-central nervous system (CNS) primary tumors. Data on demographics, clinical features, tumor characteristics, treatment modalities, and survival outcomes were analyzed.

Results: A total of 54 studies comprising 141 patients were included. The average age was 58 years, with a male predominance (66%). Renal cell carcinoma (RCC) was the most common primary tumor (46%), followed by lung (20%), thyroid (8%), and breast cancer (7%). Most metastases occurred in the lateral ventricles (80%). Treatment included surgery (38%), radiotherapy alone (29%), and combined modalities (18%). The average survival from metastasis diagnosis to death was 1.3 years. No significant survival differences were observed between patients with renal versus non-renal primaries or between isolated IVM and those with additional metastases, though isolated IVM patients showed a longer survival trend.

Conclusion: IVM are exceedingly rare, with RCC representing a disproportionate number of cases. Surgical resection remains the predominant treatment, though outcomes remain poor. Future research should focus on early detection and tailored therapeutic approaches to improve prognosis.

Other - Pain

Anterior Cingulate Cortex Activation in Cutaneous Itch and Inflammatory Pain: Role of IL-31 and IL-1

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Background: Prurigo nodularis and hidradenitis suppurativa, both chronic dermatological disorders, are associated with itch cytokine interleukin-31 (IL-31) and pain cytokine interleukin-1 (IL-1), respectively, and are characterized by significant quality of life and mental health burden. The anterior cingulate cortex (ACC) region has been shown to be involved in the processing of both itch and inflammatory pain. However, the neuronal activation patterns in the ACC in relation to skin-derived IL-31 and IL-1 are not yet fully understood.

Objective: This study aimed to investigate neuronal activation in the ACC in response to itch and inflammation mediated by IL-31 and IL-1.

Methods: Two experimental models were used. First, ACC activation in transgenic IL-31 overexpressing mice was compared to wild-type controls. Second, tdTomato reporter mice were used to visualize ACC activation in IL-31 and IL-1 expressing cells in conditions of pain and itch. Neuronal activity was quantified using cfos as a marker of neural activation.

Results: IL-31 overexpression resulted in elevated neuronal activation in the ACC compared to wild-type mice, supporting a link between IL-31-driven itch and ACC activation. In the tdTomato reporter mice, ACC activation was seen in both IL-31 and IL-1 expressing cells, indicating that both cytokines play a role in ACC activity in response to itch and inflammation.

Conclusion: These findings highlight the role of the ACC in mediating itch and inflammatory pain through IL-31 and IL-1 expression. The study provides new insights into the divergent neuronal mechanisms underlying IL-31 and IL-1-mediated disorders, such as prurigo nodularis and hidradenitis suppurativa, highlighting potential pathways for future therapeutic intervention.

Deaths from Severe Serious Adverse Events Following SARS-CoV-2 Vaccination: Focusing on Neurological Aspects

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Serious adverse events (SAEs), including neurological diseases such as Guillain-Barré Syndrome, have been reported following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination. Nevertheless, there is a paucity of research on the survival prognostics of patients with severe SAEs. We performed a retrospective cohort study involving 664 cases of reported severe SAEs in Gyeonggi Province, South Korea, between February 2021 and March 2022. We evaluated patient-specific and external factors associated with mortality in patients experiencing severe SAEs. We also analyzed the frequency of death and case fatality rates (CFR). In terms of neurological comorbidities, the death group had a larger proportion of patients with dementia (15.3%) than the censored group (9.8%). However, the distribution of stroke, epilepsy, and Parkinson's disease did not differ between the two groups. Viral vector vaccines were associated with a lower risk of mortality than mRNA vaccines. There was a difference in the risk of mortality depending on the vaccination site. Age, but not the Charlson comorbidity index (CCI), was associated with a slightly increased risk of mortality. The most frequently reported etiologies of death after severe SAEs were circulatory and respiratory disorders, and a higher case fatality rate was recorded for neoplastic and respiratory disorders. Notably, neurological diseases had a low frequency of death (N=3) and the lowest CFR (13.6%). In conclusion, these findings should be taken into consideration when managing patients with severe SAEs following SARS-CoV-2 vaccination.

Effect of Brimonidine on Retinal Ganglion Cell Function by in vivo Calcium Imaging of Optic Nerve Crush in Mice

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Purpose: Glaucoma is a group of progressive and irreversible optic neuropathy that is caused by retinal ganglion cell (RGC) death. Currently, the only effective therapy to preserve RGC survival and visual function in glaucoma is to reduce intraocular pressure (IOP). Brimonidine, an alpha-2 adrenergic agonist, has been reported to provide optic nerve neuroprotection in experimental models of glaucoma. Here, we used recently developed noninvasive live cell Ca2+ imaging methods to measure RGC function and assess the putative neuroprotective properties of brimonidine in a mouse optic nerve crush (ONC) model.

Methods: To transduce RGCs in vivo, wild-type C57Bl/6j mice were treated with intravitreal AAV2-mSncg-jGCaMP7, a live-cell Ca2+ tracer. ONC was performed to induce traumatic optic neuropathy. The mice were treated with topical brimonidine or placebo three times daily for two weeks. The calcium signals of live-cell RGCs were measured with the Heidelberg cSLO system. Retinal thickness and IOP were examined at baseline, day three, seven, and 14 days after treatment. Retinas were then collected, and the RGCs counted after RBPMS immunostaining.

Results: ONC significantly decreased RGC number (236.7±9.6 vs 51.3±9.1, $p < 0.001$, Student's t-test): the survival rate at 14 days after ONC was 21% less than in controls. The amplitude of calcium signal and cell count of ON-RGCs determined by in vivo Ca2+ imaging also decreased significantly (234.8±27.3 vs 45.3±16.7, $p = 0.005$, Student's t-test). In vivo Ca2+ imaging revealed that many ON-center RGCs converted to OFF-center RGCs after ONC. Additionally, retinal thickness increased three days after treatment induced by ONC. However, there were no significant differences in IOP, retinal thickness between the eyes treated with brimonidine or placebo.

Conclusions: In the acute optic nerve injury model, brimonidine eye drops produced no significant effects on IOP, RGC survival, or GCL thickness. However, in vivo calcium imaging revealed that brimonidine changed the Ca2+ response to UV light in RGCs, inhibiting the conversion of ON-center RGCs to OFF-center RGCs.

Other

U.T.E.R.U.S: Utilization of a Three-D Model for Education and Research in Uterine Simulation

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Background: Intrauterine procedures such as IUD insertion and uterine aspiration can be challenging to teach due to limited models that simulate the sensation of instrumentation of the cervix and uterus. Effective training assets facilitating instruction of relevant intrauterine procedures remain broadly unavailable. This study aims to develop a low-cost, reusable, high-fidelity model using 3-D printing technology for learners to practice intrauterine procedures. The hypothesis to be tested is that a 3-D printed uterine model improves training outcomes compared to existing methods.

Methods: The workflow to create a 3-D uterine training model consists of three steps including Model Creation, Review, and Production. For Creation, an anonymized female cadaver was MRI scanned, and the uterus was identified and segmented (Slicer), providing a mesh model that was subjected to artistic edits (Maya software). The Review step was achieved by uploading the model for visualization (Sketchfab and Z-Space platforms) and final alterations. After export as an .stl file, the final Production step comprised 3-D printing using a Bambu X1C printer and Bambu Studio for support and infill settings.

Results: The model dimensions are approximately 87 mm by 177 mm by 32 mm. Printing time was 4 hours and 24 minutes with tree supports and 5% infill. 41.30 grams of Polylactic Acid filament with an estimated cost of 0.83 cents to print, assuming a cost of $20 per 1 kg of filament. A looped handle was included as a mounting point for hardness. Thermoplastic polyurethane filament was also attempted to produce a more malleable model, but will need revisions for stability during printing.

Discussion: The workflow delineated here facilitates the production of a lightweight, low-cost, and ease-of-use model that can be created with an inexpensive and widely available 3-D printer. Future work focuses on assessing the instructional effectiveness of the 3-D-printed uterus.

Other

Identifying Racial Differences in Clinical Presentation of Obstructive Sleep Apnea in Native Hawaiian and Pacific Islander Patients

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Background: Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder in the United States. Disparities in the severity of OSA have been identified in minority groups, but there has been little study of OSA in the Native Hawaiian and Pacific Islander (NHPI) population.

Methods: A retrospective chart review was conducted on all patients diagnosed with OSA via polysomnography between 1/1/13 and 6/1/23 at a single outpatient sleep medicine center. Pearson's Chi-squared and Fisher's exact tests were used to identify associations between apnea-hypopnea index (AHI) severity and clinical characteristics such as BMI. Logistic regression models were utilized to estimate associations between AHI severity and race.

Results: 91 NHPI and 129 White patients with OSA were included for analysis. Among NHPIs, 76.2% were obese, compared to 48.8% of Whites ($p<0.001$). Among NHPIs, 72.5% (n=66) had moderate or severe OSA, compared to 52.7% (n=68) of Whites ($p<0.001$). The odds of NHPIs being diagnosed with moderate or severe OSA were three times greater than Whites (adjusted odds ratio (AOR) = 3.01 [95% CI: 1.31, 7.23]).

Discussion: To our knowledge, this is the first study to compare the severity of OSA in NHPIs with another racial group. With NHPIs three times more likely to be diagnosed with moderate or severe OSA than Whites, there is a need for further research on early intervention and prevention of OSA in this population.

Alignment Outcomes Following Total Knee Arthroplasty Using Handheld Navigation Versus Conventional Instruments

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Knee alignment following total knee arthroplasty (TKA) is a key predictor of its success and longevity. Conventional instrumentation has demonstrated higher rates of mechanical axis (MA) malalignment compared to robotic or computer navigated surgery. The purpose of this study is to compare the alignment and early clinical outcomes between a handheld implant agnostic navigation system (HHNS) and conventional instrumentation.

This study included 117 patients who underwent single-stage bilateral TKA. The first knee was performed using the HHNS followed by the contralateral side using intramedullary and extramedullary alignment guides. Standing anteroposterior hip-to-ankle and standard knee radiographs were taken before and after surgery to assess overall alignment. Range of motion and clinical outcome scores were obtained preoperatively and six weeks, six months, and one year postoperatively.

Navigation produced better precision but similar accuracy regarding targeted alignment goals. The mean values for MA (0.71°, -0.32°, p=0.0086), tibial slope (1.17°, 0.61°, p=0.0165), and AP tibial component angle (0.52°, 0.03°, p=0.0149) were similar, but statistically favored navigation due to smaller ranges. More HHNS knees achieved target alignment compared to the conventional group, although not statistically significant. Navigated knees had a longer tourniquet time than conventional (36 minutes, 30 minutes, p<0.0005), however, both groups had similar clinical outcomes except at six months where the HHNS group had a greater Knee Society Score (p=0.0092).

Total knee arthroplasty performed with HHNS resulted in greater precision but comparable accuracy regarding alignment without a substantial time cost compared to conventional instruments. No clinically appreciable difference was found regarding patient reported outcomes.

Other

The Implications of Perioperative Halo Traction for Adult Patients with Severe Spinal Scoliosis- A Systematic Review and Meta Analysis

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Introduction: The goal of this review is to assess available literature and report on the efficacy of perioperative skeletal traction for surgical management of severe adult scoliosis and kyphoscoliosis.
Methods: A systematic review was performed using PUBMED/MEDLINE. Outcomes of interest included percent cobb angle correction, length of traction time, maximum weight of traction, and rates of complication. Inclusion criteria were studies assessing adult patients (≥18 years of age) with severe scoliosis or kyphoscoliosis (Cobb angle > 89°), measuring one or more outcomes of interest. Exclusion criteria were studies that evaluated pediatric patients, as well as case reports/case series and articles not written in English.

Results: A total of 244 articles were identified. After inclusion and exclusion criteria, 12 studies remained. The average patient age was 25.4 years. Four types of traction were employed throughout all studies: halo-gravity traction, halo-femoral traction and halo-pelvic traction were utilized pre-operatively while skull-femoral traction was employed intraoperatively and post-operatively.
Of the pre-operative studies, four demonstrated significant improvements in pulmonary function following halo traction ($p<0.05$). Additionally, all studies showed a significant curve correction. Traction duration ranged from 4-16 weeks with average body weight traction of 30-45%. Overall complication rates were 7%, with pin site infections being the most common. The intraoperative group also showed significant curve correction with no reported complications in their study. The postoperative group had a high rate of correction, however experienced more severe complications at higher rates. Figure 1 illustrates average curve correction and complication rates amongst different traction types.

Conclusion: Perioperative halo traction is a successful technique to enhance surgical management of adult scoliosis, with preoperative and intraoperative traction providing significant improvement in pulmonary function with low complication rates. Future research is recommended for better understanding on the role of perioperative traction in severe adult spinal deformity.

Retrospective Comparison of Long versus Short Ultrasound Guided Peripheral Catheters on Extravasation Outcome in Hospitalized Pediatric Patients

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Approximately 80% of all hospitalized patients receive peripheral intravenous catheter (PIV) placement to administer fluids, nutrition, and medications. PIV placement in pediatric patients is particularly challenging due to anatomical and behavioral factors. Ultrasound-guided PIV (USGPIV) has become widely accepted for its ability to facilitate deep vein visualization, reduce puncture frequency, and improve patient satisfaction. Previous studies have highlighted the importance of catheter length for USGPIV indwelling catheter survival, but no study has investigated this directly in hospitalized pediatric populations. This retrospective chart review study aimed to compare extravasation rates and indwelling survival durations between short (≤1.25") and long (≥1.75") USGPIV catheters in pediatric patients at a tertiary pediatric and perinatal facility in Hawai'i. A total of 3,933 USGPIV placements were analyzed after exclusions. The majority of USGPIVs were short catheters (91.36%) with a 9.70% extravasation rate. Long catheters were associated with a 4% increase in extravasation risk compared to short catheters ($p=0.020$) but had a significantly longer median lifespan (67.55 hours) than short catheters (36.58 hours) ($p<0.0001$). Statistical analyses included chi-square tests and Cox proportional hazards regression, adjusting for demographic variables. Importantly, when factoring in demographic variables into the survival analysis, no significant difference in lifespan and extravasation risk was found between short and long catheters. However, the trend suggests that long catheters are less likely to infiltrate over longer periods of time. The findings suggest that long USGPIV catheters, despite a slight increase in extravasation risk, provide longer indwelling survival, reducing the frequency of PIV insertions and minimizing discomfort and complications in hospitalized children. Future prospective studies are recommended to further explore these outcomes.

BMI and Associated Health Disparities in Parkinson's Disease Risk and Progression

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Background: Previous studies have shown varied results regarding the relationship between body mass index (BMI) and the severity of Parkinson Disease (PD). While some research suggests that higher BMI may increase the risk of developing PD, other studies indicate that higher BMI might reduce disease severity and improve survival prognosis.This study aims to examine the relationship between BMI and PD severity and progression in a diverse patient population in Hawaii, while also considering factors that may influence BMI.

Method: A single-center, retrospective chart review was conducted at Hawaii Pacific Neuroscience from 2017 to 2024 on patients diagnosed with PD. A variety of variables were analyzed including ethnicity, gender, marital status, comorbidities, BMI, age at diagnosis, and LEDD scores. A Pearson's Chi-squared test and Fisher's exact test were used for statistical analyses and were performed using R software, version 4.4.1.

Results: Of the 317 patients (14 underweight, 147 healthy, 95 overweight, and 61 obese), obese and overweight patients had the earliest age of onset (66 and 69, respectively), compared to those that were underweight or healthy (71). Underweight and obese patients had a greater change in LEDD score over time. Patients with higher BMIs were more likely to be NHPIs, single, and have diabetes mellitus (DM) compared to those who were underweight or healthy.

Conclusion: PD patients with a higher BMI were diagnosed at a younger age, while those at both extremes of the BMI spectrum (underweight and obese) exhibited more rapid disease progression. Conversely, patients with healthy BMI had a lower risk of PD progression. This study suggests that maintaining a healthy BMI is an important factor in PD risk and progression. Marital status, and racial and ethnic disparities may impact BMI in PD patients.

Sleep

CPAP Therapy Compliance in Obstructive Sleep Apnea Patients in Hawai'i

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Introduction: Obstructive Sleep Apnea (OSA) is a common sleep disorder which affects over 900 million adults globally[1]. Specifically, the impact and prevalence of OSA in Native Hawaiians and Pacific Islanders (NHPI) are understudied. If left untreated, OSA can result in serious health complications, including cardiovascular disease, diabetes, and cognitive impairment, significantly reducing both quality and longevity of life. In comparison to other racial/ethnic groups, NHPI is disproportionately impacted by diseases, socioeconomic barriers, and decreased life expectancy[2]. However, previous research has shown that NHPI has the lowest rates of healthy sleep duration compared to their counterparts3-4. Additionally, OSA was found to be more severe in males with higher obesity4.

Objectives: This study investigates and evaluates CPAP adherence and compliance across Hawaii's diverse ethnocultural landscape, with a particular focus on identifying variations in OSA characteristics and adherence patterns among these groups. In addition, it seeks to evaluate any socio-behavioral factors that may impact adherence and compliance.

Methods: A retrospective chart review was conducted at Hawaii Pacific Neuroscience (HPN) for patients diagnosed with OSA (ICD10: G47.33) between June 2022 - June 2024. A total of 1,277 patients were identified. Patients were excluded if they lacked information on race/ethnicity, PAP therapy compliance, continuous PAP therapy treatment, unclassified severity of OSA, and/or if their diagnosis fell outside the specified time frame. The final analysis included 424 patients, with data collected on 15 variables, including sex, age, zip code, insurance, race/ethnicity, social history, cardiac history, BMI, weight, height, OSA severity, AHI score, type of PAP therapy, and compliance of PAP therapy.

Results: About 72.2% (n=306) of patients were males and 27.8% (n=118) were females. Majority of patients were identified as Asian (34.3%, n=133) followed by 33.2% (n=129) identified as NHPI, 25.8% (n=100) White, and 6.7% (n=26) Other Races. About 43.7% (n=185) patients had private insurance and 34.3% (n=145) had public insurance. CPAP adherence was positively associated with age (P=.009), insurance type (P=.015), and OSA severity (p<0.001). The positive association between CPAP adherence and age showed that patients with very good/excellent CPAP adherence were older with an average age of 58.3 than those with suboptimal/moderate CPAP adherence with an average age of 54.6. Only about 52.7% of patients with other insurance types (self-pay and military) had very good/excellent CPAP adherence compared to patients with private insurance (68%) and with public insurance (70%). When comparing AHI scores by racial groups, NHPI has a significantly higher average initial AHI score (43.7) than other races (P=.001). The average change in AHI scores showed a larger decrease among patients with CPAP compliance. Among all patients with CPAP compliance, NHPI patients showed a larger decrease in AHI scores compared to patients of other races.

Conclusions/Discussion: Primarily, our findings reaffirm that NHPI populations exhibit higher initial AHI levels, consistent with prior research conducted in Utah, based on initial AHI scores. By replicating these results in Hawaii, our study enhances the validity of the observed characteristics among the NHPI population, demonstrating that these patterns hold across different states and environments. Additionally, our results emphasize the importance of promoting CPAP adherence among younger patients and highlight the potential role of insurance coverage in facilitating greater adherence to PAP therapy. The observed relationship between the OSA severity and adherence to PAP therapy suggests that patients with more severe symptoms are more likely to adhere to treatment, highlighting the need for an increased emphasis on education and resources for patients with mild to moderate OSA. Understanding the factors that contribute to adherence can help develop targeted strategies to improve and implement PAP therapy adherence within Hawaii's minority-majority population. These insights may also provide valuable guidance for improving PAP therapy adherence in other diverse populations.

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Sleep

Prevalence and Correlates of Obstructive Sleep Apnea in Parkinson's Disease: A Logistic Regression Analysis

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This study investigates the prevalence of Obstructive Sleep Apnea (OSA) among patients with Parkinson's Disease (PD) and examines correlations with various medical, demographic, and behavioral factors. OSA is a sleep disorder characterized by repeated interruptions in breathing during sleep, leading to fragmented sleep and reduced oxygen levels in the blood [1]. These disturbances are associated with numerous adverse health outcomes, including cardiovascular problems, cognitive decline, and an overall diminished quality of life [2].
The connection between OSA and PD has garnered increasing attention in recent years. OSA is significantly more prevalent among PD patients, affecting 20% to 70% of this population compared to 2% to 14% in the general population [2]. Interestingly, OSA may not only co-occur with PD but could also be a precursor to it. Emerging evidence suggests that individuals diagnosed with OSA are at a higher risk of developing PD within five years, indicating that OSA may play a role in the pathophysiology of PD or serve as an early warning sign [3].

In our study, we analyzed data from 270 patients with confirmed PD, some of whom also had OSA. Our analysis included variables such as age, insurance status, body mass index (BMI), sex, ethnicity, sleeping behaviors (including insomnia and REM sleep behavior disorder), smoking history, hypertension, and the use of PD medications. We employed logistic regression to identify which of these predictors were significantly associated with the presence of OSA in PD patients. Table 1 presents the results, focusing on the nine factors with the smallest p-values from the logistic regression analysis.

Term	Coefficient	Standard Error	P-Value	VIF
Constant	-5.120	1.080	0.000	
BMI	0.111	0.039	0.004	1.10
Sex	-1.371	0.482	0.004	1.06
White	0.979	0.418	0.019	1.14
Pacific Islander	1.334	0.727	0.067	1.22
Insomnia	0.717	0.492	0.145	1.09
REM Sleep Behavior Disorder	0.564	0.541	0.297	1.08
Native Hawaiian	-0.771	0.835	0.356	1.10
Former Smoker	0.321	0.489	0.512	1.07
Hypertension	0.255	0.412	0.535	1.09

Table 1. Logistic regression results for BOA with nine predictors.
As shown in Table 1, our findings revealed that BMI was a particularly strong predictor of OSA, with higher BMI correlating significantly with increased OSA prevalence (p-value: 0.004). This reinforces the well-established link between obesity and OSA, likely due to the increased fatty deposits around the upper airway that can obstruct breathing during sleep. Additionally, sex was found to be a significant factor (p-value: 0.004), with males more prone to OSA than females, consistent with existing literature on OSA in the general population [4]. Ethnicity also emerged as a variable of interest, with White (p-value: 0.019) and Pacific Islander (p-value: 0.067) patients showing near-significant associations with OSA. These findings suggest that ethnic background may influence the risk of OSA in PD patients, potentially due to genetic factors, differences in healthcare access, or variations in disease expression. However, further research is needed to confirm these trends and understand the underlying causes.

Interestingly, predictors such as insomnia, REM sleep behavior disorder, former smoking status, and hypertension did not show significant associations with OSA in our cohort. This suggests that while these factors are important in the general context of PD and sleep disorders, their role in predicting OSA specifically may be less direct or overshadowed by stronger predictors like BMI and sex.
The implications of these findings are significant. Identifying PD patients at high risk for OSA can lead to earlier interventions, which may not only improve sleep quality but also potentially slow the progression of PD symptoms. Given the bidirectional relationship between sleep and neurodegeneration, effective management of OSA in PD patients could enhance overall treatment outcomes, improving both motor and non-motor symptoms. Future research should explore the mechanistic links between OSA and PD, particularly the role that OSA might play in exacerbating neurodegeneration. Longitudinal studies could help determine whether treating OSA can delay the onset or progression of PD.

In conclusion, this study underscores the importance of recognizing and addressing OSA in patients with Parkinson's Disease. With BMI and sex identified as key predictors, targeted screening and early intervention strategies could play a crucial role in improving the quality of life and overall outcomes for PD patients suffering from OSA. Additionally, our findings suggest that demographic factors, particularly ethnicity, may influence the risk of developing OSA in PD patients. The significant and near-significant associations observed in White and Pacific Islander patients, respectively, highlight the need for further research into how genetic predispositions, cultural differences, and healthcare disparities contribute to OSA risk.

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Evaluating Risk Factors for Back Pain in Native Hawaiian and Other Pacific Islanders

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Introduction: Back pain is a widely prevalent diagnosis in which previous research has focused on how its "multidimensional" risk factors change based on race. However, no research has focused on risk factors for back pain within the Native Hawaiian and other Pacific Islander (NHOPI) populations.

Objective: Uncover potential risk factors for back pain in NHOPI patients and explore how known risk factors have differing impact on NHOPI patients.
Methods: Retrospective chart review of 230 patients at the Spine and Pain Management Center at Hawaii Pacific Neuroscience, an outpatient neuroscience clinic. Demographic data, presentation at time of diagnosis, past medical history, treatment plan, health comorbidities, and diagnosis status were recorded.

Results: 46% of NHOPI patients reported uncategorized health comorbidities in comparison to 30% of non-NHOPI (p=0.012). 36% of non-NHOPI patients reported no health comorbidities compared to 19% of NHOPI patients (p=0.005). A parallel relationship existed for neurologic comorbidities. 23% of NHOPI patients were smokers as opposed to 8.4% of non-NHOPI patients (p=0.002). A greater proportion of non-NHOPI patients were categorized as Healthy Weight (p=0.008) and a greater proportion of NHOPI patients were categorized as Obese II (p=0.042).

Conclusions: Research has shown that smoking could negatively impact patients' pain experiences via decreased efficacy of pain medications. Adding this to the uncovered relationships with comorbidities, obesity, and smoking status suggests that there may be an emphasized social aspect to NHOPI patients' risk factors for back pain, presenting potential additional avenues for prevention and treatment of back pain.

Stroke

Examining Cerebral Small Vessel Disease (CSVD) in Native Hawaiian/Pacific Islander (NHPI) Stroke Patients: A Pilot Study

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Objective: To examine the severity of CSVD and associated risk factors in NHPI populations compared to other ethnic groups in Hawaii.

Introduction: Cerebral small vessel disease (CSVD) refers broadly to intracranial small vessel disease from various pathological processes including arteriolosclerosis and amyloid angiopathy (Li et al., 2018). It accounts for 25-30% of strokes in the United States and is a leading cause of age-related cognitive disability (Li et al., 2018). Current literature shows that NHPI populations are more than four times as likely to suffer a stroke than non-Hispanic white adults (Stroke and Native Hawaiians/Pacific Islanders, n.d.). There is a clear correlation between CSVD and stroke, but the existence of underlying differences in the prevalence of CSVD in NHPI populations as compared to other races has yet to be explored.

Methods: This is a single center, retrospective study of patients seen at Hawaii Pacific Neuroscience with ICD-10 codes identifying cerebral infarction. Presence and degree of CSVD was determined by analysis of MRI records with grading by the Fazekas scale and Global Cortical Atrophy (GCA) scale. Demographic information and other known risk factors for stroke/CVSD were also collected.

Results: Of 265 total patients, 56 were White, 73 were NHPIs, and 69 were Asians. NHPI patients experienced an earlier onset of strokes compared to other races ($p=0.002$), associated risk factors including being overweight (BMI > 25, $p=0.008$) and having type II diabetes mellitus ($p=0.032$). Elevated BMI was found to be a more significant contributing factor when comparing NHPI patients to Asian patients ($p.Chisq=0.004$). No significant differences were found in the severity of deep white matter lesions among the different races ($p=0.3$). However, there was a significant difference in GCA scores ($p<0.001$). Asians had significantly higher GCA scores than other races ($p=0.028$), especially compared to NHPI patients, and were also older at the time of stroke ($p=0.002$).
Conclusions: In this study, NHPI patients had earlier onset of strokes but no increased markers of CSVD, as compared to other racial groups. In NHPI populations, obesity and diabetes are significant risk factors for stroke compared to their counterparts. Due to small sample size, future studies are needed to confirm these findings.

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A Clever Stroke Mimic: Thrombotic Thrombocytopenic Purpura Without Schistocytes

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Introduction:

Acquired thrombotic thrombocytopenic purpura (TTP) is a rare autoimmune platelet disorder in which autoantibodies directed toward the ADAMTS13 protease leads to abnormally large uncleaved multimers of von Willebrand-factor that are hyper-adhesive to platelets, causing microthrombi formation and rapid thrombocytopenia. Since the development of therapies for TTP, survival has improved from merely 10% in historical untreated cohorts (Amorosi), to contemporary rates of nearly 90% (Vesely). However, treatment of this disease necessitates a prompt and accurate diagnosis, which can be difficult given an incidence of 1 new case/ million people, and approximately 30% of childhood and adolescent cases initially going misdiagnosed (Joly). Recognition of the disease is often delayed, as patients often present with acute neurologic deficits immediately worrisome for stroke. Furthermore, consideration for TTP is often prompted by the presence of schistocytes on peripheral smear, which in rare cases may be absent.

Case presentation:

A 79 year old female without significant past medical history presented from an outside hospital with acute onset aphasia and right sided numbness. On arrival, she complained of headache for the preceding 2 days, with difficulty naming objects and finding words. Her numbness initially originated from the face and traveled down the right upper extremity, however resolved on arrival. A neurology consultation was initiated due to concern for acute stroke. On examination she was noted to be afebrile with a blood pressure of 149/91 mmHg, demonstrated mild aphasia with loss of speech fluency, 5/5 strength and intact sensation on the bilateral upper and lower extremities, and ecchymosis on the lateral aspect of the right knee with areas in a purpuric distribution. Her National Institute of Health Stroke Score was 1. While perfusion computed tomography and magnetic resonance imaging of the head failed to demonstrate any acute intracranial abnormalities or signs of stroke, her blood work revealed a platelet count of 35 x103cells/uL, a hemoglobin of 7.8 g/dL, a total bilirubin of 2.4 mg/dL, and a lactate dehydrogenase of 876 IU/L, and a haptoglobin <10 mg/dL. A peripheral smear reviewed by an attending pathologist did not reveal significant schistocytes, and the patient had no history of thrombotic microangiopathy in the past. However, her overall clinical presentation remained suspicious for TTP, supported by a PLASMIC score of 5. High dose corticosteroids and plasmapheresis were ordered within 5 hours of admission. An ADAMTS13 was sent, and later returned with an activity level of <1%, with an elevated ADAMTS13 antibody level of 51U/mL, and a positive ADAMTS13 inhibitor, confirming the diagnosis of acquired TTP. Her neurologic symptoms did not return, and she was discharged within 6 days of hospital admission following 5 cycles of plasmapheresis. Her thrombocytopenia corrected to 336 x103cells/uL on the day of discharge. Therapy with Calpacizumab was briefly considered but deemed unnecessary following her response to plasmapheresis. She was discharged with a tapering dose of steroids and outpatient follow up with hematology, without any residual neurologic deficits.

Discussion:

TTP has rarely been documented in the literature as presenting without schistocytes, and studies have been confined to case reports and small case series no larger than 10 patients (Decker). As few as 30% of schistocyte-negative cases present during the de-novo diagnosis of TTP, instead having been more frequently documented in patients with already established TTP. In thrombocytopenic patients presenting with acute neurologic deficits and normal neuroimaging, TTP should be strongly considered, even in the absence of schistocytes. When sufficient suspicion for TTP is present, emergent initiation of immunosuppression and plasma exchange is critical in avoiding morbidity and mortality, even while confirmatory testing is still pending.

MS & Neuroimmunology

Cree/Danielle Harvey – TG Therapuetics

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Poster Title: Title: Five years of Ublituximab in relapsing multiple sclerosis: additional results from open-label extension of ULTIMATE I and II studies

Title: Five years of Ublituximab in relapsing multiple sclerosis: additional results from open-label extension of ULTIMATE I and II studies

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Introduction: In ULTIMATE I and II studies, ublituximab (UBL) demonstrated significant reduction in disease activity vs. teriflunomide (TER) over 2 years. Results from additional 3 years of open-label extension (OLE) are presented.

Objectives/Aims: To evaluate the long-term clinical efficacy and safety of ublituximab.

Methods: After 2 years of randomized, active-controlled, double-blind period (DBP), RMS patients, either continued UBL treatment, or switched from TER to UBL (TER-UBL). Adjusted annualized relapse rates (ARR) were analyzed using generalized estimating equations and 24-week confirmed disability progression (CDP 24), confirmed disability improvement (CDI 24), were estimated by Kaplan-Meier method and Cox regression model.

Results: Upon completion of DBP, over 85% of MS patients entered OLE (UBL, N=422; TER-UBL,

N=429), and over 70% stayed on UBL treatment at OLE Year 3. Patients switching from TER to UBL experienced significant reduction in ARR at 1 year post switch [58.4%; 0.182 vs 0.076; RR (95% CI): 0.416 (0.289, 0.599), P<0.0001] which continued to drop to 0.048 and 0.045 for OLE Years 2 and 3, respectively. Patients continuing UBL saw further reductions in ARR [0.053, 0.032, and 0.020 for OLE Years 1, 2, and 3 respectively]. CDP 24 at year 5 from DBP was 8.0% in UBL vs 14.3% in TER-UBL patients [HR (95% CI): 0.612 (0.414, 0.904); P=0.0126]. CDI 24 at year 5 from DBP was 17.0% in UBL vs 12.2% in TER-UBL patients [HR

(95% CI): 1.472 (1.048, 2.067); P=0.0249]. IgG and IgM levels remained stable and above LLN for patients on continuous UBL treatment for 5 years [mean (SD), 8.1 (2.23) g/L and 0.7 (0.66) g/L, respectively]. Overall, adverse events were consistent with established safety profile from pivotal trials.

Conclusions: UBL treatment for 5 years provided MS patients with sustained clinical benefit versus patients switching after 2 years of TER, with ARR reflecting 1 relapse every 50 years of treatment, and significant benefits on disability progression. Results confirm early initiation of high-efficacy treatment confers long-term benefits.

Disclosures:

Dr. Cree is a consultant for Alexion, Atara, Autobahn, Avotres, Biogen, EMD Serono, Gossamer Bio, Horizon, Neuron23, Novartis, Sanofi, TG Therapeutics and Therini; and receives grant/research support from Genentech; and is also on the advisory board for Autobahn.

Dr. Hartung has received honoraria for consulting and speaking at symposia from Bayer Pharma AG, Biogen Idec, Genzyme, Merck Serono, Novartis, Roche, Teva, and Sanofi-Aventis, with approval by the rector of Heinrich-Heine University.

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Dr. Wray has received compensation for serving on a Scientific Advisory or Data Safety Monitoring board for Biogen, Bristol Myers Squibb/Celgene, EMD Serono, Novartis, Roche/Genentech, and Sanofi/Genzyme; and has received compensation for serving on a Speakers Bureau for Biogen, Bristol Myers Squibb, EMD Serono, Roche/Genentech, and Sanofi/Genzyme. The institution of Dr. Wray has received research support from Biogen, Hope, Bristol Myers Squibb/Celgene, Novartis, Roche/Genentech, Sanofi/Genzyme, and TG Therapeutics.

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