Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium
Friday, May 24, 2019
7:30am – 9:15am
Farrell Learning and Teaching Center ~ Atrium

Poster presentations will begin at 7:30am

Awards will be presented at 9:00am

We encourage everyone to attend this important event.

Baker, Brandi

Neurosarcoidosis: clinical findings and treatment strategies at Wash U

Abstract: Disease course and disability in Neurosarcoid (NS) is highly variable, ranging from isolated cranial nerve involvement or sensory changes to myelopathy and hydrocephalus. The clinical response of individuals to treatments vary, and currently there are no defined treatment guidelines or biomarkers to guide choice or duration of therapy. The goals of these studies are to understand the clinical presentation of a cohort of NS patients here at Wash U (n=41), as well as their radiographic and CSF findings, and treatment strategies. In our NS cohort, there were a wide range of clinical symptoms at presentation, with the most common being sensory changes (50%), followed by gait instability (35.3%). The brain parenchyma was most frequently involved (44.1%), followed by the meninges (38.2%). Average nucleated cell count in our cohort was 44.8, but 40% of patients had a normal CSF profile. At diagnosis, the most frequent treatment strategy involved the use of IV steroids, followed by an oral steroid taper and initiation of a steroid sparing agent soon after (47.1%). Current therapies in these patients consist of steroids (23.5%), infliximab + MTX (17.6%) or no therapy (17.6%). These data are part of an NS repository that will eventually contain patient disability scores and biologic samples to be used for biomarker and genetic analysis.

Blattner, Margaret

Quality of documentation of distal symmetric polyneuropathy evaluation and compliance with American Academy of Neurology guidelines in the neurology resident continuity clinic

Margaret Blattner MD PhD, Lauren Langford MSN, RN, Gabriela de Bruin MD, Susan Criswell MD, MSCIDepartment of Neurology, Washington University in St. Louis

Background: Distal symmetric polyneuropathy is a common presenting problem in the resident continuity clinic. The American Academy of Neurology (AAN) has well-established evidence-based quality measures for the management of patients with distal symmetric polyneuropathy. These guidelines were not previously formally integrated into the resident continuity clinic.

Methods: Each resident reviewed the charts of patients evaluated for neuropathy in the first half of the academic year (July-November 2018), assessing how their documentation aligned with the AAN guidelines on a standardized worksheet. This process allowed for resident-directed self-assessment of compliance with the AAN guidelines. After the initial survey, residents attended an educational session about the AAN quality guidelines and an electronic medical record template was created and implemented to help residents record information included in the AAN guidelines for management of patients with distal symmetric polyneuropathy. The self-assessment worksheet was again collected for patient encounters following implementation (December 2018-March 2019) and responses were compared.

Results: Education about AAN quality guidelines and inclusion of a clinic note template improved documentation of management of distal symmetric polyneuropathy, including screening for diabetes and chronic alcohol use, impact of pain on functional status, and counseling about fall risk and medication side effects. After the intervention, residents were more confident in applying the AAN guidelines.

Conclusion: This system formalized integration of AAN quality guidelines for the management of patients with polyneuropathy into the resident continuity clinic, with the goal of promoting knowledge and application of quality care guidelines in the management of patients.

Butt, Omar

Network Dysfunction in APOE ε4 Carriers without biomarker Evidence of Alzheimer's disease is related to subclinical tau changes

Background: *APOE* ε4 has been linked to accelerated amyloid deposition and tau-tangle formation. We hypothesized that cognitively normal AD biomarker-negative individuals would exhibit synaptic dysfunction and subsequent resting-state functional connectivity (rs-fc) network disruptions related to the presence of *APOE* ε4.

Methods: Using cross-sectional analyses, we examined rs-fc from 120 cognitively-normal adults (CDR 0) with negative CSF Aβ42, CSF ptau/Aβ42, and PET (PiB-SUVR) according to established criteria (Hansson et al 2018). The cohort had a mean age of 76.4 years ±7.59 years, 15% were *APOE* e4 carriers and 65% were female. All participants had cerebrospinal fluid (CSF) and positron emission tomography (PET) evaluations. Rs-fc were aggregated into canonical cortical networks based on defined criteria (Power et al 2011). A 298x298 connectivity matrix was generated and was then masked to examine only intra-hemispheric (i.e. lateralized) and inter-hemispheric (i.e. callosal) connections between *APOE* ε4 carriers/non-carriers, with particular focus on the default-mode, memory, and salience (i.e. DMS) networks.

Results: Qualitative rs-fc differences observed in the group difference matrix (**Fig. 1A**) were quantified by averaging, with differences observed between (p = 0.03), not within (p = 0.08), the DMS cluster (**Fig. 1B**). Observed rs-fc differences were primarily due to a significant strengthening of lateralized versus callosal connections both within (p = 0.02) and between (p = 0.02) the DMS networks (**Fig. 1C, Fig. 1D**). We next modeled this dysfunction as a function of imaging and CSF biomarkers. First, participants were categorized using the amyloid, tau, neurodegeneration (A/T/N) CSF and imaging criteria (Jack et al, 2016), with subthreshold levels noted across all biomarkers (**Fig. 2A**). Next, a linear regression model of the rs-fc dysfunction revealed significant weighting for CSF p-tau (p = 0.05) and t-tau (p = 0.05) but not for CSF Aβ42 or PET-PiB (**Fig. 2B**).

Conclusions: Early changes in key rs-fc networks in cognitively-normal, AD biomarker-negative *APOE* ε4 carriers are driven by changes in local lateralized connections relative to long-range callosal connections. Linear modeling results are suggestive of an early role of tau in early network dysfunction in elderly asymptomatic *APOE* ε4 carriers without biomarker evidence of AD.

Ciotti, John

Practice patterns in management of status epilepticus at Barnes-Jewish Hospital

John R. Ciotti, MD; Lauren Langford, MSN, RN

Introduction: The Neurocritical Care Society (NCS) defines status epilepticus (SE) as 5 minutes or more of (i) continuous clinical and/or electrographic seizure activity, or (ii) recurrent seizure activity without return to baseline between seizures. Published guidelines suggest initial steps in management of SE, but American Academy of Neurology (AAN) quality measures do not define a strict timeframe for treatment initiation. Barnes-Jewish Hospital (BJH) has an acute SE management protocol, but gives significant latitude to treating physicians. This project aims to define current practice patterns in management of SE at BJH.

Methods: A retrospective chart review of patients treated at BJH between January 1, 2019 and February 19, 2019 with billing diagnosis of "Seizure," "Seizure Disorder," or "Status Epilepticus" and encounter department of 10400 ICU, 10500 SDU, 11300, 11400, or 11500 was conducted to define current SE management practice patterns by neurology residents. Information from each chart was obtained, including prior history of seizures, number and type of AEDs prescribed on arrival, etiology/trigger of SE, subtype of SE, time to initial intervention, number of seizures prior to intervention, and each intervention made to treat SE (a single intervention defined as an individual antiepileptic medication administered, or multiple medications ordered and/or given closely together), as well as other factors.

Results: Data from 28 medical charts were included. When times of SE onset and initial intervention were clearly defined, treatment was initiated within 15 minutes in 59% of cases, and delayed at least 30 minutes in 22% of cases. On average, 2.6 interventions were required to break SE, with benzodiazepines or a benzodiazepine plus levetiracetam load combination the most common initial intervention. Sixty-one percent of SE cases were successfully treated within an adapted protocol.

Conclusions: Neurology residents are largely adhering to best practices in management of SE, particularly in selection and sequence of interventions. Targeted areas for improvement should focus on rapid implementation of interventions to break SE, including initiation of treatment within 30 minutes of meeting SE criteria or prior to a third convulsive seizure.

Dionne, Kalen

Bypassing the Blood Brain Barrier (BBB) with Intranasally Delivered Nanoparticles

Abstract: Metal nanoparticles (NPs) are rapidly becoming the material of choice for nanomedicine due to the relative ease of synthesis and functionalization, combined with biocompatibility and unique optical properties. However, these materials generally do not reach the brain when injected through subcutaneous, intramuscular, intraperitoneal, and intravenous routes. The blood brain barrier (BBB) isolates the serum from the brain parenchyma, effectively blocking the passage of therapeutic agents from blood to brain. Intranasal delivery is a promising delivery technique for treating neurologic disease given that it is non-invasive and results in rapid and complete brain uptake through intraneuronal and perivascular pathways. Our recent work demonstrates that intranasally delivered gold-NPs (Au-NPs) are efficiently delivered to the mouse brain. Specifically, 5nm Au-NPs were coated with cypate fluorescent dye and instilled into mouse nares bilaterally. In vivo fluorescence imaging reveals that Au-NPs are deposited in the nasal epithelium immediately after instillation and are then progressively cleared over the span of days. Importantly, intranasally instilled NPs do not undergo hepatic clearance. Fluorescence microscopy reveals that intranasally instilled Au-NPs are deposited throughout the brain parenchyma (including the olfactory lobes, cortex, hippocampus, brain stem, and cerebellum). Ongoing research aims to target various metal nanoparticles to primary brain tumors (e.g. glioblastoma) and brain metastasis for microglial activation/phagocytosis, photothermal therapy, and Chrenkov-radiation induced therapy (CRIT).

Everett, Elyse

Appraisal of Health States Worse than Death in Patients with Acute Stroke

Elyse Everett, William Everett, Matthew Brier, Patrick White

Background: Acute stroke causes significant functional disability in many patients. Goals of care discussions are frequently required to make decisions about possible interventions. Unfortunately, many of these conversations happen without the patient as they are rendered unable to participate due to aphasia, depressed mental status, or encephalopathy. This study aimed to assess what health states patients with acute stroke deem worse than death, as well as explore possible predictors for these opinions.

Methods: Patients admitted to Barnes Jewish Hospital with acute stroke were asked to fill out a questionnaire ranking 10 different possible health/functional outcomes as better or worse than death using a 5 point Likert scale. Responses to these questions were subjected to principal component analysis (PCA), which identifies clusters of related variables and reduces them to summary components. Significant components were then subjected to linear regression analysis to identify predictive variables such as demographics.

Results: A total of 80 patients with acute stroke filled out the questionnaire. The states deemed equal to or worse than death by the majority of patients were relying on a breathing machine (66%), relying on a feeding tube (66%), being confused all of the time (62%), being unable to communicate with others (58%), and bowel/bladder incontinence (50%). PCA revealed two factors that accounted for 70.6% of the variance. The only predictor found to be statistically significant in regression analysis was race for factor one, comprised primarily of feelings about relying on a feeding tube and breathing machine, bowel/bladder incontinence, chronic pain, and being confused all of the time.

Conclusion: A substantial number of patients found multiple common outcomes of stroke to be the same as or worse than death. The only demographic factor found predictive of these opinions was race for the states that involve “life sustaining” measures. This study highlights the importance of realistic and in-depth discussions about expected functional outcomes with patients and/or their surrogate decision makers when considering goals of care after stroke.

Frerichs, Lindsay

Use of Memantine to Treat Migraine in Patients with Comorbid Bipolar Disorder: A Case Series

Lindsay Frerichs MD, Mallory Henry PA-c, Sylvia Awadalla MD

Background: Migraine is a common and debilitating condition. The prevalence of migraine in the US is 18% in women and 6% in men and it is a leading cause of disability worldwide. It is often comorbidly found in people with affective disorders. Patients with bipolar disorder were found to have a higher prevalence than the general population, overall 25.9%. In this group of patients' migraine can be difficult to treat as many of the medications commonly used to treat migraine can interact with their psychiatric medications. Memantine, which acts on the NMDA receptor has been anecdotally noted to be efficacious and well tolerated in patients with comorbid bipolar disorder and migraine and this case series seeks to document the efficacy and tolerability of memantine in this specific patient population.

Method: Retrospective chart review was conducted of patients treated with memantine in the Washington University General Neurology Clinic who carried a formal diagnosis of bipolar disorder and migraine from 2015 to present. Six patients were identified that fit these criteria. Goal of treatment was a change from baseline mean number of migraine days per month of greater than 50%. Tolerability was assessed by patient reported side effects leading to discontinuation of the medication.

Results: Of the six patients identified five of the six saw a benefit in reduction of the number of headache days per month of greater than 50%. The sixth patient was not on the medication for a long enough period to determine efficacy. Memantine was well tolerated in 5 of the 6 patients with the only adverse effect being dizziness.

Conclusion: In this series, memantine was an effective preventative migraine treatment in patients with comorbid bipolar disorder. Five of six patients received a greater than 50% reduction in the number of headache days per month when they had previously trialed and failed multiple other medications. The medication was well tolerated except for one patient who developed dizziness. This retrospective analysis provides preliminary data to suggest that memantine may be a good first line agent for migraine prevention in patients with comorbid bipolar disease, and warrants further investigation via a prospective randomized controlled clinical trial.

Gifford, Sheyna

Morbilliform Mystery: A Very Rare Case of Baclofen-Induced Rash

Sheyna Gifford, Amanda Miller

Abstract: The drug baclofen is a widely-used gamma amino butyric acid (GABA) derivative known to improve movement, decrease pain and ease alcohol dependence. A valuable alternative to opioids, baclofen has been increasingly utilized in pain pumps and for relief of musculoskeletal spasm in patients with limited response to or tolerance for anticholinerigics. More common side-effects including weakness, dizziness, and nausea are well-known to practitioners. One side effect - dermatologic in nature - has been documented less than a dozen times in the literature. Here we present a case of generalized baclofen-induced rash and discuss the potential causes, treatments, and future management options for patients who experience this rare side-effect.

Harrison, Nigel and Levasseur, Victoria

Chronic thoracic myelopathy as the initial manifestation of Susac syndrome

Abstract: Susac syndrome is an immune-mediated endotheliopathy affecting the microvasculature of the brain, retina, and inner ear, leading to the pathognomonic clinical triad of encephalopathy, branch retinal artery occlusion, and sensorineural hearing loss. Most patients ultimately diagnosed with Susac do not exhibit all features of this triad at their initial presentation and delays in diagnosis are common. We present a case of Susac syndrome manifesting with a thoracic myelopathy of two years duration before the patient developed a subacute encephalopathy complicated by a seizure and new tinnitus. A brain MRI showed features of microvascular changes in the corpus callosum, including a small callosal infarct, and additional punctate supratentorial acute and subacute infarcts. Audiometry revealed right-sided sensorineural hearing loss. A brain biopsy showed microinfarcts associated with bizarre appearing microvessels with hyalinized, thickened walls and associated hemosiderin, rare perivascular lymphocyte-predominant cellular foci without evidence of angionecrosis to suggest vasculitis, and beta amyloid plaques without evidence of amyloid deposition in vessels. A fluorescein angiogram was performed soon after discharge and showed retinal artery abnormalities consistent with Susac syndrome. Cases of Susac syndrome with associated myelopathy are rare and those reported to date are incompletely characterized. This humbling case highlights the diagnostic challenges neurologists face in evaluating patients with atypical or rare manifestations of rare conditions, and adds to the limited literature describing atypical manifestations of Susac syndrome.

Hoang, Ethan

Progressive multifocal leukoencephalopathy treated with nivolumab

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Departments of Neurology1, Medicine2, Radiology3, and Pathology and Immunology4

Abstract: Therapy for progressive multifocal leukoencephalopathy (PML) remains challenging since there are no antiviral therapies available for JC virus. Immune reconstitution has improved the prognosis in many settings where PML occurs, but it often is not possible in PML patients with hematologic malignancies.

We describe the first biopsy proven PML case where the PD-1 inhibitor nivolumab appears to have stimulated immune activation resulting in effective control of PML in a patient with hematologic malignancy.

This report supports further investigation of the utility of checkpoint inhibitors for treating PML where other immune reconstitution options are not available

Krill, Michael

Factors Affecting Return to Play After Primary Achilles Tendon Tear in NFL Players

Krill MK, Yang J, Hodax JD, Machan JT, Lemme NJ, Durand WM, Hoffman JT, Hewett TE, Owens BD

Achilles tendon tears are potentially career-ending injuries for professional athletes. For NFL players, return not only requires surgery and extensive rehabilitation, but also the ability to compete in a market with limited positions that annually introduces new, younger athletes.

We sought to evaluate factors related to return to play (RTP) and changes in performance following a primary Achilles tear. We hypothesized that "skilled" position players and those drafted in later rounds would return at a lower rate compared to "unskilled" and higher draft-round players.

Using a previously established database, 80 NFL players suffering primary Achilles tendon tears between 2009 and 2014 seasons were identified. RTP was defined as playing in a regular-season (RS) or post-season game following injury. Probability of RTP was modeled as a function of time after injury using Kaplan-Meier analysis with demographic variables assessed using generalized linear models. Twelve players (15%) suffered a subsequent Achilles tendon tear during or after the study period and were included in the overall RTP rate but were excluded from performance analyses due to confounding effects of an ipsilateral re-tear or contralateral tear.

Overall RTP rate was 61.3%. Age, number of prior seasons, position type, or draft-round status did not significantly affect RTP when evaluated with Kaplan-Meier analysis. Players who did RTP played in a significantly greater number of RS games (13.7) than players who did not RTP (8.71) in the season prior to injury ($p=0.011$). Players who did not RTP exhibited a significant decrease in performance in the season preceding injury (12.7 RS games players two seasons prior, 8.71 games RS games played one season prior, $p=0.019$). Players who returned did not display a significant change in the number of games played or started in seasons following injury when evaluating more than one season after return.

Rate of RTP following primary Achilles tendon tears may be lower than previously published. However, in those able to return, performance only in the season to be affected, as players return to pre-injury levels if given the opportunity to play more than one season after injury.

Krill, Michael

A Rare Presentation of an Atypical Rhabdoid Tumor

Michael K Krill, Alexandra Fogarty, Sindhu Jacob

Background: Pineal atypical rhabdoid tumors (AT/RT) are rare in adults with rapid progression and poor prognosis.[1] In adults, the first reported case of AT/RT was described in 1992 and over 30 cases have been reported in adults in the literature.[1] In contrast to pediatric cases which involve the cerebellum, ventricles, or frontal lobe, most adult AT/RTs are located in the cerebral hemispheres and are rarely found in the pineal region.[1]

Case Presentation: A 71-year-old male presented with acute confusion and memory loss, found to have a pineal rhabdoid tumor on head imaging (3.2x1.9x2.5cm). He underwent resection due to rapid tumor growth (5.2x3.7x4.5cm) over roughly two months. Post-operative course was complicated with hydrocephalus, subsequent shunt placement, and a cerebral empyema over the course of two months. He was admitted to an acute rehabilitation facility while he completed radiation treatment. His baseline examination demonstrated severely impaired attention, delayed initiation, and impairments with safety, judgement, problem-solving, and comprehension. He had significant deconditioning and was maximum to total assistance for transfers, mobility, ADLs, and iADLs. He demonstrated some symptoms of Parkinsonism with a short shuffling gait, cogwheel rigidity, and mild resting tremor that was not present at initial presentation. He was trialed on Sinemet with no improvement after one week. To aide with the poor initiation, energy fluctuations, and impaired attention that significantly limited participation, he was transitioned to low-dose methylphenidate (5mg) scheduled twice daily. Over the course of several weeks, his attention, initiation, and energy improved significantly and day-to-day fluctuations. At discharge, he was minimum assist with most ADLs and transfers while now able to ambulate 150' with a wheeled walker. He was still limited in comprehension, problem-solving, and memory, but his attention and initiation was significantly improved, and he was safely able to return home. He lived several months at home without decline. Immediately after starting chemotherapy, he rapidly declined further before this death from complications from metastatic, progressive disease.

Discussion: There are reports of Parkinsonism related to brain tumors, cancer treatment, or worsening of pre-existing Parkinson's disease.[2-3] This course underscores the importance of reassessing treatment plans and a multidisciplinary approach to cancer treatment for a patient with a rare and aggressive brain tumor.

References:

1. Dardis C, et al. Front Neurol. 2017.
2. Yasuhara T, et al. Open Neurosurg J. 2009.
3. Mehanna R, et al. Am J Case Rep. 2016.

Lobanov, Oleg

Resting State Functional Connectivity Patterns in Tuberous Sclerosis Complex

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Abstract: Tuberous sclerosis complex is an autosomal dominant disorder with variable expression. It is characterized by hamartomatous lesions in various organs, including the brain. Neurologic symptoms, including seizures, developmental delay and behavioral abnormalities, are a common cause of morbidity and mortality in this disease. Resting state functional MRI (rs-fMRI) can be used to identify functional brain networks which demonstrate temporally correlated spontaneous activity and are known to be co-activated by task performance. In the present study, we used rs-fMRI to characterize functional connectivity results in patients with tuberous sclerosis complex. For all children, rs-fMRI data (n=13, age: 1.1-17 years) were collected as part of routine epilepsy surgery evaluation and analyzed using standard pipelines. We demonstrated that: 1) Patients with tuberous sclerosis have a resting state brain network architecture comparable to that identified in healthy, age-matched subjects; 2) Tuberous sclerosis patients with more severe developmental delays demonstrate global reductions in homotopic functional connectivity measures; and 3) Tuberous sclerosis patients with more severe developmental delays demonstrate network-specific alterations in functional connectivity measures, including within and between the default mode, frontoparietal, ventral and dorsal attention networks. Together, these results suggest that these alterations in functional connectivity networks may underlie differences in neurodevelopmental performance in patients with tuberous sclerosis. Further studies are necessary to better delineate criteria for early identification of patients with tuberous sclerosis at greatest risk for neurodevelopmental impairment and neurocognitive disabilities.

O'Halloran, Andrew

Lance-Adams Syndrome and Neurorehabilitation

Andrew O'Halloran MD, Michael Krill MD, Sindhu Jacob MD, Barbara Hessel DPT, Katherine Gerull

Background: Approximately 150 cases of Lance-Adams syndrome have been reported in the literature. Lance-Adams syndrome is a rare form of chronic post-hypoxic myoclonus that has been described in patients following successful cardiopulmonary resuscitation.

Case Description: A 25-year-old female with a past medical history of lupus nephritis complicated by end stage renal disease on hemodialysis presented to the hospital following cardiac arrest secondary to acute pulmonary edema. She was undergoing routine outpatient dialysis when she felt short of breath and experienced acute respiratory failure necessitating emergent intubation by EMS. While in transit, she entered pulseless electrical activity requiring roughly 10 minutes of CPR and 2 doses of epinephrine prior to return of spontaneous circulation. After arrival at the hospital, she was transferred to the ICU where myoclonic jerking was observed by the critical care team 24 hours after her arrival. She underwent EEG, which revealed diffuse background slowing with intermittent background activity suppression and disorganization of background rhythms. EEG findings were consistent with diffuse cerebral dysfunction, though findings were confounded by sedating medications. MRI revealed signal abnormalities in bilateral thalami, basal ganglia, and cortex consistent with hypoxic brain injury. Neurology was consulted and recommended initiating 500mg levetiracetam nightly. As her course progressed, her respiratory status improved and she was successfully extubated. Though she was initially non-verbal and unable to follow commands, her mental status significantly improved.

Acute Rehabilitation Course: The patient was transferred to acute rehabilitation where she exhibited myoclonus in her upper and lower extremities bilaterally, which appeared to worsen with movement. Symptoms were greater in lower extremities compared to upper extremities, though myoclonic jerks occurred at approximately equal frequency bilaterally. Concurrent neurologic findings demonstrated preserved strength in all 4 extremities, lack of dysmetria with finger to nose bilaterally, and upgoing Babinski on left with equivocal findings on right. The physical therapy team initially trialed techniques traditionally applied to ataxia, though little benefit was observed, and therapy was subsequently transitioned to focus on functional mobility and postural stability. The severity of the patient's action myoclonus fluctuated with her emotional state and attentional resources, thus relaxation techniques and cognitive strategies were employed during therapy to reduce symptoms. Though she remains early in her rehabilitation course, implementation of a multimodal approach of pharmacologic intervention, physical and occupational therapies, and behavioral strategies have already yielded improvement in the severity of her myoclonus.

Plotzker, Alan

Antisense Oligonucleotide Treatment to Increase Progranulin Expression

Alan Plotzker, Kathleen Schoch, and Timothy Miller

Abstract: Mutations causing haploinsufficiency of progranulin are one of the major causes of familial frontotemporal dementia, a currently untreatable neurodegenerative disease. Previous research has identified a region in the 5'-untranslated region of the progranulin gene (GRN) that downregulates progranulin expression when present. This downregulation is thought to be related to two start codons in this region, leading to inefficient translation. We therefore hypothesized that using antisense oligonucleotides (ASOs) to block one or both of these sites would lead to increased progranulin expression. Here, we tested five candidate ASOs in human neuroglioma cells. While none of these ASOs affected GRN mRNA levels, several of them increased levels of both intracellular and secreted progranulin protein, consistent with the proposed mechanism of increasing translation rather than transcription. These ASOs have the potential to be therapeutically useful for progranulin-deficient frontotemporal dementia and also represent a new strategy for using ASOs to increase expression of a target protein.

Probst, Daniel

Educational intervention improves patient safety event reporting among PM&R residents

Daniel Probst MD, Sean Smith MD, Lauren Langford, David Carr MD, Annie C. Harmon PhD, Thy Huskey MD

Background: An important PSQI topic is resident education in patient safety event reporting. Resident physicians work long hours on the front lines of patient care and are uniquely positioned to identify patient safety events. However, residents report a disproportionately small number of patient safety events. Two factors associated with poor resident participation in patient safety event reporting are lack of education on reporting and lack of familiarity with the safety event reporting system. Through the implementation of a multifaceted educational intervention, this study sought to increase the number of patient safety events reported by physical medicine and rehabilitation (PM&R) residents at a free-standing inpatient rehabilitation hospital.

Methods: Participants in this prospective study were 14 PM&R residents. The hospital's patient safety event reporting system was launched and made available to residents at t=0 months. Baseline data on resident event reporting was collected from t=0 months to t=3 months. Data collection occurred during the intervention phase from t=3 months to t=9 months.

A multifaceted educational intervention was launched at t=3 months. The intervention consisted of the establishment of a patient safety event Trigger List, educational lectures, and step-by-step "How to Report a Patient Safety Event" posters. The Trigger List included specific patient safety events that were deemed to be a "point of emphasis" by resident physicians. Educational lectures on how to report patient safety events and the importance of patient safety event reporting were presented to all residents at t=3 months and repeated at t=4.5 months. At t=3 months, "How to Report a Patient Safety Event" posters were placed in all resident workrooms. The primary outcome was the number of patient safety events reported by resident physicians per month. The secondary outcome was the number of residents reporting patient safety events per month. Statistical analysis was performed with independent samples *t*-tests.

Results: The educational intervention led to significant increases in the number of patient safety events reported per month (pre-intervention: 3.67 events per month; post-intervention: 18.17 events per month; p=0.004) and the number of residents reporting events per month (pre-intervention: 1.00 residents per month; post-intervention 4.33 residents per month; p=0.004).

Conclusion: A multifaceted educational intervention in patient safety event reporting led to a significant increase in both the number of patient safety events reported by PM&R resident physicians and the number of PM&R resident physicians reporting patient safety events. Feedback from the patient safety event data allowed for the proposal of solutions to commonly identified patient safety events.

Probst, Daniel

Recurrent Fevers, Grimacing, and Supra-Ventricular Tachycardia: A Case of Hydralazine-Induced Lupus in a Globally Aphasic Patient

Daniel Probst MD & Thy Huskey MD

Case Diagnosis: Hydralazine-induced lupus in a globally aphasic patient

Case Description: A 55 year-old man suffered an ischemic stroke in the left middle cerebral artery distribution, causing severe global aphasia. His hospitalization was complicated by severe hypertension requiring five anti-hypertensive medications, including hydralazine 150 mg TID.

He experienced multifocal pain characterized by grimacing and moaning when various limbs and joints were palpated or moved. The specific painful joint or muscle group changed daily. He was unable to describe or answer questions regarding the pain due to his aphasia. He subsequently experienced intermittent episodes of SVT and daily fevers, which persisted despite multiple negative infectious workups.

Rheumatology was consulted and diagnosed the patient with hydralazine-induced lupus with anti-histone antibodies elevated to 3.5 (normal <1.0). He experienced fevers for 11 straight days and had near daily episodes of SVT prior to hydralazine being stopped. After hydralazine was discontinued, there was complete resolution of his fevers and SVT for the remainder of his hospitalization.

Discussion: This case highlights the complexities of working with globally aphasic patients and the importance of maintaining a broad differential diagnosis when working with patients who are unable to provide a history.

Additionally, in an acute inpatient rehabilitation setting, where a lack of telemetry monitoring prevents the use of IV medications for hypertensive crises, oral hydralazine is a commonly used. Physicians must be aware of the risk of hydralazine-induced lupus, especially at higher hydralazine doses.

Conclusion: Hypertension control is standard in post-stroke rehabilitation. Aggressive treatment often includes hydralazine. Physicians must maintain a broad differential diagnosis when treating seemingly nonspecific symptoms, especially when using hydralazine in globally aphasic patients.

Probst, Daniel

Large Ulnar Nerve Neuroma-in-Continuity Presenting as Medial Elbow Pain: A Case Report Authors:
Daniel Probst MD & Berdale Colorado DO

Setting: Tertiary academic medical center

Patient: A 20-year-old female with history of ulnar nerve laceration status post repair, presenting with medial elbow pain.

Case description: The patient sustained a left ulnar nerve transection due to an elbow laceration two years prior, and underwent ulnar nerve repair/transposition and an anterior interosseous nerve to ulnar motor nerve transfer five days after the injury. One year later, she underwent neurolysis of the ulnar nerve at the elbow and decompression of the ulnar nerve at Guyon's canal due to persistent weakness/numbness. Six weeks after this surgery, she reported increased medial elbow pain. Due to her increased pain and continued weakness/numbness, she was referred for electrodiagnostic testing.

Assessment/Results: Electrodiagnostic testing revealed a severe left ulnar neuropathy at the elbow. Ulnar motor nerve conductions to the abductor digiti minimi revealed distal latency of 4.8 ms, amplitude of 4.5 mV, and a conduction velocity of 37 m/s across the elbow. There was evidence of continuity (1 motor unit) in the flexor digitorum profundus and abductor digiti minimi on needle EMG, but no motor units seen in the first dorsal interosseous. Spontaneous activity was seen in all ulnar-innervated muscles tested. Subsequent ultrasound revealed a large ulnar nerve neuroma 2 cm proximal to the medial epicondyle with a maximum cross-sectional area measuring 109 mm^2 (normal ≤ 10 mm^2), correlating with her area of maximal tenderness.

Discussion: This case highlights the added diagnostic utility of ultrasound in conjunction with electrodiagnostic testing. It also highlights the challenge of managing neuromas-in-continuity. The patient's primary complaint of pain, her minimal ulnar nerve function despite prior surgeries, and her subsequent electrodiagnostic/ultrasound findings, all contributed to the multidisciplinary team's plan for internal neurolysis of the ulnar nerve with resection of nonviable fascicles.

Conclusion: Ultrasound in conjunction with electrodiagnostic testing can be valuable in the identification and management of neuromas-in-continuity.

Rogers, Amanda

Loss of Function Variants in the *CSTB* Gene Cause Microcephaly, a Hyperkinetic Movement Disorder, and Early Onset Epilepsy

Background: Pathogenic variants in in the *CSTB* gene, which encodes cystitin B, are associated with the autosomal recessive disorder Unverricht-Lundborg disease (ULD) or progressive myoclonic epilepsy type 1. Most patients with ULD are homozygous for an expanded dodecamer repeat in the promotor region of the gene. Compound heterozygotes who have the dodecamer repeat on one allele and a point pathogenic variant (usually loss-of-function) on the other typically exhibit a more severe phenotype. Harboring two loss of function variants in the *CSTB* gene is exceedingly rare. However, four patients with homozygous loss of function *CSTB* variants from 2 unrelated families were recently described. These patients exhibit a severe and unique phenotype characterized by microcephaly, profound developmental delay, and early onset epilepsy and dyskinetic movements of variable severity.

Design/Methods: We utilized whole exome sequencing (WES) to investigate the underlying genetic cause of microcephaly, global developmental delay, hypotonia, hyperkinetic movement disorder, and epilepsy in a 23 month old Caucasian female. We compare the phenotype and genotype in the proband with previously reported patients.

Results: WES revealed the likely pathogenic variants c.67-1G>C (IVS1-1G>C) and c.202C>T (p.R68*) in the *CSTB* gene. We report the fifth patient, to our knowledge, to harbor biallelic loss of function variants in the *CSTB* gene. While our patient is phenotypically similar to the previously described patients, she developed a more severe drug-refractory epilepsy.

Conclusions: Our data expand the phenotypic and genotypic spectra of *CSTB*-related disorders and provide additional evidence that biallelic loss of function variants in *CSTB* cause a unique phenotype characterized by microcephaly and profound developmental delay with or without early onset dyskinetic movements and epilepsy. Additional functional studies are needed to investigate the molecular basis of the allelic heterogeneity in the *CSTB* gene.

Smith, Alyssa

Magnetic Resonance Imaging Adds Prognostic Value to EEG After Pediatric Cardiac Arrest

Alyssa Smith MD, Alex Ganninger BS, Stuart Friess MD, Rejean Guerriero DO, Kristin Guilliams MD

Objective: To investigate how combined electrographic and radiographic data inform outcomes in children after cardiac arrest.

Design: Retrospective observational study

Setting: PICU of a tertiary children's hospital

Patients: Children admitted to PICU with diagnosis of cardiac arrest from 2009 to 2016.

Interventions: Electroencephalographic (EEG) monitoring and MRI

Measurements and Main Results: The first 20 minutes of EEG background was blindly scored as normal, slow-disorganized, discontinuous or attenuated-featureless. Presence and location of MRI diffusion-weighted image (DWI) abnormalities were noted. Outcomes were categorized using Pediatric Cerebral Performance Category (PCPC) scores at discharge and all neurology follow-up visits within 14 months. A "good outcome" was defined as a PCPC score of 1-3 at follow-up. A "poor outcome" was PCPC score 4-5 or death. We performed univariate analysis with Fisher's exact test between physiologic, neurophysiologic, neuroimaging findings and outcomes. Variables with $p<0.05$ were entered into logistic regression model.

Of 148 children with cardiac arrest, 129 had post-arrest EEG monitoring. Brain MRI was performed in 65 patients (43.9%), median 5 days [IQR 3-11] post-arrest. MRI diffusion abnormalities were noted in 35. Among the 60 survivors, 26 children had a good outcome. None of the 7 children with hippocampal DWI changes experienced a good outcome. In a multivariate logistic regression model, unfavorable EEG background (OR 0.03, CI [0.003,0.24]) and diffusion restriction occurring simultaneously in deep gray and hippocampal regions (OR <0.001, CI [0,0.45]) remained significant predictors of decreased likelihood of a good outcome.

Conclusion: Children with cardiac arrest have a high mortality rate and neurologic injury is prevalent among survivors. Unfavorable EEG background and MRI diffusion abnormalities in hippocampus and deep gray nuclei may predict poor outcome in children surviving cardiac arrest.

Sookochoff, Michael

Right lower extremity edema and sensory changes in a patient with low back pain and knee arthritis

HPI: A 56-year-old obese woman with history of low back pain, right knee arthritis, and previous right meniscectomy presented with edema and sensory changes in her right lower extremity. She reported insidious onset of 5-6 weeks of numbness, burning, and tingling of lateral and plantar right foot, posterior lower leg, as well as edema of the distal right leg. She also endorsed tingling pain over her posterior right thigh. Her lower extremity symptoms were exacerbated by weight-bearing and walking. In addition to her lower extremity symptoms, she also reported bilateral low back pain that was exacerbated with walking and lumbar extension. Her primary care provider had prescribed oral steroids which did not improve her symptoms. She reported a previous episode approximately 2 years prior with similar symptoms that were resolved with oral steroids. She denied any red flag symptoms.

Exam: Well developed female in no acute distress. Unremarkable HEENT, pulmonary, abdominal, and skin exam. Her vascular exam revealed right lower extremity edema distal to the knee. Her musculoskeletal and neurological exams revealed reduced sensation to light touch over the plantar right foot, positive slump-sit test on the right lower extremity for reproduction of her tingling pain over her posterior distal lower extremity, diminished Achilles reflex on the right, soft tissue mass over the posterior right knee.

Differential:
Posterior knee synovial cyst
Intraneural ganglion cyst
Thrombophlebotic syndrome/DVT
Synovial sarcoma of the knee
S1 radiculopathy

Tests & Results: MRI revealed 5x5.9x9cm multiloculated cyst posterior to the right knee compressing the popliteus muscle with mass effect on popliteal vessels and tibial nerve with evidence of denervation of tibialis posterior muscle. Ultrasound-guided cyst aspiration was attempted, though limited fluid was obtained. She was referred to an orthopedic surgeon who ultimately performed excision of the cyst. Surgical pathology ultimately revealed a multiloculated synovial cyst.
Final/working dx: Posterior knee synovial cyst measuring 5x5.9.9cm compressing the popliteal vasculature and the tibial nerve leading to peripheral neuropathy.

Discussion: Posterior knee synovial cysts are common findings in the setting of intraarticular pathology which may form secondary to accumulation of synovial fluid in the bursae of the knee or synovial herniation posterior to the joint. Rarely, such cysts may contribute to tibial nerve compression or entrapment. In our patient, her cyst nearly replaced the popliteus muscle in its mass, and compressed the popliteal vasculature and tibial nerve, resulting in tibialis posterior denervation. What makes this case unique is the sheer size of the mass, the nearly complete displacement of popliteus, as well as tibialis posterior denervation, which is rarely reported in existing literature.

Outcome: After resection, the patient continued to report improved pain but persistent weakness with toe flexion, diminished sensation over her plantar foot, and edema distal to her knee. She reported postoperative sensation of a "tight shoe laced" around her foot and also had mild surgical site scar hypertrophy.

Return to activity/follow-up: The patient was recommended to return to activity slowly and was recommended to pursue outpatient physical therapy. She was given instructions for surgical scar massage. She continued to exhibit limited toe flexion and diminished sensation to light touch over the plantar surface of her foot for at least two months postoperatively.

Wang, Yan

Rate of progression in CT-defined edema is associated with increased likelihood of intervention in acute cerebellar infarction

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Background: Edema from cerebellar ischemic stroke can be life threatening causing brainstem compression, hydrocephalus, and herniation. Unlike malignant hemispheric infarction, accurate predictors of patients who benefit from early acute medical and surgical interventions are understudied.

Objective: To determine if rate of progression in CT-defined edema predicts need for intervention in patients with cerebellar infarction.

Methods: Admissions to a tertiary medical center neurological intensive care unit (NICU) with a primary diagnosis of cerebellar infarction over a three year period were identified. Intervention cohort was defined as those needing at least one medical or surgical procedure: osmotic therapy, extra-ventricular drainage (EVD), or surgical decompression. Clinical characteristics including comorbidities and admission symptoms were recorded. Infarct volume, infarct to posterior fossa volume ratio (infarct ratio), and their rate of change on serial non-contrast head CT scans, were measured using both a manual-delineation volumetric method as well as the more pragmatic, ABC/2 formula.

Results: We identified 60 patients with cerebellar infarction admitted to NICU over a three year period. Twenty seven (45%) patients received medical and/or surgical intervention. Of those, all except one received osmotic therapy, while 15 patients required posterior fossa decompression +/- EVD. When compared with the no-intervention cohort, patients needing an intervention were more likely to be diabetic (21.5% vs 48.1%, $p = 0.03$) and their stroke involved bilateral cerebellum (24.2% vs 59.3%, $p = 0.006$). On initial CT showing evidence of infarction, using the ABC/2 method, the need for an intervention was associated with a larger infarct volume and infarct ratio on when compared with stable patients (34.3 vs 20.1 mL, $p = 0.002$; 0.22 vs 0.12, $p = <0.000$). Receiver operating characteristic analysis demonstrated that both infarct volume and infarct ratio predicted intervention (AUC = 0.725; 95% CI 0.594-0.856 and AUC = 0.755; 95% CI 0.630-0.881, respectively). An infarct ratio of 0.14 yielded optimal sensitivity of 0.74 and specificity of 0.73. Volumetric measurements yielded similar findings. The rate of early infarct growth over the first 3 days was higher in the intervention cohort compared with the no-intervention cohort (0.21 ml/hr vs 0.94 ml/hr, $p = 0.047$).

Conclusion: A larger baseline infarct volume and rapid infarct growth rate on head CT using the ABC/2 method may provide early, clinically useful markers to select patients with cerebellar infarction who benefit from medical and/or surgical intervention.

Wilks, Anson

Neurotization as a Novel Treatment for West Nile Virus-Associated Brachial Plexitis

Introduction: West Nile virus-associated brachial plexitis (WNV-BP) is a rare form of West Nile neuroinvasive disease (WNND),1,2 for which supportive care is currently the mainstay of treatment.3 The literature on brachial plexus involvement from West Nile virus infection is limited, but recovery is poor in cases reported to date.1,4,5 Neurotization is an established surgical treatment option for traumatic peripheral nerve injury and is optimally performed within 6 months of injury.6 Neurotization has been successfully used in treating poliomyelitis-like paralysis caused by enterovirus-71 and enterovirus D68,7,8 but its role in the treatment of peripheral nerve disease due to other infectious etiologies is less clear.

Case: A 63-year-old man presented with fever and encephalopathy. Testing showed an elevated WNV IgM titer and a neutrophilic pleocytosis on cerebrospinal fluid analysis, findings consistent with WNND. Brain and cervical spine MRI were normal. Two weeks after his febrile illness, he developed painless weakness of bilateral arm abduction and was referred to our center. His exam was notable for asymmetric weakness of the bilateral shoulder girdle muscles with normal strength elsewhere. The remainder of his neurologic exam was normal. Nerve conduction studies were normal. Electromyography showed severe denervation in the distribution of the bilateral suprascapular and left axillary nerves. A repeat evaluation, six months from onset, showed evidence of interval reinnervation in the distribution of the right suprascapular and left axillary nerves, but there was no evidence of interval reinnervation in the distribution of the left suprascapular nerve. Therefore, a left-sided direct end-to-end coaptation/neurotization of the distal spinal accessory nerve to the suprascapular nerve was performed.

Results: There was clinical and electrodiagnostic evidence of substantial recovery at 6, 12, and 18 months post-neurotization. At 18 months post-neurotization, he graded his recovery as 90% of his premorbid baseline.

Conclusion: Herein, we present the first successful nerve transfer for WNV-BP. The natural history of this entity is unclear, but the limited data available to date suggests that spontaneous recovery is often poor.9 Neurotization warrants further investigation as a treatment option in patients with WNV-associated brachial plexitis and/or acute flaccid paralysis, particularly those without evidence of spontaneous recovery at 6 months.

Wright, April

Utilization of Standardized Template for Review of Cardiopulmonary Data in Inpatient Sleep Medicine

April Wright, MD, Luqi Chi MD, MSCE

Abstract: The prevalence of sleep disordered breathing in hospitalized patients with comorbid atrial fibrillation, hypertension, chronic obstructive pulmonary disease, heart failure, obesity hypoventilation syndrome, and diabetes mellitus is significant. Additionally, in patients with chronic obstructive pulmonary disease-obstructive sleep apnea overlap syndrome, gas exchange abnormalities often worsen during sleep. Several cardiopulmonary factors can directly affect, both the interpretation of sleep studies and the management of patients with sleep disordered breathing. As a result, having cardiopulmonary data readily available when interpreting sleep studies of hospitalized patients, can be critical. For this project, a template was developed for inpatient sleep medicine consultations. This template included smart links and text prompts for data such as transthoracic echocardiograms, pulmonary function tests, arterial blood gas values, oxygen requirements, chest imaging, and PAP settings. Consultations were reviewed during the six week periods pre and post template to determine which test results were included. Charts were also reviewed to ascertain whether each data point was available at the time of consultation. Implementation of this template did result in an increased percentage of consultations with pertinent data including transthoracic echocardiograms, chest imaging, arterial blood gas values, oxygen requirements, and PAP settings. The percentage of consultations which documented available pulmonary function test results did not increase, although significantly fewer patients had this data available. Therefore, implementation of a permanent standardized template for inpatient sleep consultations, is likely to be beneficial to the care of sleep disordered patients.