

Enrique Alvarez, MD, PhD

(Laura Piccio and Anne H Cross)

Adiponectin Levels in Multiple Sclerosis Patients

Adiponectin, which is a member of the family of adipose tissue-specific hormones known as adipokines, is a secreted protein synthesized by adipocytes and believed to be important in glucose and lipid homeostasis. Insulin increases adiponectin levels, which tends to increase with weight loss. Adiponectin also has anti-inflammatory and anti-atherogenic roles by inhibiting the endothelial cell expression of adhesion molecules including in the blood brain barrier, suppressing the attachment of monocytes, and inducing IL-10 production by human macrophages. Previous work in the laboratory had shown that calorie restriction ameliorates disease severity in the EAE model of multiple sclerosis (MS) and led to significantly increased plasma levels of Adiponectin. Our purpose was to evaluate the levels of adiponectin in MS patients. Serum and CSF samples from patients were collected after consent was obtained. Adiponectin levels were quantitated using ELISA. We found that the levels of Adiponectin in CSF are relatively low compared to those in serum, but higher levels of Adiponectin in CSF are associated with inflammation.

Allan Azarion, MD

Electrographic seizures through anesthetic-induced burst suppression: A case of limbic encephalitis.

This is a case report of a 68 year old Caucasian male who presented with subacute course of personality changes, cognitive decline, complex partial seizures, and generalized tonic clonic seizures. Initial brain MRI showed abnormal high signal intensity on T2-weighted images (T2WI) and fluid-attenuated inversion recovery (FLAIR) in the right mesial temporal lobe. On initial continuous video EEG monitoring, the patient had subclinical and clinical seizures of right temporal onset, with a clinical correlate of behavioral arrest and oral automatisms. After one week of seizure control with valproic acid (VPA) and oxcarbazepine (OXC), the patient's disease progressed to involve the left temporal lobe as evidenced by a follow-up brain MRI showing abnormal high signal intensity on T2WI and FLAIR in the bilateral temporal lobes. Subsequently the patient's EEG began to show left temporal lobe focal electrographic slowing as well as subclinical seizures. Given non-convulsive status epilepticus despite higher doses of both VPA and OXC, burst suppression was induced by phenobarbital and midazolam. The patient continued to have seizures through burst suppression. CSF studies showed mild lymphocytic pleocytosis with negative viral PCR studies. A CSF antibody to a novel neuronal surface antigen was identified, suggesting a previously uncharacterized limbic encephalitis. Electrographic seizures through burst suppression have not been previously reported in the literature.

Debrah Bauer, MD and Karan Johar, MD

PREDICTORS OF FALLS IN INPATIENT REHABILITATION: A QUALITY IMPROVEMENT STUDY

Objective: We conducted a Quality Improvement project to evaluate our facilities current fall screen (Morse Fall Index) and to compare it to other admission variables such as demographics, medical conditions, and the Functional Independence Measure (FIM) scores.

Design: We selected 100 charts for a retrospective chart review which included new admissions from two similar months separated by one year (January 2008 and January 2009). The primary predictor measure was whether the patient had a fall during their admission.

Setting: The setting is The Rehabilitation Institute of St. Louis (TRISL), an 80-bed inpatient rehabilitation facility that serves a variety of patients across several service lines including; stroke, spinal cord injury, brain injury, deconditioning and weakness, and post-surgical patients.

Participants: 104 participants met inclusion criteria for the study. The average age was 57.8 + 17.1 years, 58% were males, 40% were African-American and 52% of this sample had at least one fall during their admission.

Main Outcome Measures: The main outcome was whether the patient fell during their inpatient stay.

Results: Fallers were more likely to use muscle relaxants, were tube fed, had indwelling foley catheters and had more impaired FIM subscores and total FIM scores (except for walking and shower transfer). There was no difference in fallers and nonfallers between a simple sum of the Morse Fall Index or for the weighted summary total scores. ROC curves showed good ability for all FIM measures to individually discriminate between fallers and non-fallers (AUC=.71-.76). Stepwise logistic regression models for predicting falls in our facility included three FIM subscores, including two cognitive scores (comprehension, expression) and bladder management resulting in a 76% correct classification rate.

Discussion: Clinicians should be aware that medications such as muscle relaxants, use of a G-tube, or presence of a foley catheter may indicate an individual who is at risk for a fall in the inpatient rehabilitation setting. However, due to the low prevalence of these conditions, their presence was not able to identify the majority of the patients that fell in our facility. Similarly, the Morse Falls Index was not predictive of falls in our sample. Most FIM subscores were strongly associated with falls, especially those related to cognition and bladder management.

Conclusions: Further study is needed to determine if admission FIM scores are useful in a larger sample and could be used to risk stratify patients at-risk for falls in inpatient rehabilitation settings.

Robert Bucelli, MD, PhD

(Patrick E¹, Wang LH¹, Bucelli RC¹, Alvarez E¹, Lim M¹, DeBruin G¹, Sharma V¹, Benzinger T², Ward BA¹, Ances BM¹.)

¹Washington University School of Medicine, Department of Neurology.

²Washington University School of Medicine, Department of Radiology.)

Diagnostic Evaluation of Patients with Sporadic Creutzfeldt-Jakob Disease (sCJD) and Rapidly Progressive Dementias (RPD) at Barnes Jewish Hospital from 2005-2010

Background: Sporadic Creutzfeldt-Jakob disease (sCJD) is a prion disorder that classically presents as a rapidly progressive dementia. According to WHO criteria, definitive diagnosis of sporadic CJD requires tissue confirmation of the disease via biopsy or at autopsy but is frequently impractical (WHO, 1998). Other modalities commonly used in assisting in the diagnosis include cerebrospinal fluid (CSF) analysis, brain magnetic resonance imaging (MRI), and electroencephalography (EEG). However, the sensitivity and specificity of each method varies (Collins et al., 2006; Wieser et al., 2006; Zerr et al., 2009). We assessed if additional non-invasive diagnostic procedures including brain diffusion tensor imaging (DTI) and polysomnography (PSG) may assist in the diagnosis of sCJD.

Methods: We characterized the clinical, MRI (including DTI), CSF, EEG, and PSG findings in 26 patients evaluated at Barnes Jewish Hospital for possible sCJD over a 5 year period. Additional age and sex matched controls without symptoms of dementia were also used for comparison in imaging studies. For DTI fractional anisotropy (FA) and mean diffusivity (MD) were determined for sCJD, non-CJD, and control subjects within seven brain regions including the right and left: precuneus, posterior limb of the internal capsule, caudate, frontal lobe, corpus callosum, temporal lobe, and pulvinar. An ANOVA was performed for each region of interest with subsequent Bonferroni correction applied ($p < 0.04$). 4 patients with sCJD and 5 non-CJD controls were evaluated by overnight polysomnography.

Results: 12 patients were confirmed to have sCJD by tissue diagnosis with one additional case of probable CJD without tissue confirmation, while 13 cases were diagnosed with other neurological disorders. No significant differences in age or sex existed between sCJD and non-CJD cases. CSF 14-3-3 and EEG were neither sensitive nor specific for sCJD. However, DTI showed significant decreases in FA and increases in MD in sCJD patients when compared to other groups. Sleep efficiency and architecture were severely disrupted in both CJD and non-CJD patients.

Conclusion: DTI and PSG may be additional non-invasive methods to assist in the diagnosis of CJD. Future larger longitudinal studies are required to further evaluate their efficacy.

Collins SJ, Sanchez-Juan P, Masters CL, et al. Determinants of diagnostic investigation sensitivities across the clinical spectrum of sporadic Creutzfeldt-Jakob disease. *Brain* 2006; 129: 2278-2287.

Wieser HG, Schindler K, Zumsteg D. EEG in Creutzfeldt-Jakob disease. *Clinical Neurophysiology* 2006; 117: 935-951.

World Health Organization. Consensus on criteria for diagnosis of sporadic CJD. *Wkly Epidemiol Rec* 1998; 73: 361-365.

Zerr I, Kallenberg K, Summers DM, et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. *Brain* 2009; 132: 2659-2668.

Miguel Chuquilin, MD

Motor Neuropathies and Serum IgM Binding to NS6S Heparin Disaccharide or GM1 Ganglioside

Background: Serum IgM binding to GM1 ganglioside (GM1) is often associated with chronic acquired motor neuropathies. We compared the frequency and clinical associations of serum IgM binding to a different antigen, a disulfated heparin disaccharide (NS6S), with results of IgM binding to GM1 in patients with motor, and other, neuropathies.

Methods: We retrospectively studied serums and clinical features from 75 patients with motor neuropathies who were evaluated at Washington University in Saint Louis. Controls (134) included ALS, CIDP and sensory neuropathies. We also reviewed clinical correlations of positive IgM anti3GM1 testing found in 27 of 2,113 unselected serums from our patients evaluated in our Clinical Neuromuscular Laboratory. Serum testing for IgM binding to NS6S and GM1 used covalent antigen linkage to ELISA plates.

Results: High titer IgM binding to NS6S and GM1 each occurred in 43%, and to one of the two in 64%, of motor neuropathy patients. The presence of motor conduction block in motor neuropathy patients was not associated with the frequency of either antibody. IgM binding to either GM1 or NS6S was more frequent in motor neuropathy patients with serum IgM M3proteins (100%). Motor neuropathy syndromes were present in 25 of 27 patients with high titer serum IgM binding to GM1 in the series of unselected serums from our clinic patients. IgM anti-GM1 or NS6S antibody-related motor neuropathy syndromes usually have asymmetric weakness predominantly involving the distal upper extremities.

Conclusions: IgM binding to NS6S disaccharide is associated with motor neuropathy syndromes and occurs with similar frequency to IgM binding to GM1. Testing for IgM binding to NS6S in addition to GM1 increases the frequency of finding IgM autoantibodies in motor neuropathies from 43% to 64%. IgM binding to NS6S or GM1 in motor neuropathies is more common in the presence of IgM M-proteins. High titers of serum IgM

binding to GM1, tested using a covalent ELISA methodology, have high specificity (93%) for motor neuropathy syndromes.

Michael Ciliberto, MD

(Powers A⁺, Limbrick D⁺, Munro R⁺, Smyth M⁺)

Palliative Hemispherotomy in patients with Independent Bilateral Seizure Onset

Background: Intractable epilepsy is a significant burden on families and the development and quality of life of patients. Surgical options are generally considered in patients with unilateral EEG abnormalities or MRI lesions and in some institutions are contraindicated in individuals with independent bilateral seizure onset. In intractable epilepsy however, a palliative hemispherotomy has been shown to lead to a significant increase in cognitive outcomes and quality of life.

Methods: In this retrospective case series, we report eight patients with independent bilateral seizure onset noted on routine and/or video-EEG monitoring. We note surgical complications, quality of life, neuropsychological, and seizure outcomes.

Results: Seven of eight patients (87.5%) achieved an Engel Class I or II level of seizure control. There were no significant complications to the surgery. Two patients (25%) had an improvement in neuropsychological parameters. One patient developed a hemiparesis. All patients noted a subjective increase in quality of life and do not regret the surgery.

Conclusion: Hemispherectomy for medically intractable epilepsy can be of significant benefit to patients who undergo this procedure. It is generally reserved for patients with unilateral MRI lesions or epileptiform abnormalities. We present 8 patients who benefitted from surgery despite independent bilateral seizure onset. Therefore, we believe that surgery should be presented as an option for certain patients even if they do not fit heretofore “ideal” candidacy requirements.

Jamika Hallman, MD

(Paciorkowski AR (St. Louis, MO), Ciliberto MA (St. Louis, MO), McDaniel SS (St. Louis, MO), Lenox JA (St. Louis, MO), Shoffner JM (Atlanta, GA), Hyland K (Atlanta, GA), Brunstrom-Hernandez JE (St. Louis, MO))

Cerebral Folate Deficiency in Patients with Cerebral Palsy

Objectives

To estimate the prevalence and identify significant risk factors of cerebral folate deficiency (CFD) in a cohort of patients with cerebral palsy (CP).

Methods

Retrospective chart review of medical records from the CP Center was performed to identify all patients with CSF 5-Methyltetrahydrofolate (5-MTHF) levels checked between January 1, 2009 and December 1, 2009. Patient demographics, characteristics, and laboratory data were obtained. Normative data provided by the laboratory performing the CSF 5-MTHF testing was used to compare levels between patients and controls. Descriptive and statistical analyses were employed.

Results

76 patients had CSF 5-MTHF levels measured. 18 patients had 5-MTHF levels <48 nmol/L (1st quartile) with 11 (14.5%; age 2- 46 years) having levels <40 (below the reference range). Mean 5-MTHF levels were significantly lower in two CP age groups (5 to 10 years and >15 years) compared to controls. A significant correlation was found between hydrocephalus and low 5-MTHF levels ($p < 0.001$); 8 of 9 (89%) patients with hydrocephalus (shunted) had levels below 32. No correlation was found between MTHF levels and CP subtype, tone abnormality, movement disorder, gestational age, GMFCS, epilepsy, or periventricular leukomalacia.

Conclusions

CFD, a treatable cause of neurologic dysfunction, is common among patients with CP and hydrocephalus is a major risk factor for CFD among these patients. Many symptoms of CFD are found in patients with CP including abnormalities of tone, movement, gait, sleep, cognition, behavior and epilepsy. Evaluation for CFD should be considered in patients with CP, particularly those with hydrocephalus.

Miranda Lim, MD, PhD

(Jae-Eun Kang, Liam P. Smyth, Randall J. Bateman, David M. Holtzman)

The sleep-wake cycle affects amyloid-beta deposition in a mouse model of Alzheimer's Disease

Amyloid-beta accumulation in the brain extracellular space is a hallmark of Alzheimer's disease. Previous studies using in vivo microdialysis in mice have shown that the brain interstitial fluid levels of amyloid-beta correlate with the sleep-wake cycle. Amyloid-beta levels are highest during wakefulness, acute sleep deprivation, and during orexin infusion; they are lowest during both physiologic sleep and with the administration of sleep-inducing drugs such as a dual orexin receptor antagonist.

The goal of these experiments is to determine whether chronic sleep restriction or sleep enhancement can affect long-term amyloid-beta plaque deposition in a transgenic mouse model for Alzheimer's Disease. We found that chronically sleep restricted mice showed significantly greater amyloid plaque burden compared to age-matched controls. Conversely, mice that underwent pharmacologic enhancement of sleep showed significantly less amyloid plaque burden compared to age-matched controls. These results suggest that sleep and orexin could play a role in the pathogenesis of neurodegenerative disease, and optimization of sleep could be a potential target for therapeutics.

Sharon McDaniel, MD

(Nicholas R. Rensing, Liu Lin Thio, Kelvin A. Yamada, and Michael Wong)

The ketogenic diet inhibits the mammalian target of rapamycin (mTOR) pathway

Rationale

The ketogenic diet (KD) is an effective treatment for pediatric epilepsy, and although it has been in use for nearly a century, its mechanisms of action remain poorly-understood. Unlike other treatments for epilepsy, there is evidence that the KD possesses antiepileptogenic as well as anticonvulsant properties. mTOR is a protein kinase that regulates numerous cellular functions including growth, proliferation, survival, and synaptic plasticity. mTOR is activated by PI3K/Akt signaling in the presence of nutrients and growth factors, and inhibited by AMPK in the setting of energy starvation. Dysregulated mTOR signaling has been implicated in epileptogenesis in models of genetic and acquired epilepsies including tuberous sclerosis complex (TSC) and kainic acid (KA)-induced status epilepticus (SE). Given the ability of mTOR to integrate nutrient and energy signals, we investigated the effects of the KD on mTOR pathway signaling in normal animals as well as rodent models of epilepsy.

Methods

Sprague Dawley rats were given ad libitum access to KD (F3666; Bioserv, Frenchtown, NJ) or standard diet (SD) beginning at P21. For the KA model, rats were injected with 15mg/kg KA i.p. to induce SE, and started on KD or SD after resolution of SE. For TSC experiments, conditional GFAP *Tsc1* knockout mice (*Tsc1*^{GFAP}CKO) and littermate controls were weaned to KD or SD at P21. mTOR activity was assessed using western blot (WB) for phosphorylation of its downstream target S6 (pS6) compared to total ribosomal protein S6. Upstream signaling was evaluated by WB for phospho Akt (pAkt), total Akt, phospho AMPK (pAMPK), and total AMPK. Tissue was harvested for WB after two weeks of KD or SD in

normal rat and TSC experiments, and 1, 7, or 21 days after SE in the KA model.

Results

In normal rats, KD reduced pS6 and pAkt in hippocampus (24% and 14%, respectively, $p < 0.05$ for both) and liver (45% and 54%, $p < 0.05$ for both), but not neocortex. KD increased pAMPK only in liver ($p < 0.001$). *Tsc1*^{GFAP}CKO mice on SD had higher pS6 ($p < 0.01$) and lower pAkt ($p < 0.05$) than controls. KD decreased pS6 and pAkt in combined neocortex and hippocampus of control mice (22% and 19%, $p < 0.05$ for both), but not *Tsc1*^{GFAP}CKO mice. There was no effect of KD on brain pAMPK in control or *Tsc1*^{GFAP}CKO mice. KA-induced SE increased hippocampal pS6 acutely and at 7 days, with return to baseline by 21 days, and KD blocked this elevation at 7 days.

Conclusions

KD inhibited mTOR activity in hippocampus and liver of normal rats, most likely via decreased Akt signaling in both regions, as well as increased AMPK signaling in liver. KD also inhibited mTOR in control mouse brain. In contrast, KD had no effect on mTOR hyperactivation in the TSC model, possibly due to an inability of KD to bypass the genetic inactivation of *Tsc1*. However, in the KA model, KD blocked the SE-induced mTOR activation. As pharmacological inhibition of mTOR by rapamycin prevents epilepsy in some models, these results suggest that the KD may also have antiepileptogenic actions via inhibition of the mTOR pathway.

Alex Paciorkowski, MD

(Christina Gurnett, Shashikant Kulkarni, William B. Dobyns, Liu Lin Thio)

Infantile Spasms Registry & Genetic Studies: Preliminary report on EEG data and power analysis of sample size

Objective: Infantile spasms (ISS) are a group of disorders with unresolved questions concerning etiology and outcome. A disease registry of adequate sample size has the potential to address these questions.

Methods: An international, parent-centered, web-based registry for patients with ISS was implemented. A novel EEG score was derived to quantify hypsarrhythmia. Power analysis was performed using t-test to calculate sample size (power=0.8; significance level=0.05) required for clinical outcome questions.

Results: *Subjects:* 40 subjects from 6 states and 5 countries have enrolled in the registry. Of these 19 are male, 21 are female, and the mean age at enrollment is 2.8 years. Mean developmental score was 8.1 (score of 13=normal development). 25 subjects are genotype-unknown and 15 are genotype-known, including 8 subjects with trisomy 21 and infantile spasms. *EEG:* 11 patients had Level 1 EEG evidence, 2 patients had Level 2 EEG evidence. Of subjects with Level 1 and 2 EEG evidence, none had classical hypsarrhythmia, 12 had modified hypsarrhythmia, and 1 did not have hypsarrhythmia. *Power analysis:* 198 subjects will be required to determine whether degree of hypsarrhythmia is associated with autism, movement disorder, or intractible epilepsy.

Conclusions: The ISS Registry defines a cohort for further clinical/genetic studies, treatment trials, and includes a subgroup of children with trisomy 21 and ISS. Most subjects had modified hypsarrhythmia, and a quantifiable EEG scoring system will allow correlation with outcome. Power analysis for sample size indicated 198 subjects will be needed for selected outcome questions.

Alex Paciorkowski, MD

(Liu Lin Thio, Christina Gurnett, Shashikant Kulkarni, Wendy Chung, Eric Marsh, William B. Dobyns)

Bioinformatic analysis of published and novel copy number variants suggests candidate genes and networks for infantile spasms

Objective: Infantile spasms (ISS) are a developmental epilepsy (DEVE) that overlaps Ohtahara syndrome and early myoclonic epileptic encephalopathy. Several causative genes for ISS/DEVE have been identified through copy number variants (CNVs) and/or genomic translocations, including CDKL5, MAGI2, MEF2C, and STXBP1. A major challenge of genomic disorders is the evaluation of large amounts of gene content data to identify potentially causative genes. Bioinformatic analysis of published and novel CNVs and translocations may identify candidate genes for further study and reveal gene networks that explain pathogenesis.

Methods: (1) *Identification of CNVs from the literature.* Search of all PubMed indexed abstracts and Decipher to identify published CNVs and translocations in patients with ISS/DEVE. (2) *Identification of novel CNVs.* Clinically obtained de novo chromosomal microarray (CMA) results from subjects with ISS/DEVE were referred to the Infantile Spasms Registry & Genetic Studies. (3) *Bioinformatic analysis of CNV gene content.* Gene content in published and novel CNVs was organized using the Chromosomal Locus Evaluation Workspace (CLEW 1.0), a PHP/Perl software linked to a MySQL database. Molecular function for each gene was determined from the Gene Ontology database. Gene expression in the brain was evaluated using mouse databases BGEM, GENSAT, MGI, and the cumulative summaries available at ArrayExpress and BioGPS. PubMatrix was used to search PubMed for evidence of a role for identified brain-expressed genes in specific stages of brain development. (4) *Network analysis.* Candidate genes in the 1p36 locus were evaluated for network relationships using GEDI and relationships between nodes (genes) were then manually verified. Networks identified were visualized using String 8.2.

Results: (1) Literature search identified 10 published CNVs at 1p36, 2p22.1p21, 4p16.1-4pter, 12p, 13q21.2q31.2, 14q32, 15q11q13, 16p11.2, 19p13.13, Xq26.3, and 4 translocations at (1;7)(p13.3;q31.3), (2;6)(p15;p22.3), (2;6)(q34;p25.3), (6;14)(q27;q13.3). (2) Seven novel CNVs were identified at 2p16.1p15, 3p26.3, 14q32.33, 19q12, 20p13, 20q13.33, 21q21.1q21.2. (3) Bioinformatic analysis of gene content of published and novel CNVs and translocations identified 27 genes from the novel CNVs that were expressed in the brain, and of these 6 genes (BCL11A, CHL1, FKBP1A, NCAM2, REL, and SNPH) had molecular function and CNS expression patterns suggesting a possible role in ISS/DEVE pathogenesis. (4) Analysis of candidate gene content of 1p36 revealed 3 genes (FRAP1/MTOR, HES5, and PIK3CD) related by a common network, and associated with the mTOR pathway. Interestingly, this network also included FKBP1A.

Conclusions: CMA is helpful in identifying loci associated with ISS/DEVE, and yields large amounts of gene content for further analysis. Bioinformatic tools to evaluate gene content require coordination to identify specific candidate genes for sequencing studies. CLEW 1.0 is a method of organizing gene content that is database-linked. Six novel ISS/DEVE candidate genes are reported here. Network analysis of genes deleted at 1p36 revealed an association with the mTOR pathway, and a possible pathogenesis for ISS and brain malformation in deletion 1p36 patients. ISS in deletion 1p36 and 20p13 patients may be due in part to deletions of genes in this network. Similar analysis in other loci may provide additional evidence for network dysfunction in ISS/DEVE.

Peiqing Qian, MD

(Anne H Cross MD and Robert T Naismith MD)

Assessment of Pain in Neuromyelitis Optica

Introduction

Pain is a frequent and disabling symptom among demyelinating diseases. The characteristics of pain in patients with neuromyelitis optica (NMO) have not been defined.

Objective

To characterize pain in NMO, along with its relationship to depression, fatigue, sleepiness, cognition, CNS medication usage, physical and cognitive function.

Methods

Cross-sectional study of those who meet NMO research criteria. Measures included the McGill Pain Score (MPS), the Short Form 36 QOL Scale (SF36), the Center for Epidemiologic Studies Depression Scale (CES-D), Modified Fatigue Impact Scale (MFIS), Epworth Sleepiness Scale (ESS), characterization of pain medications, Expanded Disability Status Score (EDSS), Multiple Sclerosis Functional Compositive (MSFC), and Symbol Digit Modality Test (SDMT).

Results

Pain syndromes of the spinal cord are frequent in NMO. These include: repetitive tonic spasms, tingling and burning in the limbs, a squeezing sensation around the trunk, and radiating sharp pain throughout the body. The average McGill pain score was markedly elevated at 49.5 out of a maximum 78. This was associated with decreases in both the mental (41.8 +/- 11.3) and physical components (25.3 +/- 9.1) of the SF36. Fatigue was also noted (MFIS 43.7 +/- 14.0). Polypharmacy for pain was common, with frequent use of opioid derivatives, anti-epileptics, and tricyclic antidepressants. Depression was also common (CES-D 22.3 +/- 13.0), as was use of anti-depressant medication.

Conclusions

Patients with NMO will frequently have pain. This may contribute to a lower mental quality of life, increased fatigue, and worse depression. Many patients would describe their pain as one of the most disabling symptoms of NMO. Treatment of pain and other symptoms can be effective, and deserves special attention in clinic visits. Despite the use of multiple medications for pain, very few would characterize the response as excellent.

Tomoko Sampson, MD, MPH

(Rajat Dhar, M.D.¹, Gregory J. Zipfel, M.D.^{1,2})

Departments of Neurology¹ and Neurosurgery²)

Cerebral infarction following a seizure in a patient with subarachnoid hemorrhage complicated by delayed cerebral ischemia

Background: Seizures are a recognized complication of subarachnoid hemorrhage (SAH). They can increase cerebral metabolic demands and lead to cardiopulmonary compromise. This could be detrimental in the setting of delayed cerebral ischemia (DCI), when brain tissue is vulnerable to further reductions in oxygen delivery or increases in demand. An association between seizures and worsening ischemia could influence the decision to use antiepileptic drug (AED) prophylaxis in patients with vasospasm.

Case Description: A 64 year-old woman developed confusion, aphasia, and right hemiparesis on day 7 after aneurysmal SAH. Angiography confirmed severe anterior circulation vasospasm. She initially responded to hypertensive therapy with almost complete resolution of her ischemic neurological deficits. However, on day 10 she had a single generalized seizure and required intubation for airway protection. Her blood pressure dropped with AED initiation, necessitating an increase in previously stable dose of vasopressors. She developed aphasia and worsening hemiparesis that did not resolve despite hemodynamic augmentation. Subsequent head CTs revealed new infarction in the left anterior cerebral artery territory not present previously. She had received prophylactic phenytoin for only 3 days, as per our SAH protocol.

Conclusion: AED prophylaxis is typically used early after SAH when risk is high and a seizure may precipitate aneurysmal rebleeding. This case illustrates how a later seizure in the setting of vasospasm can lead to decompensation of DCI, with potential for irreversible infarction. Therefore, patients with vasospasm may benefit from extended durations of prophylaxis to prevent such complications.

Victoria Sharma, MD

(Gabriela deBruin, MD)

Amyloid- β -Related Angiitis – An Unusual Cause of Transient Recurrent Neurological Symptoms

Amyloid- β -related angiitis is a rare form of primary CNS angiitis caused by vascular deposition of β -amyloid (β A). It is believed to be a distinct entity from cerebral amyloid angiopathy and to share some characteristics with primary CNS vasculitis. Clinical presentation varies and may include confusion, headache, seizures, and transient focal neurological symptoms. Treatment with steroids and other immunosuppressants has been found to be effective.

We present a case of a 69 year-old male who presented with transient, recurrent right arm and face weakness, numbness, paresthesias, and dysarthria. He had a negative TIA workup including a conventional angiogram. Video EEG monitoring during the episodes in question did not reveal any epileptic activity. However, the episodes subsided once anti-epileptic therapy was initiated. Brain MRI showed left parietal, temporal, occipital and right temporal T2 hyperintensities, subarachnoid hemorrhage, and leptomeningeal enhancement. He underwent a brain biopsy which revealed β A deposition within the cerebral cortex vessels and leptomeningeal vessel walls. There was also leptomeningeal vessel angiitis with a marked inflammatory infiltrate. The patient received steroids with improvement in symptoms and a follow brain MRI showed resolving lesions.

Transient neurological deficits in the elderly that are not otherwise explained present a diagnostic challenge and should raise suspicion for amyloid- β -related angiitis.

Mathula Thangarajh, MD

(Marcus Kessler[‡], David Loy[‡], and Todd Schwedt^{*})

^{*}Department of Neurology, Washington University School of Medicine, Saint Louis, MO 63110;

[‡]Mallinckrodt Institute of Radiology, Washington University School of Medicine, Saint Louis, MO 63110)

Dural arteriovenous fistula as an unusual cause of reversible encephalopathy

A 54 year-old right-handed man presented with a one-week history of confusion, behavioral change, and loss in work-related productivity. His neurological examination was notable for short-term memory loss, inability to do serial subtractions, and a right pronator drift. Complete blood counts and metabolic panel were normal; HIV, RPR, and vasculitic work-up were negative. Cerebrospinal fluid analysis was normal except for mild elevation in protein. Brain magnetic resonance imaging (MRI) showed T2 hyperintensities in both thalami, and in the medial occipital lobes. Cerebral angiogram revealed a dural arteriovenous fistula (AVF) with multiple feeding vessels in the region of the vein-of-Galen. He underwent Onyx embolization of the dural AVF with complete obliteration of the feeding vessels. At his follow-up visit three months after the embolization, he was noted to have improvement in his neurological symptoms. Follow-up brain MRI showed partial resolution of bilateral thalamic hyperintensities. Dural AVF with venous hypertension can be a rare but reversible cause of acute encephalopathy.

Ford Vox, MD

Digital Plasticity: Brain-Computer Interfacing After Stroke

Our successful trials of ipsilateral cortical control of a computer program with BCI-2000 processed EEG signals in stroke patients with severe corticospinal tract damage points to the feasibility of interfacing exoskeletal functional orthoses and the design of acute rehabilitation trials. A discussion of the theory and our initial testing results on several stroke subjects.