Washington University
School of Medicine
Department of Neurology

Neurology Academic Symposium

Friday, May 26, 2023
7:30am – 9:00am

Farrell Learning and Teaching Center ~ Atrium

Poster presentations will begin at 7:30am

Research awards will be presented at 8:45am

We encourage everyone to attend this important event.

Ahmadi, Saumel and Mwangi, Martin

Hydrogel electrodes for neonatal long term EEG

Saumel Ahmadi, Martin Mwangi, Keri Wallace, Emily Walsh, Melanie Sewkarran, Paige Ardnt, Lauren Langford, Lydia Goodyear, Carly Wheeler, Zachary Vesoulis, John Zempel

Neonatal seizures are the most common neurologic emergency in the NICU, affecting upto 150 patients per 100,000 live births. Long term EEG is necessary in the high-risk neonatal population given that only 10% seizures might have clinical correlate seen by hospital staff, and the risk of electroclinical dissociation after treatment with GABAnergic agents. It is known that up to 8.5% neonates can suffer from electrode injuries related to long term EEG monitoring. Additionally, conductive hydrogels have increasingly being used because of their favorable tissue like mechanical properties, with reasonably good electrical properties. Hence we hypothesized using hydrogel electrodes to potentially reduce neonatal electrode related injuries. We first analyzed the impact of gestational age, birth weight, length of EEG on stages of injuries, and found no impact of these variables on the stages of injury. Interestingly, we also found the frontal regions to be impacted the most by electrode related injury, and hence we trialed hydrogel electrodes in mainly the frontal and occipital regions and found a trend towards decreased electrode related injuries with these hydrogel electrodes. Taken together hydrogel electrodes give reliable EEG recordings and can potentially decrease neonatal electrode related injuries.

Assael, Wendy

A Case of Multiple Cranial Neuropathies

Wendy Assael, MD
Neurology Residency Program, Washington University in St. Louis

Introduction: Patients presenting with multiple cranial neuropathies are relatively common. The differential is broad, including mass lesions, vascular infarctions, infections with bacterial, viral, fungal, and parasitic organisms, and inflammatory disorders.

Case Presentation: A 68-year-old woman presented with diplopia. Over the course of 2 months, she successively developed cranial nerve deficits. This started with decreased taste and decreased hearing in the left ear, followed by left face weakness, then double vision. On review of systems, she had chills and 5 pounds of weight loss over the past 3-4 months. Exam showed limited right eye abduction, weakness of left eyelid closure, and sensorineural hearing loss of the left ear. Serial CSF testing showed persistent pleocytosis with lymphocytic predominance, progressively worsening hypoglycorrhachia, elevated protein, 7 unique oligoclonal bands, and negative serial flow cytometry and cytology. Differential diagnosis included infections (Lyme, Syphilis, TB, HSV, EBV, CMV, HIV, Cryptococcosis, and Histoplasmosis), inflammatory conditions (sarcoidosis, connective tissue disease, vasculitis), neoplasm (carcinomatous meningitis due to lymphoma or metastasis, meningioma, schwannoma) or vascular abnormality (aneurysm). Infectious testing including TSpot, HIV, RPR, Serum treponemal Ab, Crypto, bacterial blood culture, Fungal blood culture, AFB culture, HSV, CMV, VZV, Lyme, Histoplasmosis, and Blastomycosis testing was negative. Autoimmune workup including ANA, ANCA, RF, and ENA were negative. Initial MRI after onset of hearing loss and facial weakness showed a mass in the left cerebellopontine angle. Follow up MRI after development of diplopia was significant for nodular leptomeningeal enhancement of the right frontal lobe, hypothalamus, left CN V, left CN VII, and left CN VIII. She then underwent brain biopsy, and pathology resulted with Large B-cell Lymphoma, confirming diagnosis of primary CNS lymphoma.

Discussion: This case demonstrates a case of primary CNS lymphoma causing multiple cranial neuropathies.

Bashardost, Leeda

Abstract to Follow

Butler, Michael

Analysis of medical student responses during standardized patient encounters

Abstract: Medical student clinical education is challenging, particularly given the multiple subspecialty areas within medicine and surgery as well as the ever-expanding and increasingly detailed level of knowledge and information within each of these arenas. Standard approaches to medical education have remained relatively stagnant, and in order to better prepare medical students for clinical practice and ensure they feel confident in their assessment and diagnostic skills, clinical and medical student education should continuously evolve to mirror the progress of medicine as a whole. Neurology training for medical students presents a unique challenge given the reliance on detailed histories and correct implementation and interpretation of exam maneuvers, especially given the need to adapt and expand upon specific examination techniques depending on the clinical scenario. Given the rapidly expanding and changing field of neurology with greater recognition of neurologic disease within the medical community, it is imperative that medical student training in neurology evolve and adapt to ensure the next generation of physicians feel comfortable and above all capable of appropriately evaluating and diagnosing neurologic disease in any field of medicine or surgery. Standardized patients represent a crucial assessment and evaluation tool in medical student training and education. Critically analyzing the history gathering, diagnostic reasoning, and decision-making rationale in the context of standardized patient encounters will provide medical educators within neurology (e.g., faculty, residents, fellows, etc.) with invaluable data with which to better train and coach medical students as they progress through their training.

De Carvalho Paixao, Luis

Abstract to Follow

Everett, Will

A Challenging Case of Intravascular B-Cell Lymphoma with Late-Presenting Strokes

A 64 year old man with rheumatoid arthritis presented with new onset headache, gait instability, and confusion. He was treated for migraine and discharged.
Over the following 6 weeks, he had multiple presentations for worsening headache, vision changes, and altered mental status. He underwent broad CSF and serum workup for inflammatory and infectious etiologies which were unrevealing. His imaging showed nonspecific T2/FLAIR abnormalities and changes in the posterior cortex that were thought to be possible artifacts. During this time he was diagnosed with PRES due to methotrexate and idiopathic intracranial hypertension.

Two months after initial presentation, the patient began to have stroke-like episodes with slurred speech and facial weakness. MRI now showed multifocal FLAIR hyperintensities with susceptibility artifact without diffusion restriction or contrast enhancement. CSF protein trended to a marked elevation (150->186->238). Suspicion was high for cerebral amyloid angiopathy-related inflammation versus amyloid beta-related angiitis and the patient was treated with high dose steroids with improvement.

Two weeks later, MRI showed increase in FLAIR abnormalities with susceptibility and now areas of leptomeningeal enhancement. He suffered a left PICA occlusion after angiography requiring transfer to ICU. Brain biopsy was performed. The patient's mental status continued to be poor, and the patient's family elected to transition to comfort care. The biopsy showed vascular spaces distended with accumulated atypical tumor cells with staining pattern consistent with large B-cell lymphoma.

This case illustrates the difficulty of diagnosing intravascular lymphoma. The patient had several typical symptoms for this disease that are however quite nonspecific. Due to the late presentation of stroke, intravascular pathology was not considered until late in the disease course.

Ferguson, Katie

Anti-Seizure Medication Administration in the Emergency Department

Patients with epilepsy on anti-seizure medications (ASMs) often do not receive their maintenance medications when they are in the SLCH Emergency Department (ED). We evaluated patients with epilepsy on at least one ASM who presented to the SLCH ED and were admitted to the neurology service. In our initial evaluation, 46% of patients who were due for their ASMs while in the ED did not receive their ASMs. Our aim is to increase the percentage of patients admitted to the neurology inpatient service who receive their ASMs on time in the ED by 20% in 3 months. We are instituting an Epic advisory for all patients who are prescribed an ASM in their medication list. This advisory will alert the provider that this patient is prescribed an ASM and to please ask the family if they are due for the medication.

Gilbert, Laura A

Identifying upper extremity features of dystonia in people with spastic cerebral palsy

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1 Toni S Pearson,2 Bhooma R Aravamuthan1

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Objective: To identify expert-cited features of upper extremity dystonia in people with cerebral palsy (CP).

Background: Dystonia in CP is debilitating yet underdiagnosed, particularly when co-existent with spasticity. Subjective expert consensus remains the diagnostic gold standard, but the specific features leading experts to make a dystonia diagnosis remain unclear.
Design/Methods: To determine expert-cited features of dystonia, we performed a conventional content analysis of consensus-building discussions between three pediatric movement disorder specialists as they evaluated upper extremity dystonia severity in 26 neurologic exam videos of seated subjects with CP and spasticity.

Results: 45.8% of discussion codes related to body region, actions, movement features, laterality, or examination features (with the remainder on severity score deliberation and dystonia diagnostic difficulty). Experts cited involvement of the "shoulder" significantly more frequently as dystonia severity increased ($p<0.005$, chi-squared test) as opposed to the "hand" which was cited less frequently ($p<0.0005$, chi-squared test). "Mirror movements" were cited significantly more frequently in videos with no or mild dystonia ($p<0.005$, chi-squared test). Though "unilateral" was the top cited laterality code (72%) and "variability over time" was the top cited movement feature code (34%), neither were significantly associated with dystonia severity ($p=0.09$, $p=0.052$ respectively, chi-squared test), in contrast to our previous lower extremity dystonia analysis findings. In videos where diagnostic consensus was reached only after consensus-building discussion (4/26 videos), the repetitive hand "open/close" exam maneuver was the top cited exam maneuver (28%) and was referred to significantly more frequently than for videos where consensus was reached prior to any discussion ($p<0.005$).

Conclusion: Experts use distinct movement features to diagnose upper extremity dystonia in people with CP and spasticity. Efforts like this can be used to target examinations and codify the defining features of dystonia in people with CP, thus helping to facilitate dystonia diagnosis.

Gilman, Carley

ATP1A3-related epilepsy with response to ketogenic diet: A case report and review

Abstract: ATP1A3 is a gene that encodes for sodium/potassium ATPase pump with high expression in GABAergic neuronal cells, cochlear membrane and some cardiac myocytes. Classic variants in this gene have been associated with alternating hemiplegia of childhood, rapid-onset dystonia-parkinsonism and CAPOS syndrome (cerebellar ataxia, areflexia, pes cavus, optic atrophy and sensorineural hearing loss)1. Here we describe an infant with a severe developmental and epileptic encephalopathy (DEE), a rare ATP1A3-related phenotype, his profound clinical response to the ketogenic diet (KGD), and a proposed therapeutic mechanism.

Herman, Collin

An EMU/NNICU communication model to benefit interdisciplinary education and team satisfaction

Collin Herman MD, Jonathan Williams MD, Salah Keyrouz MD

Purpose: Electrographic seizures are frequently encountered in the neuro ICU (NNICU). Delays in diagnosis and treatment can result in prolonged hospitalization and worse clinical outcomes. Diagnosis is based on clinical suspicion by treating intensivists and electroencephalogram (EEG) interpretation by epileptologists or neurophysiologists. Our project aims to establish a model for communication between the epilepsy monitoring unit (EMU) and NNICU as a fellow-centered education and quality improvement initiative.

Methods: We prospectively implemented a communication process for EMU/NNICU sign-out from April 1, 2022 to September 30, 2022. The intervention consisted of a virtual or in-person EEG review of all continuous video EEGs between the EMU and NNICU teams at a set time each day. Reviewed items included duration of monitoring, EEG background, epileptiform discharge patterns, seizure frequency/duration, and proposed changes to treatment regimen. A ten-question survey assessing satisfaction, educational value, and comfort level with EEG interpretation was distributed to the NNICU faculty and fellows prior to the intervention period. Post-intervention surveys were distributed at one, two, and six months.

Results: Ten (62.5%) of the NNICU faculty/fellows participated in the surveys. There was an increasing trend towards positivity in all survey questions as the intervention period progressed. Team satisfaction (90% very satisfied/satisfied from 43.3% pre-intervention) and educational value (90% very satisfied/satisfied from 30% pre-intervention) both showed significant improvement post-intervention, while comfort with EEG interpretation/terminology showed a more modest improvement (63.3% very comfortable/comfortable from 56.7% pre-intervention).

Conclusion: Our communication model was feasible and effective based on survey results. Future projects may directly evaluate patient-centered outcomes using this communication model.

Heuermann, Robert "BJ"

Dopaminergic regulation of pain processing in the central amygdala

Pain is one of the most common nonmotor symptoms in Parkinson disease (PD), but is often under-recognized and under-treated. In addition to musculoskeletal sources of pain due to dystonia and abnormal posture, there is evidence of aberrant central pain processing in both human studies and animal models of PD. To investigate the potential mechanisms behind this central sensitization, we used the TRAP mouse line (Transient Recombination in Activated Populations) to fluorescently label neurons activated by a painful stimulus. Labeled cells were identified in several brain regions including the central amygdala (CeA), an important node for pain processing. Applying dopamine reduced excitability of labeled CeA neurons in patch-clamp recordings. In preliminary behavioral experiments, ablating dopamine terminals in the CeA using 6-hydroxydopamine led to increased nocifensive behavior in the formalin test. These studies may lead to better understanding and treatment of pain in PD.

Jaafar, Nesreen

Carbidopa/levodopa for Spasticity in Amyotrophic Lateral Sclerosis and Primary Lateral Sclerosis

Abstract:

Background: Spasticity is a disabling symptom in patients with amyotrophic lateral sclerosis (ALS) and primary lateral sclerosis (PLS). There is a lack of effective treatments in management of spasticity in ALS and PLS. Motivated by the success of dopaminergic drugs in treating rigidity in Parkinson's disease, and by the improvement of spasticity with carbidopa-levodopa in children with spastic quadriplegia and cerebral palsy, along with positive results from unpublished data at our institution, this study was designed to evaluate efficacy of carbidopa-levodopa in treating spasticity in ALS and PLS patients.

Hypothesis: Carbidopalevodopa can improve spasticity in ALS and PLS using patients' reported outcome measure and objective measures.

Methods/Design: We conducted an interventional, placebo-controlled, double-blind randomized crossover clinical trial at Washington University in Saint Louis. We included 16 consecutive ALS and PLS patients with spasticity seen at the Neuromuscular clinic. Participants were randomized to receive either placebo or carbidopa-levodopa for a period of three weeks in a AB/BA treatment sequence. The dose of carbidopa-levodopa used was 25/100 mg three times daily. Spasticity, muscle spasm, and pain were assessed via a subjective numerical rating scale and objective measures were assessed using modified Ashworth scale as the primary outcome along with MRC strength scale, Timed Up and Go, 10 meter walk test and the 9-Hole Peg Test.

Results: A total of 16 subjects were screened for eligibility, and 15 subjects were randomly assigned to receive carbidopa-levodopa or placebo (average age 56.81, SD 12.33; ALS 9, 56.3%, PLS 7, 43.7%. The study did not find evidence that carbidopa-levodopa was effective in the treatment of spasticity. Primary outcome meet did not reach statistical significance. The mean total modified Ashworth score for the treatment arm was 8.67 (95% CI: 6.94, 10.40) and 8.06 (6.31, 9.80) for the placebo arm (difference, p = 0.2926). Secondary outcomes did not differ significantly between treatment arms. The sequence of treatment did not affect the results.

Conclusion: The present study did not show effectiveness of Carbidopa-Levodopa in treating spasticity in ALS and PLS patients when comparing it to placebo. However, our study is limited by its small number of patients and the severity of their spasticity.

Khasawneh, Mohammad

Carotid Webs: Exploring the Pathology and Implications for Acute Ischemic Stroke

Background: Carotid webs are rare vascular anomalies characterized by fibromuscular dysplasia of the carotid artery. These webs typically appear as thin shelf-like intraluminal projections within the carotid artery, causing turbulent blood flow and subsequent thrombus formation. Carotid webs have been reported to occur in approximately 0.9-1.5% of patients with ischemic stroke [1][2]. Despite their low frequency, carotid webs are increasingly recognized as an important cause of acute ischemic stroke, particularly in young and middle-aged individuals [2].

Case Presentation: We present the case of a 43-year-old female with a previous medical history of hypertension and relapsing-remitting multiple sclerosis, who presented with right-sided hemiplegia and aphasia. CT head imaging revealed hypoattenuation in the distribution of the left middle cerebral artery (MCA). The patient was not eligible for thrombolytics due to a high Alberta Stroke Program Early CT Score (ASPECTS). Computed tomography angiography (CTA) demonstrated left M1 occlusion. Angiography revealed occlusion of the left terminal internal carotid artery (ICA) and the presence of a left ICA carotid web. The patient underwent successful mechanical thrombectomy for acute stroke treatment, followed by a comprehensive stroke workup. The final diagnosis was acute ischemic stroke secondary to the carotid web. Carotid stenting is planned as a future intervention after the patient's discharge from the hospital.

Discussion: Digital subtraction angiography (DSA) is considered the gold standard imaging modality for diagnosing carotid webs [3]. However, CTA and magnetic resonance angiography (MRA) have emerged as valuable non-invasive alternatives for carotid web diagnosis. CTA, especially with an oblique view, allows for detailed assessment of the carotid artery, enhancing the detection of carotid webs [4]. Patients with carotid webs are at an increased risk of recurrent strokes, with reported recurrence rates ranging from 44% to 64% [5][6]. This high recurrence rate emphasizes the need for appropriate treatment interventions. Several treatment options have been explored, including medical management, antiplatelet therapy, and endovascular interventions such as carotid stenting. A systemic review examining the efficacy of different treatment modalities for carotid webs showed that carotid stenting had the highest success rate in preventing recurrent strokes compared to medical management alone [7].

Conclusion: Carotid webs are rare anomalies of the carotid artery that can lead to acute ischemic stroke. Carotid stenting has shown promise as an effective treatment option for patients with carotid webs, providing a favorable outcome in terms of stroke prevention. Further research and larger studies are warranted to validate these findings and establish optimal management strategies for this condition.

References:

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Klinman, Eva

Age-associated changes in cytoskeleton structure and organelle behavior in micro-RNA reprogrammed human neurons

Abstract: Age is the primary risk factor for the development of dementia and many other neurodegenerative conditions, however, modeling changes associated with age in human neurons is challenging. Neurons derived from induced pluripotent stem cells are stripped of their age-associated epigenetic signatures, and animal models cannot capture the complexity of the human proteome. The Yoo lab has pioneered a novel method to permit the study of aging in human neurons using microRNA to directly convert human skin fibroblasts into neurons (microRNA-induced neurons or miNs). These miNs retain the age-specific epigenetic and cellular properties of the donor fibroblast, permitting evaluation of healthy aging in neurons in vitro. In this project we compare miNs from healthy young and old donors, focusing on cytoskeleton components that support cellular health and regeneration, as well as the behavior and function of critical organelles, specifically mitochondria and autophagosomes. Preliminary data suggests that aging decreases actin dynamics resulting in reduced actin turnover, while the characteristics of the microtubule binding protein tau change to favor smaller more frequent tau "islands" with advanced age. We additionally identified trends towards increased fusion and motility of mitochondria in older individuals, without notable changes in mitochondrial size or density. Further work will focus on functional acidification of autophagosomes, and the role of cytoskeleton changes in disruption of microtubule-based transport.

Langton, Erin

Electrodiagnostic Findings of Infant Botulism: a Case Series

Abstract to Follow

Newman, Joshua

Myopathy Antibody Testing: A tale of two panels

Joshua D. Newman, MD, and Robert C. Bucelli, MD PhD

Abstract: Immune myopathies are among the more common and treatable acquired muscle disorders. The landscape of immune myopathy antibody testing has evolved in recent years with the discovery of new antibodies and the evolution of our understanding regarding the specificity of certain antibodies and their association with specific immune myo-pathologies. The most commonly used myositis autoantibody testing panels are the Myomarker 3 panel out of RDL labs and our own Washington University Myopathy antibody panel. Ordering patterns vary widely among centers, across specialties, and between providers regarding which panel or panels are ordered. The Myomarker 3 panel uses an ELISA assay and Immunoprecipitation (RIPA). The Washington University panel uses ELISA and Western Blot assays. ELISA assays can have issues with sensitivity and specificity related to multiple factors. Western blot is less sensitive, but more specific and for this reason is often used for confirmation of ELISA results. The Myomarker 3 panel is among the highest volume and cost send out tests from BJH. The two panels have 12 overlapping antibodies, but each panel also has several antibodies not tested on the other. We sought to compare the two panels regarding their positivity rate for both unique and overlapping antigens, and to look for any notable differences in results. Ultimately, we hope this preliminary study identifies any notable differences between the tests, so that we may optimize our testing to maximize sensitivity and specificity of myositis antibody testing for our patients.

Overmann, Christina

Inpatient Code Strokes: Neurologists Acting as Chaos Coordinators

Presentation of the yearly resident wide QI project which focused on highlighting challenges often faced in the inpatient setting during code strokes, interventions we made, and outcomes of data collected before and after.

Qiao, Min

Disseminated Histoplasmosis causing cerebrovascular disease

Histoplasmosis is a common endemic mycosis that most often affects immunocompromised individuals. CNS involvement occurs in about 5-10% of cases of disseminated histoplasmosis and carries a higher mortality rate and worse prognosis. The most common presentations of CNS histoplasmosis include chronic meningitis, encephalitis, hydrocephalus and focal brain lesions. Cerebral vascular events and vasculitis is a rare complication of CNS histoplasmosis and to date has only had 6 cases reported in the literature. Here we describe a case of a 61-year-old female who presented initially with decreased PO intake, nausea and unintentional weight loss and was later found to have disseminated histoplasmosis causing multifocal strokes from CNS vasculitis.

Roach, Drew

Plasma p-tau 181 and p-tau 217 are elevated in ALS

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Background: Phosphorylated tau (p-tau) isoform, p-tau 217, in plasma is a highly sensitive and specific biomarker for amyloid plaque pathology and predicts further neurodegeneration in Alzheimer's disease (AD). Plasma p-tau 181 is also increased in AD but is typically less accurate than p-tau 217. These biomarkers are less explored in other neurodegenerative conditions. Recent work indicates plasma p-tau 181 is increased in amyotrophic lateral sclerosis (ALS) and is associated with lower motor neuron (LMN) dysfunction. However, p-tau 217 has not been investigated and compared to p-tau181 in ALS. We sought to measure p-tau 181 and p-tau 217 in plasma from the WashU ALS Biorepository and correlate these measures to clinical characteristics, including LMN burden.

Methods: We measured plasma p-tau 181, p-tau 217, corresponding t-tau levels and p-tau/tau ratios in a cohort of 30 ALS patients and 32 healthy controls using tau immunoprecipitation coupled to nano liquid chromatography - mass spectrometry (LC-MS). Neurofilament light chain (NfL) was quantified in the plasma using single-molecule array (Simoa) platform. A retrospective chart review was performed to obtain cohort demographics, disease duration, site of onset, ALSFRS-R decline, clinical examination findings, and electrodiagnostic data.

Results: Absolute and normalized plasma P-tau 181 and p-tau 217 were elevated in ALS patients relative to healthy controls ([pT181]ALS = 0.0020 ± 0.0099 ng/mL, [pT181/T181]ALS = 22.3 ± 4.60 %, n = 30; [pT181]Ctrl = 0.0095 ± 0.00043 ng/mL, pT181/T181Ctrl = 16.6 ± 2.95 %, n = 32; [pT217]ALS = 0.000096 ± 0.000059 ng/mL, pT217/T217ALS = 0.86 ± 0.37 %, n = 30; [pT217]Ctrl= 0.000059 ± 0.000048 ng/mL, pT217/T217Ctrl = 0.66 ± 0.30 %, n = 32). P-tau 181 was associated with longer disease duration (Spearman's r= 0.45, p= 0.011) and with lower motor neuron dysfunction in the lumbosacral region (p= 0.046). There was no correlation between NfL and p-tau 217 or p-tau 181.

Conclusions: Plasma p-tau 181 shows promise as a biomarker for lower motor neuron dysfunction in ALS. Further studies of p-tau 181 and other p-tau isoforms in ALS are warranted to understand their potential as disease biomarkers.

Rudman, Michelle

Effects of pharmacologic lowering of APOE using statins on glial lipid metabolism and the development of tau pathology

Abstract: Apolipoprotein E (APOE) is the strongest genetic risk factor for Alzheimer's disease (AD) and has three alleles which confer variable risk for developing AD – APOE2, APOE3, and APOE4. Compared to the most common variant APOE3, APOE4 increases the risk of developing AD, while APOE2 decreases the risk. The mechanisms by which APOE modulates AD risk are still incompletely understood. APOE functions in the trafficking of lipids and is expressed primarily by glia. In AD mouse models, glia accumulate lipid droplets suggesting dysregulation of lipid metabolism, and this effect is exacerbated by the APOE4 isoform. In addition, the Holtzman laboratory has shown that decreasing APOE protein levels decreases tau-mediated neurodegeneration. While studying pharmacologic methods to decrease APOE, they also recently discovered that cholesterol-lowering drugs known as statins, and particularly the brain-penetrant statin simvastatin, can substantially lower murine ApoE in the brain. Thus, we hypothesize that (1) APOE isoforms differentially regulate lipid metabolism and the APOE4 isoform results in pathologic dysregulation of lipid trafficking in the brain in the setting of AD pathology, and (2) treatment with statins may abrogate aberrant lipid metabolism and inhibit neurodegeneration and cognitive decline in a mouse model of tauopathy.

To test these hypotheses, P301S-Tau mice expressing human APOE2, 3, or 4 will be sacrificed at 6 or 9.5 months of age. Half the brain will be used for histology to assess lipid droplet accumulation while the other half will be processed for lipidomic analysis to characterize differences in lipid species in whole brain or FACS-purified astrocytes and microglia. Based on unpublished results, I anticipate the lipidomic analyses will show APOE isoform-dependent shifts in astroglial and microglial cholesterol and lipid species. We will then perform parallel analyses in P301S-Tau;APOE4 mice treated with simvastatin or vehicle to determine whether statins alter lipid profiles or lipid droplet accumulation. To determine whether statin treatment may inhibit the development of neurodegeneration, P301S-Tau;APOE4 mice will be treated with simvastatin or vehicle from 6 to 9.5 months of age, and compared to APOE knockout mice as a positive control. At 9.5 months, memory and learning will be assessed and then half the brain will be processed for histology for atrophy and multiple pathologic markers of neurodegeneration while the other half will be analyzed for expression of APOE and APOE receptors or RNAseq in forebrain homogenate and FACS-purified astrocytes and microglia to elucidate cell-specific effects.

These experiments will provide important mechanistic insights into the effects of APOE isoforms on brain lipid metabolism in the setting of tau pathology and whether modulation of APOE using statins may ameliorate aberrant lipid metabolism, neurodegeneration, and/or cognitive deficits in a mouse model of Alzheimer's disease pathology

Vaquer Alicea, Ana

Plasma and CSF Proteomic Signatures of Acutely Sleep-Deprived Humans

ABSTRACT: Sleep deprivation affects both central and peripheral biological processes, but previous research has mainly focused on specific proteins or pathways in one biofluid or tissue. To gain a more comprehensive understanding of the biological processes impacted by sleep deprivation, we collected plasma and cerebrospinal fluid (CSF) from human participants during one night of sleep deprivation and control normal sleep conditions. 1300 proteins were measured at hour 0 and hour 24 using a high aptamer-based proteomics platform and a systems biological database. Our findings suggest that acute sleep deprivation has a significant effects on differential protein expression by decreasing differential protein expression and biological pathways in plasma and increasing them in CSF. Protein pathways were affected by sleep deprivation include immune response, inflammation, phosphorylation, membrane signaling, cell-cell adhesion, and extracellular matrix organization. The modification across biofluids adds to growing evidence that acute sleep deprivation has important and clinically relevant impacts on biological pathways that can negatively affect human health.

Wang, Hannah

Effectiveness of Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea at a Major Tertiary Academic Sleep Center

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Introduction: The use of hypoglossal nerve stimulation (HGNS) for treatment of obstructive sleep apnea (OSA) has been reported to be efficacious in up to 75% of patients with a 68% improvement in the 3% apnea hypopnea index (AHI).1 Based on these results, HGNS is an increasingly widespread alternative treatment for OSA patients who are intolerant of Positive Airway Pressure (PAP) treatment. It is unknown if HGNS is equally efficacious outside of the highly controlled setting of a clinical trial. Here, we performed a retrospective cohort study from patients who underwent implantation of a hypoglossal nerve stimulator at our academic institution and reported the efficacy based on improvement in AHI.

Methods: Adult subjects with a diagnosis of OSA, who were intolerant of PAP therapy and underwent implantation of HGNS at Barnes Jewish Hospital in St. Louis, Missouri from 4/4/2019 to 1/19/2023 were included in this retrospective cohort study. The efficacy of HGNS was evaluated by comparing the AHI on subjects' polysomnography before and after the HGNS was implanted and activated. Analysis of the data was done using paired t-tests to determine efficacy of HGNS via a reduction of at least 50% of the AHI and a reduction in AHI to less than 20 events per hour.2

Results: 111 subjects were implanted of which 1 subject did not sleep during titration study and lost to follow-up, 18 patients were still awaiting titration study and 24 subjects were lost to follow-up. Of the remaining 68 subjects, the median AHI decreased 83% from 29.25 to 4.85 events per hour ($p<0.0001$). There was a reduction of at least 50% of the AHI in 82% of subjects and a reduction of AHI to less than 20 events per hour in 85% of subjects.

Conclusion: HGNS achieved significant therapeutic results in the majority of patients with OSA who were intolerant of PAP therapy. These results add to the growing body of evidence reproducing the original clinical trial in a "real-world" setting free of any conflict of interest. Future studies examining predictive factors influencing the effectiveness of HGNS are needed.

Citation:

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Zolno, Rachel

Functional and safety outcomes of therapeutic plasma exchange for children with neuroimmunologic diseases

Background: Therapeutic plasma exchange (TPE) is established as a safe and effective treatment for adults with acute neuroinflammatory or demyelinating neurological disease. There are a limited number of small case series and retrospective chart reviews looking at the use of TPE in the pediatric population which do suggest that TPE is a safe treatment in children. However, the lack of available data has resulted in limited use of TPE for neuroimmunologic conditions in many pediatric centers, reserved only for cases that are refractory to first- and second- line immunomodulatory therapies.

Objective: To investigate the safety of and functional outcomes of TPE in patients with neuroimmunologic conditions.

Design/Methods: This study included all pediatric patients (≤18 years) who received TPE at St. Louis Children's Hospital for neurological indications from 1/1/2014-7/31/2021. A retrospective electronic medical record review was performed, focused on the first hospitalization in which the patient received TPE. Data collected included diagnosis, number of TPE cycles, complications of TPE, and additional disease modifying therapies used. To assess functional outcomes, a Modified Rankin Scale (mRS) was assigned at initiation of TPE and at hospital discharge. This study was approved by the Institutional Review Board.

Results: 51 patients were included. The most common diagnoses were central nervous system demyelination (N=24, 47%), autoimmune encephalitis (N=9, 18%), peripheral nervous system demyelination (N=5, 10%), and acute flaccid myelitis (N=3, 6%). The number of TPE cycles were 3 to 11 with a mean of 5.9. There were no complications from TPE in 30 (59%) of patients. 14 (28%) experienced 1 complication, and 7 (14%) experienced 2 complications. The most common complications were hypotension (N=10), hypocalcemia (N=5), technical (N=5), and central line infection (N=2). There were no long-term sequelae and no life-threatening complications. At initiation of TPE, 34 (67%) patients had an mRS score of 5, corresponding to severe, bedridden disability. In 41 (80%) of patients, there was improvement in functional mRS score at discharge, with 12 (24%) having a score of 1 (minimal symptoms with no disability) or 0 (no symptoms).

Conclusions: There were no complications related to TPE in the majority of our cohort. Of those who did experience complications, all were readily addressed with symptomatic management at the time of treatment (e.g., fluid boluses for hypotension, calcium supplementation for hypocalcemia) or treated successfully with intravenous antibiotics for the two central line infections. These results support that TPE is a safe treatment modality for pediatric neuroimmunologic conditions in centers with a dedicated pediatric apheresis program and suggest TPE may contribute to improved functional outcomes in patients receiving TPE. This study demonstrates that TPE is a highly effective treatment modality for pediatric patients with neuroimmunologic conditions when clinically indicated.