Neuroscience Day 2009 Abstracts

Aaron Mammoser- Bevacizumab (Avastin) is an important treatment option for high grade gliomas and possibly for cerebral radiation necrosis. Bevacizumab administration is associated with a small risk of DVT/PE and bleeding, including intracranial hemorrhage. Of clinical concern is whether the risk of intracranial hemorrhage from Bevacizumab is increased when therapeutic anticoagulation is concurrently administered to treat patients with a DVT /PE. We retrospectively reviewed glioma patients treated with Bev who also had a DVT/PE managed with therapeutic anticoagulation. We determined the frequency of recurrent DVT/PE and of bleeding complications, including ICH.

Amanda Rabquer- Proximal EMG Tests in patients with multifocal motor neuropathy and motor neuron disease

Unfortunately, lower motor neuron disease (LMND) remains an untreatable disorder that results in progressive limb weakness. LMND may mimic an inflammatory demyelinating multifocal motor neuropathy (MMN). It is important to accurately differentiate patients with MMN, which is treatable with immune modifying therapy, from patients with LMND. In order not to misdiagnosis MMN patients as erroneously having LMND, many patients who present with symptoms of either disorder are treated with immune modifying therapy, intravenous immunoglobulin (IVIG). IVIG therapy is an extremely expensive treatment that has potential side-effects including anaphylaxis, chemical meningitis, renal failure, and thrombotic events. After treatment with IVIG therapy, those patients who respond to treatment with improved motor strength are diagnosed with MMN and those who do not respond to treatment, LMND. Therefore, diagnostic tests that would accurately distinguish between patients with MMN or LMND would be very useful.

Electromyographic (EMG) testing is done to look for electrophysiologic evidence of demyelination seen in MMN but not in LMND. EMG evidence of demyelination includes prolonged proximal motor nerve responses called F-waves. Whether or not this standard EMG test, F-waves, can differentiate MMN from LMND is unknown. We hypothesized that F-wave EMG tests are useful in predicting patients ultimately diagnosed with MMN, as evidenced by a positive response to IVIG therapy, rather than LMND. Therefore, we performed a retrospective data analysis of 34 patients. Proportions and means with standard deviations were calculated for baseline clinical characteristics and demographic variables. Univariable logistic regression was used to assess the relationship between having the diagnosis of MMN and the following variables: one nerve with an abnormal F-wave, one nerve with definite conduction block, or one nerve with probable conduction block. The statistical analysis is underway at this time. The results of this study may alter clinical practice in identifying patients who will best respond to IVIG therapy. It would also provide information regarding patients who may not need to be exposed to the potential side-effects of IVIG therapy.

Angela Mark- **A randomized crossover study of standard NIPPV and low expiratory pressure NIPPV in ALS patients**

Introduction: Tolerance to noninvasive positive pressure ventilation (NIPPV) prolongs survival and improves quality of life in ALS patients with respiratory muscle weakness. Yet, only a small proportion of ALS patients who meet American Academy of Neurology practice parameter guidelines for NIPPV treatment are actually using the therapy, in large part due to NIPPV intolerance. Methods for improving ALS patient NIPPV tolerance are desperately needed.

One reason for NIPPV intolerance may be the requirement to breathe out against expiratory positive airway pressure (EPAP), likely increasing dyspnea and respiratory fatigue. EPAP is used in standard bi-level NIPPV machines to prevent CO_2 re-breathing. However, portable lap-top ventilators eliminate the possibility of re-breathing expired CO_2 by having two separate circuits for inspiration and expiration. This allows NIPPV to be administered as IPAP (inspiratory positive airway pressure) only.

Objective: to conduct a randomized, crossover study comparing standard NIPPV with IPAP-only NIPPV, with respect to objective NIPPV use, quality of life, patient satisfaction, and side effects.

Methods:

Study subjects: 18 patients with probable or definite ALS who have been using NIPPV for 2 months or more will be recruited from the University of Michigan , Motor Neuron Disease clinic. Patients must also have a maximal inspiratory force (MIF) < 60 cm/H_2O or forced vital capacity (FVC) < 50% predicted.

Study Design: The study is a randomized, crossover study of two different NIPPV settings. Subjects will be randomized on a 1:1 basis to one of two groups differing in the sequence of NIPPV settings ((a) standard followed by IPAP-only or (b) IPAP-only followed by standard). Subjects will then spend 6 weeks using the first NIPPV set-up before crossing over to the other NIPPV treatment for 6 weeks. Viasys Healthcare lap-top ventilators will be used to provide both the standard and IPAP-only treatments. For standard treatment, IPAP and EPAP will be set to the patients¿ current, bi-level IPAP and EPAP settings. For IPAP-only treatment, IPAP will be reduced by 4 cm H_20 and EPAP will be lowered to 0 cm H_2O to maintain the identical pressure support.

Study Outcomes: The primary outcome is NIPPV use, as summarized by weekly means and standard deviations of objective hours of use for the two NIPPV set-ups (standard and IPAP-only) over weeks 2-6 of each treatment period. Secondary outcomes measured at the end of each treatment period include quality of life, dyspnea, and patient satisfaction, measured with validated scales.

Statistical Methods:

Sample Size: Eighteen subjects are required to detect a 2-hour difference in the primary outcome assuming the following: power of 80%, an alpha = 0.05, with 2-sided testing. This is based on the assumption that the within-patient standard deviation of the response variable is 2 hours, and there will be negligible carryover effects.

Analysis Plan: The primary analysis will be conducted using repeated measures analysis of variance. The treatment effect will be adjusted for time period to account for any increase in NIPPV through the study period due to, for example increased respiratory muscle weakness. This adjustment is conducted by including a main effect for period in the model. Treatment effect will be tested at the 0.05 significance level. Quality of life and dyspnea, secondary outcome measures, will also be analyzed in a similar fashion with a repeated measures analysis.

Conclusion: Funding (ALS Association, PI: Gruis) and IRBMED approval were secured. Enrollment has begun. An update on the first 7 enrollees will be provided.

Anthony Wang- Imaging of Intrinsic Optical Signals in Human Neocortex: A Quantitative Analysis

The optical properties of cortical tissue are known to vary as a function of neuronal activity. The technique of using these optical changes to map neuronal activity is known as Imaging of Intrinsic Optical Signals (IIOS). One potential application of IIOS is in the localization of epileptogenic neocortex. Limited accuracy in mapping neocortical epileptogenic tissue has long hindered improvement of outcomes in patients being treated for neocortical epilepsy by surgical resection. In order to develop IIOS as a viable intraoperative tool for epilepsy surgery, it is necessary to determine if optical imaging can reliably identify epileptic activity. To this end, the optical changes must be characterized quantitatively with statistical linear models, according to their association with afterdischarge activity.

Purpose: To quantitatively characterize distinguishing properties of activity-evoked optical signals that can be used to reliably identify epileptic activity in human neocortex.

Methods: Data recorded prospectively from 15 patients undergoing surgical resection for treatment of intractable neocortical epilepsy were analyzed. In each of these experiments, the minimal electrical stimulation required to reliably elicit ictal (i.e. afterdischarge) activity was first determined. Data from 10 such stimulation trials, from which the stimulation current was 16mA, were used to quantify the optical properties associated with ictal activity. Regression analyses were performed to study correlations between the duration of afterdischarge activity, as determined by simultaneous surface EEG recordings, and the magnitude and duration of the optical signal.

Results: 159 trial runs from 34 surgical patients were analyzed. Regression analyses revealed statistically significant linear positive correlations between the duration of ictal activity and the maximum percentage change of the optical signal ($p < 0.001$), as well as with the duration of the optical signal ($p < 0.001$). Surprisingly, there did not appear to be a significant relationship between the recorded stimulation current and the duration and amplitude of the optical changes, across the entire population. All of these results held true for both groups of trial runs---those with epileptiform afterdischarge activity, and those without.

Once the absolute amplitude of the stimulation current had been corrected using the described method, a linear positive correlation between the magnitude of stimulation current and the maximum percentage change of the optical signal ($p < 0.001$) was identified. 3 points were excluded as outliers, due to extremely high stimulation current magnitudes, though they would not have affected the correlation.

With the measured absolute magnitude of the stimulation current, a statistically significant linear positive correlation between magnitude of stimulation current and the maximum percentage change of the optical signal ($p < 0.05$).

Conclusion: These data suggest quantitative linear relationships between the duration of ictal activity and the magnitude and duration of the optical signal. In addition, the magnitude of stimulation and the resultant optical change are also linearly related, as indicated by our data. This relationship is distinct for epileptiform afterdischarge activity, when compared with that of solely stimulation-evoked electrical activity. Our results imply that both the magnitude and duration of activity-evoked optical signals, as a function of current, provide an objective measure for the identification of epileptic activity with IIOS. These new findings, in addition to ongoing characterization, will be used to create spatial maps of epileptogenic neocortex. Potential benefits of further refinement of this imaging modality include elimination of the initial surgical implantation of an electrode array in the current treatment for intractable epilepsy. In addition, the spatial resolution afforded by IIOS might allow for a dramatic reduction in the amount of cortical tissue resected.

Beata Ruprecht- Evaluation of staring spells in children and adolescents, a pilot study.

Background: Staring spells are a common presenting symptom in children and adolescents referred to the pediatric neurology clinic for evaluation. The differential diagnosis of staring spells is broad, and it is not always obvious simply from clinical history as to the etiology and nature of the spells. These could range from epileptic seizures (either absence or complex partial), to non-epileptic spells of inattention, part of stereotypic spells, etc. Various techniques are employed to assist in diagnostic evaluation, but it is not clear which test(s) are optimal to arrive at a diagnosis.

Objective:

1. To describe various diagnostic techniques used in the diagnostic evaluation of staring spells.
2. To describe the prevalence of the various final diagnoses made after the diagnostic evaluation of staring spells.

Methods: The study design will be a retrospective review of the medical data of pediatric patients referred for the evaluation of staring spells, behavioral arrest, spells of unresponsiveness and absence seizures. Medical records will be reviewed to obtain clinical information about the spells, and assess what diagnostic testing is ordered for further evaluation of the spells. The outcome of the test(s) and the final diagnosis as to the nature of the staring spells will also be assessed. For the initial pilot study, data from patients seen in our clinic from January 1, 2009 through March 31, 2009 will be reviewed. The ultimate goal is to include 100 subjects from the Pediatric Neurology clinic as the study cohort.

Significance: This study will provide important information with regards to prevalence of various conditions that can present as staring spells. It may also help to determine preferred diagnostic testing, and possibly which tests are more cost-effective.

Brian Abaluck- Changes in Cognition During and After Internship

Research Protocol

Goals of the study

5-1.1 Objectives: The goals of this prospective cohort study are to assess changes in cognition across medical internship and to evaluate the roles of sleep deprivation, mood changes, and sleepiness as partial mediators of changes in cognition.

5-1.2 Specific Aims:

Aim 1. To assess cognitive functioning before, during, and after frequent call nights that are required during one year of medical internship (n=17 interns) or absence of overnight call during one year of dental residency (n=4 residents). Medical interns and dental residents have similar levels of education.

Hypothesis 1. Compared to dental residents, cognitive functioning in medical interns will show greater decline after several months (2nd time point) and one year (final time point) of training.

Aim 2. At similar time points and in the same groups, assess subjective sleepiness and depression.

Hypothesis 2a. After baseline measurement, medical interns in comparison to dental residents will show greater subjective sleepiness and depression.

Hypothesis 2b: In statistical models, sleepiness and depression will each partially account for differences in cognitive performance observed between physician interns and dental trainees.

Brian Callaghan- Remission and relapse in an adult refractory epilepsy population

Rationale: To investigate remission and relapse in a refractory epilepsy population followed prospectively.

Methods:

In 2000 we identified a cohort of 246 patients at the University of Pennsylvania Epilepsy Center who met a pre-specified definition of drug refractory epilepsy (failure of at least two antiepileptic drugs and seizure frequency greater than once per month). Median age at entry was 40, mean duration of epilepsy was 25 years, and mean duration of intractability was 20 years. We have now followed this cohort for over six years. Follow-up methods included chart review, and for those not seen within the past year, additional attempts at direct contact using last known phone number. We used Kaplan-Meier methods to estimate the cumulative risk of achieving a 12-month seizure remission and subsequent relapse. Cox regression analysis was used to evaluate clinical predictors for seizure remission and relapse.

Results:

At 7 years, the estimated cumulative incidence of 12-month seizure remission was 35% (95% confidence interval, 26-44%) for all cases and 33% (95% confidence interval, 25-44%) when limited to those treated only with medication. For the subset of patient who underwent surgery, the cumulative risk for 12-month seizure remission at 4 years was 45% (95% confidence interval, 16-41%). The cumulative risk of relapse in the entire cohort was 56% (95% confidence interval, 42-70%) by 2 years after achieving a one year remission and 71% (95% confidence interval, 55-86%) by 5 years. Negative predictors of remission included mental retardation, symptomatic generalized epilepsy, duration of intractability, and number of antiepileptic medications failed. The only statistically significant negative predictor of relapse was localization related epilepsy.

Conclusion: Among patients with refractory epilepsy, the cumulative risk for remission continues to be substantial over a long period of follow up. Followin g remission, the cumulative risk of relapse in this population is also significant with a large proportion occurring even after the first year of remission. Intere stingly, approximately four fifths of relapses after a significant remission occur within the first two years after achieving a one year seizure remission. Epilep tologists should be cautious when counseling drug refractory patients about possible cure or when recommending return to driving.

Chris Fox- Factors Associated with Vasospasm Refractory to Endovascular Therapy

Introduction: We define refractory vasospasm as that which requires more than one endovascular treatment based upon clinical examination and radiographic imaging. The pathophysiology and risk factors as well as the best method of treatment for this devastating condition are unclear.

Methods: We retrospectively reviewed our clinical database to evaluate the rate of refractory vasospasm in patients treated for ruptured intracranial aneurysms between January 2006 and August 2007. Type and number of endovascular treatments, aneurysm location, presenting Hunt Hess and Fischer score, open versus interventional aneurysm treatment, demographic, and outcomes data were evaluated using Fisher¿s, chi-square and student t-test analysis.

Results: 48 patients and 97 interventional procedures for vasospasm were identified. 22 patients (46%) had refractory vasospasm. 30 patients (63%) had their aneurysms clipped; 16 (33%) underwent endovascular coiling. Angiography negative subarachnoid hemorrhage occurred in 2 patients (4%). 37% of post-clipping versus 56% of coiled patients were refractory to treatment (p=0.23). Death occurred in 23% of patients with refractory vasospasm. Patients with refractory vasospasm were significantly more likely to undergo balloon angioplasty (p=0.04). There were no statistically significant differences in patient demographics, post-bleed day, clipping versus coiling, aneurysm location, intraarterial verapamil dose during first treatment, or death.

Conclusion: In this series, 46% of patients with vasospasm were refractory to endovascular treatment. These patients are significantly more likely to receive aggressive therapy with balloon angioplasty in

combination with other strategies such as intraarterial medication. In addition, we often treat patients with refractory vasospasm on multiple occasions, especially those whose interventional treatments consist of intraarterial medication alone (patients who have not undergone balloon angioplasty). In these patients, the effect of intraarterial medications such as verapamil often lasts less than 24 hours, and multiple treatments may prevent vasospasm-induced stroke. It remains challenging to predict which patients will develop refractory vasospasm. Further investigation is necessary and may help identify those patients at risk for this difficult problem.

Eric Adelman- Patient Initiated Device Removal in the Neurosurgical ICU

Introduction

Neurosurgical ICU patients have multiple devices placed over the course of a hospitalization. These patients often suffer from delirium as a result of their underlying disease. This confusion can lead to inadvertent removal of indwelling devices, which not only puts the patient at risk for complications, but is also costly. Restraints are often used to ensure the safety of agitated patients.

Background

Prior studies have shown that nasogastric tubes are the most commonly removed device, followed by vascular catheters. In some series, nasogastric tubes were accidentally discontinued in up to 40% of patients. Instructing staff to be vigilant about optimal restraint use (keeping hands >20cm from device) reduces the rate of device discontinuation.

Patients will frequently remove devices despite being restrained. This often occurs at night, in the setting of agitation. Predictive factors for device removal include longer duration of ICU stay, increasing amounts of sedation, and less time on mechanical ventilation. In one 20 bed study, annual cost of device removal was about $250,000. In this study, 8% of patients accounted for 70% of removals and 76% of the cost.

No studies have had a large number of neurology or neurosurgery patients.

Methods

We collected data every nursing shift (12 hours), for every patient in February 2008. Information collected included number of devices, if a device had been self-discontinued, and the circumstances surrounding the removal. Devices included: arterial catheters, central venous catheters, endotracheal tubes, nasogastric tubes, peripheral IVs, PICC lines, and ventriculostomies. The frequency of accidental device removal was calculated.

Results

There were a total of 1745 device-shifts. Fifteen devices were accidentally removed. The majority of these were nasogastric tubes (n=9). The remaining were: arterial catheters (n=2), ventriculostomies (n=2), peripheral IV (n=1), and unspecified (n=1). No central venous catheters, endotracheal tubes, or PICC lines were removed. Circumstances surrounding device removal included: loose restraints; removed despite restraints; removed despite staff intervention; tape failure; excess movement; and patient unawareness.

Conclusions

Inadvertent device removal is uncommon in our neurosurgical ICU. Our study has several important limitations. We do not have data on the frequency of individual device placement. Because we lack this denominator information, we are unable to calculate the rate of accidental removal by device type. We also do not have individual patient data to determine if a single patient removed multiple devices. A strength of our study is that it included an entire ICU, not just a subset of patients as in many other studies.

Further research will focus on what factors keep patient initiated device removal rates low in our NICU as well as effective use of restraints to minimize accidental device removal.

Fauziya Hassan- Sufficient sleep may be more common among overweight than non-overweight asthmatic children.

Introduction: Asthma in adults is associated with overweight and poor quality sleep, but these relationships have scarcely been studied in children. We used a nationally representative U.S. survey data to examine retrospectively whether caregiver-defined ¿sufficient¿ sleep differed between asthmatic children with higher or lower body mass index (BMI), after adjusting for sociodemographic variables and asthma severity.

Methods: The 2003 National Survey of Children¿s Health included question-items on demographics, height and weight, doctor-diagnosed asthma and number of nights of sufficient sleep (0-3, 4-7) obtained in the past week as perceived by a caregiver. Subjects were divided into 2 subgroups by BMI z-scores (adjusted for age and gender). Normal weight was defined as 5^{th}-84^{th} percentile; at risk or overweight as a BMI ¿ 85^{th} percentile.

Results: In 2003 among 6,908 asthmatics aged 6-17 years, unadjusted bivariate logistic regression showed that overweight or at risk children in comparison to those of normal weight had higher odds of having 4-7 nights per week of sufficient sleep (OR=19.6, 95% CI: 4.0-98.0). In a logistic regression model that adjusted for race, gender, income, household education and asthma severity, the association persisted (OR=6.0, 95% CI: 1.1-35.3).

Conclusion: Data from this nationally representative dataset indicate that asthmatic children who are overweight or at risk may obtain more rather than less sleep than their counterparts who have normal BMI. These surprising results highlight the importance of developing a better understanding of complex and probably bidirectional relationships between asthma, sleep and overweight.

Heidi Orme-

Abstract: Dropped head syndrome (DHS) is characterized by severe neck extensor muscle weakness, resulting in a chin-on-chest deformity in the standing or sitting position, which is correctable by passive neck extension. It may be a prominent sign in several neuromuscular conditions and can involve multiple sites of pathology such as the motor neuron, peripheral nerve, neuromuscular junction, or muscle. Some of these conditions presenting with DHS are progressive, and may even have a grave prognosis, whereas others are medically treatable. We present four cases of dropped head syndrome from our neuromuscular clinic. Routine clinical and laboratory data, including electrophysiologic, radiologic, and pathologic studies are reviewed. We review the literature on DHS, emphasizing the broad differential diagnosis, management and outcome, with the goal of providing clinicians with a useful clinical approachto patients presenting with DHS, either in isolation or in association with additional neurologic signs and symptoms.

Jenn Strahle- Increased DJ-1 expression under oxidative stress and in Alzheimer's disease brains.

Mutations in the DJ-1 gene have been linked to autosomal recessive familial Parkinson's disease. To understand the function of DJ-1, we evaluated DJ-1 expression in both zebrafish and post mortem human brains. We found that DJ-1 was expressed early during zebrafish development and throughout adulthood. Knock down (KD) of DJ-1 by injection of morpholino did not cause dramatic morphologic alterations during development, and no loss of dopaminergic neurons was observed in embryos lacking DJ-1. However, DJ-1 KD embryos were more susceptible to programmed cell death. While a slight reduction in staining for islet-1
positive neurons was observed in both DJ-1 KD and H2O2 treated embryos, the number of apoptotic cells was significantly increased in both KD and H2O2 treated embryos. Interestingly, DJ-1 expression was increased in brains of zebrafish under conditions of oxidative stress, indicating that DJ-1 is a part of stress-responsive machinery. Since oxidative stress is one of the major contributors to the development of Alzheimer's disease (AD), we also examined DJ-1 expression in AD brains. Using DJ-1 specific antibodies, we failed to detect a robust staining of DJ-1 in brain tissues from control subjects. However, DJ-1
immunoreactivity was detected in hippocampal pyramidal neurons and astrocytes of AD brains. Therefore, our results strongly suggest that DJ-1 expression is not necessary during zebrafish development but can be induced in zebrafish exposed to oxidative stress and is present in human AD brains.

Jennifer Simpson- Mexican Americans with Atrial Fibrillation and Stroke have a Higher Risk of Recurrent Stroke than Non-Hispanic Whites

Objective: We studied post-stroke recurrence and survival in Mexican Americans (MAs) compared with non-Hispanic whites (NHWs).

Methods: Using surveillance methods from the Brain Attack Surveillance in Corpus Christi (BASIC) Project, cases of ischemic stroke/ TIA with atrial fibrillation were prospectively identified January 2000-June 2008. Recurrent stroke (found by BASIC) and all-cause mortality (identified through state /national databases) were compared by ethnicity with survival analysis methods.

Results: A total of 236 patients were included (88 MA, 148 NHW). MAs were younger than NHWs (75 vs. 81, $p<0.001$), with no ethnic differences in stroke severity or proportion discharged on warfarin. By the end of follow-up, 37% of MAs and 22% of NHWs had recurrent stroke (Kaplan-Meier estimates). Elev ated stroke recurrence risk in MAs persisted despite adjustment for age and gender (hazard ratio 2.45, 95% CI: 1.18, 5.08). No ethnic difference in survival after stroke occurred in unadjusted analysis ($p=0.90$) or adjusting for demographics and clinical factors ($p=0.59$).

Conclusions: MAs with atrial fibrillation have a higher risk of recurrent stroke than NHWs, but no difference in all-cause mortality. Aggressive stroke prevention measures in this population are warranted.

Jim Burke- Participation of women and minorities in NINDS trials.

Introduction

Women and minorities are underrepresented in clinical trials, although results vary based on disease state. Race, ethnic, and gender participant distribution has not previously been reported for neurologic disease.

Methods

All phase 3 trials funded by NINDS were identified using clinicaltrials.gov. Completed trials with published results were included. Reporting of race, ethnicity, and gender information was abstracted from published trials. The number of trials that reported any data on race/ethnic enrollment was calculated as was the proportion of enrollment for African Americans and Hispanics. Spearman¿s rank correlation coefficients were calculated assessing the correlation between year of trial publication and the number of trials reporting race/ethnicity and gender, as well as the percentage of minorities and women enrolled. Analysis was performed with Microsoft Excel and R: A language and Environment for Statistical Computing.

Results

Of the 53 trials identified, all reported the number of women enrolled. Of the 40,401 total subjects enrolled, 17,197 (42.6%) were women. 40 (75.5%) trials reported any race data. Of the 26 (49.1%) studies that reported specific race data, 22.3% of the enrollees were African American. Of the 10 (18.9%) studies that reported on ethnicity, 8.8% of the enrollees were Hispanic. There was little change in race/ethnic reporting over time (for African American reporting, p=.95, for Hispanic reporting, p = .49). There has been a statistically significant (p=.02) increase in the percentage of women participating in NINDS trials. No significant trend was identified between time and the percentage of African Americans (p=.09) or Hispanics enrolled (p=.52).

Conclusions

Reporting of minorities in NINDS clinical trials has been poor and has not significantly improved over time. The possibility of outcome reporting bias limits definitive conclusions about minority participation.

Over the time period evaluated, women were significantly underrepresented relative to their proportion in the population, a trend that improved over time. In the subset of studies that report African American participation, African Americans appeared to be relatively well-represented. In the small subset of studies reporting Hispanic participation, Hispanics were quite under-represented.

John Betjemann- Quality of life and long-term psychosocial outcomes following surgery for mesial temporal lobe epilepsy

With a prevalence of 0.5%-1.0% epilepsy is a common disease with enormous financial impacts on the individual as well as society. Studies have estimated that approximately 70% of patients with epilepsy can achieve complete remission or significant reduction in seizures with one or multiple antiepileptic medications. Of those that remain refractory to medications, a significant proportion have focal onset seizures arising from the temporal lobe that are amenable to temporal lobectomy. Studies have shown that patients undergoing temporal lobe surgery for focal onset seizures can expect a 50% -70% rate of complete seizure control. What is less well established is the effect of temporal lobe surgery and seizure control on long-term quality of life.

The Quality of Life in Epilepsy-31 (QOLIE-31) is a 31 question validated instrument aimed at addressing this issue. In our study, we created a brief phone questionnaire involving various outcome measures related to quality of life including employment, driving status, relationship status (married/significant other) and current or past mental health issues. We administered this questionnaire to all patients with a radiographic or pathologic diagnosis of mesial temporal sclerosis who underwent selective or anterior temporal lobectomy at the University of Michigan between the years 2000-2004. We examined the relationship between current rate of seizures (according to Engel Classification), the above mentioned outcome measures and the patient¿s perceived quality of life (as measured on a standard 1-5 Likert Scale). Our preliminary data reveals that a large percentage of patients met Engel Class I criteria and have a perceived improvement in quality of life, however, this is not always reflected in their employment status, interpersonal relationships, driving status and severity of current mental health issues. These results may indicate a disconnect between perceived quality of life and more objective quality of life measures, and may point to a need for improved pre- and post-op psychosocial support for epilepsy surgery patients.

Joe Krainin- Resident Performance on a Simulated Case-Based Medical Decision Making Task after Heavy Call and Alcohol Consumption

Introduction: Sleep deprivation during postgraduate medical education is common and associated with deleterious effects on neurobehavioral performance parameters equivalent to low doses of alcohol. We compared residents¿ actual and self-rated performance on an on-line simulated medical decision making task (MedCases) under four conditions: rested (Light Call; LC), sleep loss (Heavy Call; HC), Rested + Alcohol (LC/Alcohol), and Sleep Loss + Placebo (HC/Placebo).

Methods: Twenty-seven pediatric residents (13 women, 28.7 ± 2.9 years, 10 PL-1, 14 PL-2, 3 PL-3) completed 4 on-line, medical cases in a counterbalanced order after a month of light call (LC and LC/Alcohol) and post-call after a heavy-call (q 4 or q 5) month (HC and HC/Placebo). Subjects were presented with an initial case presentation of a typical outpatient problem and selected appropriate differential diagnoses (DD), laboratory tests (LT), final diagnoses (FD) and treatment plan (TP) from a range of options within 15 minutes. Participants self-rated performance post-test from 1 (extremely good) to 7 (extremely poor) and effort from 1 (very little) to 4 (extreme). Primary outcomes included appropriate selections (%Hits), Omission, and Commission Errors for DD, LT, and TP (%Hits for FD), and self-ratings of performance and effort.

Results: Subjects completed the cases in less time in LC/Alcohol (8.78 ± .4 minutes) and HC/Placebo (9.11 ± .5 minutes) compared with LC (11.01± .5 minutes) and HC (10.89 ± .5 minutes) ($F_{3,26}$=14.75, p <0.0001). No differences among the conditions in Hits or Errors of Omission/Commission were found for DD, LT, TP, or FD. Subjects self-rated performance worst in the HC conditions, followed by LC/Alcohol, and LC ($F_{3,26}$=4.95, p = 0.0075). No differences in effort ratings were found.

Conclusions: Residents rated their performance worse following heavy call compared to alcohol, but no objective differences in simulated medical decision making were evident.

Lisa Cook- a retrospective study looking at the incidence of triphasic waves seen on EEGs and underlying diagnoses

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Mirko Villanueva- Snoring, Obesity, and Gestational Hypertension in the Last Trimester of Pregnancy

Introduction: Obesity during pregnancy increases the risk of maternal complications. Emerging data suggest that habitual snoring, a cardinal symptom of sleep-disordered breathing (SDB), during pregnancy is also associated with adverse outcomes. The goal of this study is to determine the relationship between habitual snoring, obesity, and gestational hypertension.

Methods: Women with singleton pregnancies were invited in their last trimester to answer several sleep-related questionnaires. Risk for SDB was defined as the presence of habitual snoring (¿3-4 nights/week). Pre-pregnancy BMI was used to classify subjects as underweight (BMI<20); normal weight (BMI 20-24.9); overweight (BMI 25-29.9) and obese (BMI >30). Subjects were further grouped according to whether their absolute weight gain exceeded Institute of Medicine (IOM) recommendations, which are 28-~~40lbs for underweight women, 2535lbs for normal weight women, 15~~ 25lbs for overweight women, and ¿15lbs for obese women. Medical records were reviewed after delivery to obtain information on gestational hypertension.

Results: Of 363 subjects, 90 (25%) were obese. Weight gain in excess of IOM recommendations was an independent predictor of SDB risk (OR: 1.9 [1.2-3.1]) after adjusting for pre-pregnancy BMI, maternal age, and race. Compared to non-obese women, obese women were more likely to be at risk for SDB (61% vs. 27%, p<0.002) and gestational hypertension (30% vs. 14%, p<0.001). In a logistic regression, after adjusting for confounders including pre-pregnancy BMI and excess pounds gained, SDB risk remained an independent predictor of gestational hypertension (OR: 2.0 [95%CI 1.11-3.6]). A significant interaction was observed between obesity and SDB risk for gestational hypertension (OR: 4.1 [2.1-7.8]; p<0.001).

Conclusions: Weight gain greater than IOM recommendations during pregnancy independently increases risk for SDB, as reflected by habitual snoring. Th ese data suggest that SDB may help explain why obesity and excess weight gain promote gestational hypertension.

Nadir Osman- Menin-A new central player in metabolic & energy homeostasis

Objective: Menin is a 67kDa protein product of the MEN1 locus (11q13) described as tumor suppressor gene, loss of which is associated with MEN 1 syndrome. The MEN 1 syndrome is characterized by tumors of the pituitary, pancreas and parathyroid, as well as overproduction of a cocktail of endocrine hormones (*Science* 18; 276(5311): 404-7, 1997). This study tested the hypothesis that menin expression in the central nervous system is down-regulated by hyperinsulinemia associated with type-2 diabetes mellitus and obesity.

Methods: 2.5 month old wild-type C57BL/6 mice, (n=4) and 2 diabetic mouse models (ceacam 1 knockout and Agouti mice, with corresponding WT litter mates), n=2, were euthanized and brains perfused with PBS and 4% formalin for 24hrs. Sections were obtained for immunoflourescence staining with specific antibodies, for mapping of menin within the brain. Wild-type C57BL/6 mice fed on regular diet, high fat diet and high fat high carbohydrate diet for 2 months (n=6) were euthanized and whole brains isolated for RNA extraction and cDNA preparation prior to real-time PCR analysis. Wild-type C57BL/6 mice fasted and re-fed after 1-, 4-, 7- and 24 hrs, (n=6) were euthanized and whole brains analyzed by real-time PCR.

Results: We determined that menin is expressed in the cytoplasm of cells within specific regions of the brain, namely, hypothalamus (arcuate nucleus) and hippocampus. Conditions that lead to hyperinsulinemia resulted in down-regulation of menin within the

hypothalamus but not in other regions. Menin expression in the brain was not affected

with physiological changes on levels of insulin, such as by fasting and re-feeding.

Conclusion: These data are the first to show that menin is located in areas related to

metabolic/energy homeostasis in the central nervous system. Menin in the brain colocalizes

with metabolic/energy homeostasis signals such as insulin receptor, ceacam 1

and glucagon-like peptide 2. The results are consistent with the possibility that menin

serves as an important sensor that reflects on insulin levels, and by acting on discrete

responses in the hypothalamus orchestrates metabolic and neuro-endocrine adaptations

to the type of nutrients absorbed and their availability.

Namath Hussain- Pediatric melanotic neuroectodermal tumor of the calvarium presenting after trauma: Case report

Melanotic neuroectodermal tumor (MNET) is a rare condition that typically presents spontaneously within the first few months of life usually in the maxilla or mandible. These tumors are not known to usually involve the skull. A thorough review of the literature revealed a few other cases arising in the cranial vault; however, only one previous case presented after trauma. We report a second case of the MNET presenting after trauma.

A five-year-old male presented for evaluation following a fall where he violently hit his head on steel bleachers at a sporting event. The patient did not experience any loss of consciousness and was neurologically intact. There was no posttraumatic nausea or vomiting.

After presenting several months later with intractable headaches, routine computed tomographic imaging in the emergency department revealed a large left parieto-occipital mass that involved the skull and underlying dura. MR imaging was later performed. Based on the findings, the preliminary differential diagnosis included meningioma, fibrous dysplasia, and osteoma. The patient was operated on and gross total excision of the mass was completed. Pathology revealed MNET.

A thorough review of the neurosurgical literature for previous reports of MNET of the calvarium revealed scarce cases. Hered et al report an orbital MNET that was treated with subtotal excision due to its invasion of the sclera and chemotherapy. Several cases of MNET of the maxilla have been reported. Kumari et al report a case involving the maxilla presenting in a 13 day old neonate. The tumor recurred three weeks after removal. The patient was later treated with repeat wide surgical excision. De Oliveira et al report two cases of MNET of the maxilla.

There have been a few previous reports of spontaneous development of calvarial MNETs, however, there has been only one report in the literature regarding MNET associated with head trauma. Paueksakon et al describe a case of 7-month-old female who developed an enlarging frontal mass after falling out of bed onto a concrete floor. Radiography showed only a depressed right frontal skull fracture. Computed tomography revealed a hyperdense extra-axial mass widening the metopic suture with associated hyperostosis. Gross pathology upon resection showed a calcified epidural lesion appearing like an unusual hematoma. Although MNET cells produce melanin, pigmentation may not be clinically evident in most cases. Microscopic examination of this mass revealed chronic hematoma and MNET.

MNET has an unusually high rate of recurrence when gross total resection with adequate margins is not possible. However, in cases where good margins are possible, the disease is surgically curable.

Naricha Chirakalwasan- Oral appliance therapy for treatment of residual obstructive sleep apnea after uvulopalatopharyngoplasty

Introduction: Uvulopalatopharyngoplasty (UPPP) is the most common surgical procedure performed to treat obstructive sleep apnea (OSA) with an overall success rate of approximately 40%. To our knowledge, there is currently only one publication regarding the use of oral appliance (OA) as a salvage intervention after UPPP [(1)]. The University of Michigan has established a multi-disciplinary Alternatives to CPAP clinic in which patients with OSA who are unable to use CPAP are evaluated for alternative treatments. Data from this clinic was used to evaluate the efficacy of OA for persistent OSA after UPPP.

Method: We performed a retrospective chart review to identify patients with residual OSA after UPPP who were subsequently treated with an OA between December 1997 and August 2008. Demographics included age, sex, and BMI. Three polysomnograms were analyzed for each patient; diagnostic baseline, post-UPPP, and while using the OA. Successful treatment of OSA was defined as AHI<10 or AHI<20 with ¿50% reduction while using OA compared both to baseline and to the post-UPPP results.

Results: Sixty-three patients underwent UPPP, with 12 (all male) who subsequently received an OA. Mean age was 41.3±13.7 years and 8 of these (66.7%) met the criteria for successful treatment of OSA. There were no significant differences in demographics between the group who was considered successfully treated versus the group who was not. Mean baseline AHI was 31.8±21.0 and did not change after UPPP (31.2±14.9). There was no significant change in any sleep parameters between baseline and post-UPPP polysomnograms. There was a reduction in total AHI between post-UPPP and OA from 31.2±14.9 to 13.5±15.6 ($p<0.05$). This change was mostly due to a reduction in NREM AHI (30.6±19.0 to 10.3±13.9; $p<0.05$).

Conclusion: The use of an OA for the treatment of residual OSA after UPPP should be considered as a salvage treatment after unsuccessful UPPP.

Preeti Gupta- Treatment of obstructive sleep apnea with cholinesterase inhibitors in myasthenia gravis

Obstructive sleep apnea and myasthenia gravis are each highly prevalent conditions. As many as 36% of patients with myasthenia gravis are thought to have sleep apnea, in comparison to 15 to 20% of the general population. The physiology of obstructive sleep apnea is directly related to the relaxation during sleep of muscles that line the upper airway, leading to recurrent episodes of upper airway collapse. Many patients with myasthenia gravis have bulbar weakness, which could cause or exacerbate sleep apnea. Acetylcholine esterase inhibitors, such as pyridostigmine, may reduce bulbar weakness and consequently mitigate the severity of obstructive sleep apnea. However, the standard preparation of pyridostigmine has a half-life of 200 minutes. Thus, it is possible that a dose taken before bed may reduce apneic episodes only in the first part of the night. Whether myasthenia directly contributes to sleep apnea risk, or whether lack of adequate treatment through the night might explain the high frequency of obstructive sleep apnea in myasthenia gravis, has not been explored. We therefore propose to characterize the nocturnal distribution and characteristics of apneic events in myasthenia gravis patients and non-myasthenics matched for overall apnea severity, age, and gender. These comparisons are anticipated to provide suggestive evidence that acetylcholine esterase inhibitors, while still active in the first third of the night, can reduce sleep apnea. This would in turn support the hypothesis that myasthenia can worsen or cause obstructive sleep apnea. Additional aims are to compare sleep stages, sleep fragmentation, and sleep positions in myasthenia gravis patients with sleep apnea to those in matched apneics who do not have myasthenia gravis. Differences between groups could provide preliminary evidence for effects of cholinesterase inhibitors on cholinergically-mediated REM sleep or sleep-disordered breathing, whereas differences in sleeping position also could help to explain increased sleep apnea in myasthenics.

Ravi Pande- Low Serum Vitamin D Concentration as a Predictor of Short Sleep Duration: A NHANES 2005-2006 Analysis.

Introduction: The daily rhythmic melatonin production from the pineal gland is considered a vital process in the modulation of circadian rhythms. The suprachiastmatic nucleus which is the main input to the pineal gland is shown to be immunoreactive to Vitamin-D dependent calcium binding proteins (Calbindin-D9k, Calbindin-28K). We therefore hypothesized that low serum Vitamin-D would directly affect the synthesis of endogenous melatonin and in turn alter the sleep-wake cycle.

Methods: The National Health and Nutrition Examination Survey (NHANES) 2005-2006 is a cross-sectional multistage survey of the US civilian non-institutionalized population. Participants answered demographic, health, and sleep related questions and serum Vitamin-D levels were measured. The two sleep related questions; "How much sleep do you get (hours)?" and "How long does it take to fall asleep (minutes)?", were analyzed using multivariable logistic regression models, controlling for age, gender, race, overweight, arthritis, cancer, parathyroid levels, night-time leg jerks and daily consumption of milk.

Results: There were 3,028 participants (46% male) with a mean age of 50.1±18.7years who had complete data available. In a multivariate analysis, Vitamin-D level was found to be a significant predictor of sleeping <5 hours ($p<0.0005$). The participants were further categorized by serum vitamin-D quartiles (¿14 ng/ml; 15-20 ng/ml; 21-26 ng/ml; ¿27 ng/ml). Relative to the top three Vitamin-D quartiles, the lowest quartile was significantly more likely to sleep <5 hours (odds ratio [OR] 1.79 [95% Confidence Interval (CI) 1.25-2.57]). Lower Vitamin-D quartiles also showed a trend towards taking >30 minutes to fall asleep (OR 1.20 CI [0.87-1.65]).

Conclusion: Low serum Vitamin-D levels (¿14 ng/ml) are associated with an increased risk of sleeping <5 hours. Our results also show a trend towards difficulty in sleep onset in participants with lower Vitamin-D levels. The role of Vitamin-D in the reduction in total sleep time remains unclear.

Sara Afshari - Unnecessary Surgeries Related to Misdiagnosis of Motor Neuron Disease

Motor neuron diseases are a group of progressive neurological disorders that result in degeneration of lower and/or upper motor neurons. Lower motor neuron deficits present as muscle wasting, weakness, and fasciculations; Upper motor neuron deficits present as hyperreflexia and spasticity. The major site of motor neuron degeneration classifies the disorders. Diseases that fall under this spectrum include: primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), progressive bulbar palsy, spinal muscular atrophy (SMA), spinobulbar muscular atrophy/Kennedy¿s disease (SBMA), and amyotrophic lateral sclerosis (ALS). Misdiagnosis continues to be a problem as early presentation can mimic arthropathy, myopathy, mononeuropathy, radiculopathy, and myelopathy, which can subsequently result in inappropriate and ineffective surgeries. We retrospectively reviewed the medical charts of 333 patients evaluated in initial consultation and/or follow-up at the Motor Neuron Disease/ALS clinic at the University of Michigan between 2007 and 2009, for surgeries performed prior to diagnosis and their subsequent outcome.

Sachie Arankie- Surgical resection is the treatment of choice in patients with medically refractory and focal epilepsy. Ictal SPECT scan is often useful in localizing the epileptogenic foci. We performed a retrospective review of the seizure outcomes of patients, who had an ictal SPECT scan and epilepsy surgery, with respect to the location, pathology, and surgical technique for resection of the epileptogenic area.

Sophos Geroulis- A patient with Wolf Hirschorn Syndrome that we monitored on video EEG and will discuss some of the typical EEG features that we found in this patient as well as in those previously described.

Soumya Madala- Sleep Disruption and Mode of Delivery in Pregnant Women

Introduction:

Sleep disturbances are known to impact physical and psychological wellbeing. Limited available data from women with a moderate-to-high socioeconomic background suggest that poor sleep in late pregnancy is associated with an increased risk for cesarean section. Such an association has important clinical implications. However, the impact of sleep disruption on mode of delivery has not been investigated in a heterogeneous sample of pregnant women attending a large academic medical center.

Methods:

Pregnant women ¿18 years, carrying a single fetus, were recruited from the labor and delivery unit and invited to complete several sleep questionnaires including the General Sleep Disturbance Scale (GSDS). Total score ranges from 0-147 and a mean score ¿3 is considered a threshold for poor sleep. Wo men with snoring ¿3 nights/week were considered to have habitual snoring. Non-pregnant women of child bearing age (18-45 years) were recruited as controls. Medical records were accessed to obtain delivery information.

Results:

In total, 141 pregnant women and 83 controls have been studied. Mean ages were 29.8±5.7 years vs. 32.7±8.0 years respectively. There were no differences in pre-pregnancy BMI between groups (26.5±7.2 vs. 26.7±7.1kg/m^2). Total GSDS score was higher for pregnant women than controls (61.6 ±17.6 vs. 47.8±15.7; p<0.001). In addition, pregnant women were more likely than controls to have a mean GSDS score ¿3 (55% vs.19%; p<0.001) and report habitual snoring (34% vs. 17%; p=0.006). Overall, 38% of pregnancies resulted in a cesarean section. In a logistic regression with mode of delivery as the dependent variable, and controlling for previous cesarean section, parity, maternal age, BMI, gestational age, and birth weight, no sleep-related parameters were found to be significant predictors of mode of delivery.

Conclusion:

Contrary to previous findings, our data do not support the hypothesis that sleep disruption in pregnancy associated with an increased risk for cesarean section.

Vessela Giger-Mateeva- The Pale Tremor Mutant: Analysis of a Mouse Model for Charcot-Marie-Tooth Disease Type 4

Charcot-Marie-Tooth disease (CMT), also referred to as hereditary motor and sensory neuropathy (HMSN), is the most common form of inherited peripheral neuropathy. The genetic basis of CMT is complex and over 40 different genes have been identified. Different subtypes of CMT diseases have been reported (CMT disease type 1-4). The 'demyelinating' neuropathies (CMT disease types 1 and 4) are genetically heterogeneous, but their common feature is that the primary defect perturbs myelination. Demyelination leads to axonal degeneration, a common final pathway of all CMT diseases.

Over the past years transgenic mouse models have become available that mimic specific types of CMT disease. Mouse models provide new opportunities to study the mechanisms of CMT disease genes and also guide the development of strategies to diagnose and treat the disease. Genes involved in phosphoinositide regulation cause CMT type 4. A newly identified gene that causes CMT type 4 is FIG4 (encoding a PI(3,5)P(2) 5-phosphatase). FIG4 is the gene mutated in the pale tremor (plt) mouse, as recently reported by Chow et al., (Nature, 2007; 448(7149):68-72). FIG4 regulates levels of membrane bound phosphoinositides which are thought to be important for vesicle trafficking in eukaryotic cells.

The plt mouse (null for FIG4) shows a multi-organ disorder with neuronal degeneration in the central nervous system, peripheral neuronopathy, and diluted pigmentation (giving the mouse its name). To examine whether the Fig4 gene is important for proper myelination of CNS fibers, the optic nerve of wild-type and plt mice was analyzed at the light microscopic and ultra-structural level. Electron microscopy revealed a severe demyelination phenotype in plt mice compared to age-matched wild-type controls. In three week-old plt mice, there is a significant decrease in the number of myelinated axons in the optic nerve. Commensurate with the demyelination phenotype, biochemical studies revealed that levels of myelin-associated glycoprotein (MAG) and Oligodendrocyte myelin glycoprotein (OMgp) are decreased by more than 50% in plt brain extracts compared to age-matched wild-type controls. To assess whether axon demyelination observed in the optic nerve leads to functional impairments, the conduction velocity (CV) of optic nerve explants was assessed *in vitro*. Consistent with the anatomical findings, CV studies showed that in plt optic nerve there is a shift toward slow conducting axons.

In sum, these studies reveal that loss of FIG4 leads to peripheral but also central demyelination in vivo. In future studies the plt mouse will be further characterized to determine how loss of the FIG4 gene product leads to demyelination and neuronal degeneration.

Vikas Kotagal- Parkinson and Alzheimer-selective hyposmia measures have different neurochemical substrates in patients with Parkinson¿s disease.

OBJECTIVE: To investigate the relationship between Parkinson versus Alzheimer-selective hyposmia measures and dopaminergic and cholinergic activity in the striatum, amygdala and hippocampus in non-demented patients with Parkinson¿s disease (PD).

BACKGROUND: Olfactory deficits may be part of the prodromal stages of both PD and Alzheimer's disease (AD). Previous studies using the University of Pennsylvania Smell Identification Test (UPSIT) have shown disease-selective deficits in odor identification deficits in both PD and AD. For example, we reported a PD-selective measure derived from 3 odors (UPSIT-3; J Neurol 2007;254:84-90). Similarly, Tabert et al reported an AD-selective UPSIT scale (Tabert-10; Ann Neurol 2005;58:155-160). A random distribution of PD or AD-related neuropathology in the olfactory tubercle is unlikely to explain such disease-selective hyposmic deficits. However, specific neurochemical deficits, especially in brain areas involved in higher order odor cognitive processing, may provide an alternative explanation.

METHODS: Nineteen non-demented PD patients (age 67.89.3; Hoehn and Yahr stages I-III, UPDRS motor score 26.97.3, MMSE score 28.81.9) underwent (+)-[C-11]DTBZ (VMAT2) monomaminergic and [C-11]methyl-4-piperidinyl propionate (PMP) acetylcholinesterase (AChE) brain PET imaging and olfactory testing using previously reported Parkinson (UPSIT-3) and Alzheimer-selective (Tabert-10) hyposmia scores derived from the UPSIT.

RESULTS:

UPSIT-3 scores correlated well with striatal VMAT2 binding (R=0.57, P=0.013) but not with hippocampal and amygdala AChE hydrolysis rates. Similarly, Tabert-10 scores correlated robustly with AChE hydrolysis rates in the amygdala (R=0.77, P=0.0001) and hippocampus (R=0.67, P=0.002) but not with VMAT2 binding in the striatum.

CONCLUSIONS: Previously reported PD and AD-selective hyposmia scales appear to have specific neurochemical correlates in PD without dementia. Th e combined use of these selective hyposmia scores may ultimately prove useful not only in identifying subjects at risk for PD but also PD subjects at risk for dementia.

Khoi Than- Gliadel (BCNU) wafer plus concomitant temozolomide therapy after primary resection of glioblastoma multiforme

Object. Gliadel (BCNU) wafer and concomitant temozolomide (TMZ) therapy, when used individually as adjuvant therapies, extend survival from that achieved by resection and radiation therapy (XRT) for glioblastoma multiforme (GBM). It remains unstudied whether combining Gliadel and TMZ therapy is safe or further improves survival in patients with newly diagnosed GBM. The authors reviewed their initial experience utilizing combined Gliadel, TMZ, and radiation therapy for the treatment of GBM.

Methods. All cases involving patients undergoing primary resection of GBM with or without Gliadel wafer

(3.85% BCNU) implantation and adjuvant XRT over a 10-year period (1997--2006) were retrospectively reviewed.

Beginning in 2004, concomitant TMZ became the standard of care at the authors¿ institution and all patients with Gliadel implantation also received concomitant TMZ (Stupp protocol). Overall survival and treatment-related morbidity were assessed for all patients treated with Gliadel plus concomitant TMZ (XRT + Gliadel + TMZ). Age-matched (¿ 70 years) comparison of survival and morbidity was performed between the XRT + Gliadel + TMZ (post-2003) and XRT + Gliadel (pre-2004) cohorts.

Results. Thirty-three patients were treated with XRT + Gliadel + TMZ. The median survival in this group was 20.7 months, with a 2-year survival rate of 36%. Six-month morbidity included surgical site infection in 1 case (3%), perioperative seizures in 2 cases (6%), deep-vein thrombus in 1 (3%), pulmonary embolism in 3 (9%), and cerebral edema requiring admission for intravenous dexamethasone in 1 case (3%). Myelosuppression required premature termination of TMZ in 7 patients (21%) (thrombocytopenia in 5, neutropenia in 2 cases). In patients ¿ 70 years of age, XRT + Gliadel + TMZ (30 patients, post-2003) was independently associated with improved median survival (21.3 vs 12.4 months, p = 0.005) versus XRT + Gliadel (78 patients, pre-2004), with 2-year survival of 39 versus 18%, respectively. In these patients, XRT + Gliadel + TMZ was not associated with an increase in perioperative morbidity in comparison with XRT + Gliadel.

Conclusions. In this experience, concomitant TMZ therapy in addition to Gliadel wafer implantation was associated with a median survival of nearly 21 months without increased perioperative morbidity. Temozolomide can be safely administered to patients receiving Gliadel wafers after resection of GBM.

Lesli Skolarus- Antihypertensive therapy delays door-to-needle time and may adversely affect patient outcomes

Background: Guidelines for the management of blood pressure in patients undergoing thrombolysis with IV t-PA recommend blood pressure less than 185 /110. Patients with elevated blood pressures receive antihypertensive treatment for modest blood pressure reduction. The investigators in the NINDS t-PA stroke study followed these guidelines in 20% of the hypertensive patients receiving t-PA, with no adverse effects occurring in those who did not receive antihypertensive therapy. To our knowledge, there are no randomized trials exploring the relationship of blood pressure, antihypertensive therapy and thrombolytics. We hypothesized that administration of blood pressure medications leads to a delay in delivery of thrombolytics resulting in worse outcomes for patients treated with antihypertensive therapy.

Methods: We prospectively collected data from 130 consecutive patients from March 1, 2004 to December 31, 2007 who presented to our tertiary care emergency department with acute ischemic stroke who were administered t-PA. We defined favorable outcome as discharge to home or inpatient rehabilitation. Symptomatic intracerebral hemorrhage was defined as an intracerebral hemorrhage within 36 hours of symptom onset accompanying any decline in neurological status.

Results: Among the 130 patients who were administered t-PA, 28 (22%) received antihypertensive treatment prior to t-PA administration according to current guidelines. The patients receiving antihypertensive therapy were older (74 years vs. 67 years; p=0.02) and more likely to have diabetes mellitus (p=0.02). There was no difference in sex, race, admission NIHSS or history of previous stroke and hypertension. Patients who received antihypertensive therapy prior to t-PA administration had an increased door-to-needle time of 15 minutes (57 minutes vs. 72 minutes; p=0.002). Patients who did not receive antihypertensive therapy demonstrated a trend towards a favorable outcome (p=0.08, one-tailed) and improved NIHSS within 72 hours (p=0.179) compared to those who received hypertensive therapy. There was no difference in number of symptomatic intracranial hemorrhages (p=0.94)

Conclusions: Rigid guidelines regarding antihypertensive therapy in t-PA candidates may contribute to inferior outcomes secondary to prolonged door-to-needle times. Moreover, the guidelines exclude a number of patients from receiving t-PA who would likely benefit from the medication. Further studies are needed to determine the optimal management of hypertension in t-PA candidates.

Daniel Orringer- A COMBINED CRANIAL WINDOW AND IMPLANTED GLIOMA MODEL FOR EVALUATING INTRAOPERATIVE CONTRAST AGENTS

Objective: Previous evaluations of optical contrast agents for brain tumor delineation have been carried out in *ex vivo* specimens from animals with implanted gliomas that may not reflect the true visual parameters encountered during brain tumor surgery. This study describes a novel model system designed to evaluate the ability of optical contrast agents to delineate brain tumor margins *in vivo*.

Materials and methods: Biparietal craniectomies were performed on 8-week-old Sprague-Dawley male rats. 9L glioma cells, were injected intraparenchymally. A cover slip was bonded to the margins of the craniectomy with cyanoacrylate glue. Tumor growth was observed daily. When the tumor radius reached 1mm, coomassie blue was administered intravenously and the appearance of the cortical surface was recorded using a video microscope. A computerized image analysis of the RGB components was used to quantify visible differences between tumor and normal brain tissue.

Results: After transient initial weight loss, all rats gained weight appropriately following surgery and demonstrated no neurologic deficits. 2mm tumors were observed after an average of 10.4 days (range 7-20 days). The margin between tumor and normal brain was subjectively difficult to distinguish prior to contrast administration. Following contrast administration, the border between tumor tissue and normal brain was readily apparent. The red component intensity in tumor decreased 2-3 fold versus normal brain tissue at 50 minutes post-contrast administration ($p<0.002$).

Discussion: Placement of a window overlying an implanted glioma is technically possible and well tolerated in the rat. In this model, the appearance of glioma adjacent to normal cortex is similar to the intraoperative appearance of a superficial human brain tumor after surgical exposure. The border of normal brain and implanted 9L glioma is enhanced by the administration of optical contrast material.

Conclusion: The brain tumor window model is a valid system for evaluating optical contrast material designed to delineate brain tumor margins. To our knowledge, we have described the first *in vivo* model system for evaluating optical contrast agents for tumor delineation.

Elia M Pestana Knight - 17-year-old with CNS and systemic infarcts as a complication of bronchial artery embolization with microspheres

Introduction: Bronchial artery embolization (BAE) has been effectively used to treat hemoptysis. Although a relatively safe procedure, main complications are chest pain, dysphagia, and spinal cord ischemia in a small percentage of cases.Case : A 17-year-old female with history of cystic fibrosis, B. cepacia lung colonization and pancreatic insufficiency underwent routine bronchoscopy. She subsequently developed hemoptysis from an exposed vessel in the left mainstream bronchus. She underwent left bronchial artery embolization with Embosphere particles 300-500um and 500-700um, under general anesthesia. Hours after the procedure she developed altered mental status with periods of agitation alternating with lethargy, and headache. Initial examination showed no motor deficits, but there was hyperreflexia of all limbs with clonus of knees and ankles. Brain MRI showed multiple embolic strokes affecting mainly of the posterior circulation (cerebellar vermis, bilateral cerebellar hemispheres and thalami, both cerebral hemispheres). The following day she developed pain in the left 5th digit and cyanosis of the distal 2/3 of her finger. ECHO documented no intracardiac shunt. Both CNS and systemic embolism were attributed to the embolization with Embosphere particles. Spine MRI weeks later showed no spinal cord embolization. She made a full neurological recovery over the next several weeks.

Literature review: There are three other cases of cerebral and systemic embolism following BAE with microspheres. All patients had evidence of lung disease (tuberculosis, focal vascular abnormality, pulmonary metastases). Presenting symptoms were delirum, headache and leg weakness. All patients made a functional neurological recovery.

Conclusions: Cerebrovascular embolism is a rare complication of BAE with miscrospheres, reported in 1.4% of cases. From an anatomic/vascular standpoint, embolization to spinal cord is more likely. In our case and the others reported in the literature, it is possible the chronic lung disease leads to shunting between the pulmonary arterial and venous circulation, predisposing these patients to cerebral and systemic embolism during BAE.

Debbie K. Song- Surgical management of melanoma brain metastases in patients treated with systemic immunotherapy

Introduction. Despite the increasing use of immunotherapy in the treatment of metastatic melanoma, the effects of this therapy on the management of patients with associated brain metastases are not completely defined. To gain insight into the effect of immunotherapy on brain metastasis management, we analyzed melanoma immunotherapy patients with brain metastases that were surgically resected.

Methods. Consecutive patients with metastatic melanoma treated with immunotherapy within 2 months of metastasis discovery and who developed brain metastases that were surgically resected between September 1998 and February 2007 were included. Patient characteristics, tumor properties, response to immunotherapy and use of adjuvant whole-brain radiation therapy (WBRT) were analyzed.

Results. Forty-one patients (median age, 44.4 years; range, 19.2 to 63.1 years) underwent resection of 53 brain metastases (median metastases, 1; range, 1 to 4). Median metastasis volume was 2.5 cm^3. Fifteen patients underwent WBRT, while 26 patients did not undergo WBRT. Survival from the time of brain metastasis diagnosis was not significantly different between patients who received WBRT (mean, 24.9 months) and those who did not (mean, 23.3. months) ($p>0.05$). Local and distant brain recurrence rates were not statistically different between WBRT (7.1%; 28.6%, respectively) versus non-WBRT (7.7%; 41.0%) tumor groups for the duration of follow-up ($p>0.05$). Objective systemic response to immunotherapy was associated with an increased survival ($p<0.05$).

Conclusion. Surgical resection of melanoma brain metastases in immunotherapy patients provides excellent local control with low morbidity. An objective response to systemic immunotherapy is associated with a prolonged survival in patients who have undergone resection of melanoma brain metastases. M oreover, adjuvant WBRT in melanoma immunotherapy patients with limited metastatic disease to the brain does not appear to provide a significant survival benefit.