Neuroscience Day 2010 Abstracts

Affa Shamim-Uzzaman - Restless Legs Syndrome in Pregnancy: Frequency and Correlates.

Introduction: Restless legs syndrome (RLS) affects approximately 14% of females in the general population. Several studies have shown that RLS is increased during pregnancy but little is known about its true frequency or correlates.

Methods: As part of a larger prospective study on sleep in pregnancy, women were surveyed about their sleep during their third trimester. Validated screening questionnaires included the General Sleep Disturbance Scale (GSDS) and a 4-item Brief Restless Legs Scale. Sleep disturbance was considered present if the mean total score or any subscale score (poor sleep quality and poor daytime functioning) was $\geq$ 3. Positive responses to the first 3 question items on the brief RLS scale signified RLS. Item 4 provided information on RLS severity.

Results: Thus far, 1387 women pregnant with single fetuses (mean age 29.7±5.7 years and mean gestational age 34.2±3.8 weeks) have participated in this study. Of these, 487 (35%) were found to have RLS. Caucasian women were most likely (37%) and African American women were the least likely (25%) to report RLS. Overall, 70% of women with RLS reported symptoms occurring $\geq$ 2 nights/week and 33% reported symptoms $\geq$ 4 nights/week. Compared to women without RLS, women with RLS had a significantly higher frequency of total sleep disturbance (55% vs. 38%), poor sleep quality (79% vs. 67%), and poor daytime functioning (80% vs. 66%; all p-values <0.001). Using logistic regression and controlling for age, ethnicity, Epworth sleepiness score, BMI, and sleep disordered breathing, RLS independently predicted poor sleep quality (OR 1.57, 95%CI 1.2-2.1; p=0.002) and poor daytime functioning (OR 1.70, 95%CI 1.3-2.3; p=0.001).

Conclusion: RLS is highly prevalent in pregnancy. While pregnancy is associated with sleep disturbances, the presence of RLS may further impair sleep quality and daytime functioning. These findings suggest potential opportunities to improve women's sleep during pregnancy.

Albert Ho - Periodic leg movements and daytime sleepiness in children

Introduction: Periodic leg movements during sleep (PLMS) may negatively impact sleep quality, but no studies have supported an effect on daytime sleepiness using objective measurements in children. Our aim was to determine whether children with frequent PLMS based on polysomnographic criteria, and without evidence for sleep-disordered breathing (SDB) or narcolepsy, would demonstrate excessive daytime sleepiness as defined by mean sleep latency on a Multiple Sleep Latency Test (MSLT).

Methods: Our retrospective database analysis included polysomnograms and MSLTs performed from 1987-2003 on children referred for clinical suspicion of sleep disturbances. Analyzed variables included PLMS (PLMS per hour of sleep), AHI (apnea-hypopnea index), and mean sleep latency. Children were classified as having SDB if AHI $\geq$ 5; frequent PLMS if PLMS $\geq$ 5; or narcolepsy if $\geq$ 2 sleep-onset REM periods occurred in the absence of SDB.

Results: Among 153 children, 79 had neither PLMS, SDB, or narcolepsy, and 13 had a combination of more than one sleep problem. Of the remaining 61 children (ages 5-18 years), 16 had PLMS, 25 had SDB, and 20 had narcolepsy. Children with narcolepsy had shorter sleep latencies than those with SDB and PLMS (5.7±4.8 vs. 9.8±5.9 and 11.2±4.2 minutes; p=0.01 and p=0.002 respectively). Mean sleep latency did not differ between the SDB and PLMS groups (9.8±5.9 and 11.2±4.2 minutes; p=0.38). No correlation was found between PLMI and mean sleep latency ($r= -0.064$, p=0.44).

Conclusion: These results suggest similar objective levels of daytime sleepiness in children with frequent PLMS and those with SDB, whereas narcoleptics have worse sleepiness. Lack of correlation between PLMI and mean sleep latency matches previously reported findings in adults. However, preadolescent norms for mean sleep latency (19±3 minutes) suggest that children referred to our sleep clinic and found to have PLMS alone did also have evidence of excessive sleepiness on MSLTs.

Amanda Rabquer - Screening Laboratory Studies in the Initial Evaluation of Peripheral Neuropathy

Background, Significance, Rationale: Peripheral neuropathy is a common condition affecting approximately 2.4% of the population and an even higher percentage of the elderly[1]. Many different causes of peripheral neuropathy exist and there is clinical uncertainty about which tests should be performed in the initial evaluation of patients presenting for symptoms consistent with peripheral neuropathy. Recently, the American Academy of Neurology (AAN) published guidelines for the evaluation of the most common type of peripheral neuropathy, distal symmetric polyneuropathy[2]. Based on a systematic review of the literature, the AAN concluded that the highest level of evidence to support the use of commonly used screening laboratory tests (i.e., blood glucose, serum B12, and SPEP) was level C (possibly useful)[2]. The guideline statement did not address the many other tests, including rheumatologic studies and thyroid function tests, which are frequently ordered in evaluation this condition. Given the current health care climate, which places a premium on cost-effective medicine, further studies are needed to determine which tests should be performed in these patients.

Statement of Hypotheses and Specific Aims:

Specific Aim #1: To determine how often thyroid and rheumatologic screening tests are abnormal and/or change management in the evaluation of peripheral neuropathy.

Hypothesis #1: The yield of these studies will be incredibly low.

Hypothesis #2: When abnormal, these studies will only rarely change the management of a patient with peripheral neuropathy.

Specific Aim #2: To determine the factors that can predict whether these screening tests will be abnormal.

Hypothesis #1: Neuropathy type (mononeuritis multiplex), history of thyroid or rheumatologic disease, and signs and/or symptoms of thyroid or rheumatologic disease will be the only predictive factors for a positive test.

Research Designs and Method: We will obtain the names of all new patients seen in the neuromuscular clinic from 1/1/2007 to 12/31/08. We will identify those patients whose primary problem is peripheral neuropathy excluding those with compression neuropathies, traumatic neuropathies, and radiculopathies. We will perform a retrospective cross sectional study.
We will obtain information on gender, age, time since symptom onset, time since diagnosis of neuropathy, neuropathy subtype (AIDP, CIDP, mononeuropathy multiplex, DSP, sensory neuropathy, motor neuropathy, small fiber predominant neuropathy). We will also obtain information on suspected etiology, the presence or absence of pain, weakness on examination, demyelinating features on electrodiagnostic testing, any NCS abnormality, any EMG evidence of denervation outside of the foot attributed to the neuropathy, history of thyroid or rheumatologic disease, signs/symptoms of thyroid or rheumatologic disease.

We will identify those patients who have had blood tests for thyroid (TSH, free T3,4) and rheumatologic conditions (ESR, CRP, ANA, ANCA, adsDNA, RF, SSAB or ENA) and document the results as normal or abnormal. If abnormal we will document whether the test changed the suspected etiology or management of the patient. We will include tests whether they were ordered here (near the time of evaluation) or at an outside institution if included in the evaluation notes.

For statistical analysis we will perform chi square and Cox regression analysis using SAS software.

_Anticipated Results and Potential Problems:_ We anticipate that the yield of these tests will be quite low despite the relatively common use of these tests in the evaluation of peripheral neuropathy. Potential problems include inadequate information on previous work up since most patients have been seen by another neurologist prior to evaluation here at the University of Michigan. However, we have an excellent system for the documentation of outside hospital records and are unlikely to miss laboratory values that were available to the evaluating U of M neurologist.

_Future directions:_ We plan to continue to study the value of tests in the evaluation of peripheral neuropathy. Currently, we are trying to further define the potential for excellent durability in hearing preservation with a low incidence of complications.

**Anthony Wang**

**Background:** The middle cranial fossa approach is a microsurgical technique described as a primary option in the treatment of small, intracanalicular schwannomas involving the eighth cranial nerve. Excellent rates of complete tumor resection, hearing preservation, preservation of facial nerve function, and low complication rates have been reproduced using this technique. However, the durability of hearing preservation using the various treatment options has not been adequately assessed. Our purpose is to evaluate the durability of long-term hearing preservation in patients with vestibular schwannoma treated via the middle cranial fossa approach. We hypothesized that hearing preservation in these patients will prove to be quite durable.

**Methods:** Review was performed of 100 consecutive patients undergoing resection of vestibular schwannoma via a modified middle cranial fossa approach from 1999 through 2008. Patients in whom surgical goals were gross total resection and hearing preservation were included. Pre- and post-operative hearing assessment was done using standard audiometry, and classified according to American Academy of Otolaryngology-Head and Neck Surgery guidelines as a primary outcome measure. Outcomes and neurologic complications initially, and at one, three, and five years following operation, were analyzed.

**Results:** Initial hearing preservation rates were in keeping with the best previously-published results. Good hearing results were achieved in 83% of patients presenting with Class A hearing, and in 84% of all patients.

In order to assess the durability of hearing preservation in our patients, we evaluated hearing function at regular intervals after the initial post-operative audiometric follow-up. At 5-year follow-up, good hearing was preserved in 94% of patients with Class A hearing at initial post-operative follow-up, and in 98% of all patients.

**Conclusion:** In resecting small intracanalicular schwannomas of the eighth cranial nerve via the middle cranial fossa approach, the surgeon offers the potential for excellent durability in hearing preservation with a low incidence of complications.

**Beata Ruprecht**

**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:** This 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.

**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.

**Daniel Orringer**

**Introduction:** Achieving maximal resection of remains an important, yet elusive goal in brain tumor surgery. Nanotechnology provides a unique solutions for improving the accuracy of tumor surgery. We set out to create a tumor-targeted, dye-loaded nanoparticle capable of improving the extent and accuracy of resection by visibly delineating tumor margins during surgery.

**Methods:** Dye-loaded nanoparticles were created by reverse micelle polymerization of coomassie blue (CB)-linked acrylamide and targeted with a tumor targeting peptide, F3. Targeted, dye-loaded nanoparticles were intravenously injected at doses of 125-500mg/kg in brain tumor window animals and tumor delineation was recorded using digital videography for 6 hours following injection. Tumor delineation was quantified using a proven method for computerized image analysis. To evaluate the uptake of nanoparticle into brain tumors on a histologic level, animals bearing tumors expressing green-fluorescent protein were injected with rhodamine-labeled tumor-targeted nanoparticles.
Results: Qualitatively, dye-loaded nanoparticles at a dose of 250 mg/kg or greater visibly delineate brain tumor margins in the brain tumor window model. There is a quantifiable, improvement in tumor delineation with increasing nanoparticle dose. Moreover, peptide-based targeting of dye-loaded nanoparticles imparts a significant improvement in tumor delineation in comparison to non-targeted nanoparticles and free CB (p<0.00004). Nanoparticle-mediated tumor delineation remains visually detectable for greater than six hours in comparison to 2 hours for free dye. Based on histologic analysis, nanoparticles delineate tumor margins by accumulating within the angiogenic tumor vasculature.

Conclusions: Tumor targeted, dye-loaded nanoparticles are capable of delineating experimental brain tumor margins in a dose-dependent fashion for over 6 hours. Molecular targeting improves the efficiency of tumor margin delineation. Tumor delineation is likely achieved by the accumulation of nanoparticles within angiogenic vasculature. In summary, further preclinical testing is warranted to develop dye-loaded nanoparticles to advance the current surgical treatment of brain tumors.

Emily Lehmann - Representation of reward prediction and motivation in the ventral pallidum related to conditioned stimuli presented in association with drug reward.

Introduction: Much research has been done to evaluate the functional role of the basal ganglia in regards to control of movement, encouraged by the success of first stereotactic lesions, followed by stimulation, of deep brain structures for the treatment of movement disorders. Recently, interest has grown surrounding the use of stimulation in other regions of the brain in order to treat disorders as varied as epilepsy, depression, obsessive-compulsive (OCD) disorder and obesity. Dysfunction of the brain’s reward circuitry is thought to be common to OCD and obesity, as well as other addictive behaviors. It is thought that the nucleus accumbens (NAcc) and ventral pallidum (VP), because of their connections with prefrontal cortex and the amygdala, are involved in neural processing of reward. In order to better understand how the brain codes the value associated with rewarding stimuli, we will explore the response of the VP to conditioned stimuli related to drug rewards.

Temporal relation of the conditioned stimulus to the reward (unconditioned stimulus) can alter the motivational importance of that stimulus. Previous work in the Aldridge lab showed that, when presented with two sequential conditioned stimuli (CS1+, CS2+) prior to a sugar pellet reward, each stimulus was represented differently by the VP. It has been previously described that the first stimulus has more predictive information, while the second one has more incentive motivation (Tindell et al. 2005). Drugs of abuse, such as cocaine and amphetamine, alter dopamine signaling within the basal ganglia and amphetamine has been shown to increase the response of the VP to conditioned stimuli presented in association with food reward (Tindell et al. 2005). It is our intention to study the difference of the signals in the VP in response to CS1+ and CS2+ when the reward itself is a drug. Improved understanding of the brain’s processing of drug as a reward may allow for future treatments of addiction.

Methods: We will implant intravenous catheters into the internal jugular vein of male Sprague-Dawley rats. The rats will undergo Pavlovian conditioning, being presented with two temporally distinct stimuli (CS1+, CS2+) paired with an intravenous dose of a drug (amphetamine or cocaine). We will subsequently implant recording microelectrodes into the caudal ventral pallidum. Following implantation of the electrodes, we will record neuronal activity from single units in the caudal ventral pallidum to determine the response of this region to cues and drug rewards. Response of individual neural units will be assessed surrounding the individual stimuli and both the change in response rate and the number of units responding to a particular stimulus will be evaluated.

Expected Outcome and Interpretation: We expect that the firing rate of neurons in the caudal ventral pallidum will be altered following presentation of the stimuli corresponding to the intravenous administration of the drug reward. In previous work in the Aldridge lab, amphetamine sensitization as well as acute administration increased the firing rate as well as number of units responding to CS2+ presented in association with a food reward, perhaps indicating an increased incentive motivation toward the reward. Drugs of abuse may increase the incentive motivation associated with their own cues, creating a feedback loop magnifying the response of the ventral pallidum. This may represent the process by which addiction to drugs of abuse is established and then continued, and may indicate why cues related to drug-taking behavior can lead to relapse.

Eric Adelman - Outcomes from the use of pentobarbital: a retrospective analysis

Status epilepticus has a high mortality and can be difficult to treat. Pentobarbital is often used as a third or fourth line agent—after others have failed to control the seizures. Pentobarbital coma is also used to treat refractory intracranial hypertension. We reviewed UMHS pharmacy data to find adult patients who had received pentobarbital from 2004 through 2008.

Twenty-two patients received pentobarbital to treat status epilepticus (8) and intracranial hypertension (14). Toxic-metabolic conditions were the most frequent underlying etiology requiring pentobarbital use. Complications, including hypotension, renal failure, and pneumonia were common. Fourteen patients died in the hospital. Of the 8 patients who were alive at the time of discharge: 3 were discharged to acute rehabilitation, 2 to extended care facilities, 1 to sub-acute rehabilitation, 1 to hospice, and 1 to home. There was no significant association between mortality and reason for pentobarbital use (status epilepticus versus intracranial hypertension). Patients treated for an underlying toxic-metabolic problem were more likely to die than those treated for other etiologies.

Pentobarbital use is associated with significant morbidity and mortality. However, almost 20% (4/22) of patients treated with pentobarbital were discharged home or to an acute rehabilitation facility.

Jennifer Simpson – Background: The Joint Commission, the American Heart Association/American Stroke Association have developed specific measures to improve patient outcome after stroke. Our institution wishes to follow these guidelines to provide quality patient care.

Methods: Patients will be identified using ICD-9 codes 433 and 434 or MDSRG codes 61, 62, 63, 64, 65, 66, 67, and 68. Reason for admission, statin prescription at discharge, aspirin administration within 48 hours of admission, use of DVT prophylaxis, therapy referrals, use of other anti-thrombotic/anti-coagulation, length of stay, and disposition will be abstracted. General demographic characteristics and stroke risk factors (such as diabetes, coronary heart disease, congestive heart failure, hypertension, hyperlipidemia, atrial fibrillation, tobacco use, history of previous stroke) may also be obtained. If the patient was not managed by the neurology service, assessing the proportion of neurological consultations will also be studied.

Results: 343 charts have been reviewed thus far, 272 admitted the neurology service and 47 admitted to other services. Occupational therapy was less likely to be consulted (p=0.01), aspirin was administered less often within 48 hours (p=0.01), Aggrenox was less likely to be used as an antplatelet agent (p=0.02), and a statin was less likely given at discharge (p=0.02) by services other than neurology. Patients on the neurology service are more likely to have hyperlipidemia (p=0.01) and less likely to have chronic heart failure (p=0.03) as co-morbid conditions. 68% of patients had neurology consultations when on other services, and an additional 12% were transferred to the neurology service. Twenty-three patients were excluded from the study due to improper identification (hemorrhage, venous sinus thrombosis, subdural hematoma, no stroke findings during admission, etc)
Identification of areas to improve quality of care in stroke patients is necessary in the neurological patient population and on other medical and surgical services.

Jennifer Strahle –

Introduction: Type I Chiari Malformation (CM), defined as cerebellar tonsillar herniation greater than or equal to 5 mm below the foramen magnum, is a common pediatric diagnosis that is occasionally treated surgically. CM can also lead to spinal cord syrinx formation as a result of abnormal flow of cerebral spinal fluid at the foramen magnum. The true prevalence of syrinx in CM is not well defined as most reports are from small surgical case series. Additionally, the natural history of CM and syrinx is not well known. A greater understanding of the prevalence and natural history of these related conditions may lead to improved treatment decisions.

Methods: A retrospective review of all patients ages 0-18 with brain or cervical spine MR imaging at the University of Michigan from 11/1997-8/2008 was performed. The records of 14,116 consecutive individuals were reviewed. In those patients with CM on imaging, we recorded demographic information, symptoms, surgical information, and clinical and radiographic follow-up information.

Results: 509/14,116 patients had CM by imaging criteria (3.6%). 117 (23%) of these patients also had a spinal cord syrinx, and 86% of these syringes started in the cervical spine. The MR prevalence of CM with syrinx was 1.8% in girls and 0.5% in boys. CM was associated with hydrocephalus (11%) and scoliosis (22%). The degree of tonsillar herniation did not vary by age of CM diagnosis and averaged 10.15 mm. The severity of impaired CSF flow was associated with amount of tonsillar herniation (p<0.0001) and conformation of the tonsils (p=0.0001). 35% of CM patients underwent surgical treatment for this condition. These patients exhibited more severe tonsillar herniation (12.8mm vs. 8.6 mm, p=0.0001) and impaired CSF flow (p<0.0001) compared with patients who did not undergo surgery. 5% of patients with previously normal MRIs demonstrated interval development of CM with an average time to radiographic diagnosis of 1115 days.

Conclusions: This study describes the prevalence and natural history of CM and its association with syrinx and other abnormalities. CM is a frequent incidental finding on imaging that only occasionally requires surgical treatment. CM is associated with spinal cord syrinx, though less frequently than reported in prior series of surgical patients. Asymptomatic CM is associated with an excellent natural history; symptomatic or radiographic progression is rare in these patients.

Jocelynn Owusu - Habitual Snoring, Racial Background, and Gestational Hypertension in Pregnant Women

Introduction: Gestational hypertension is one of the leading causes of maternal mortality and morbidity. Outside pregnancy, obstructive sleep apnea (OSA) is a common condition and independent predictor of hypertension. This raises the possibility that OSA may play a role in gestational hypertension (GHTN). Both GHTN and SDB are more common among African-American women than Caucasian women. Therefore, we hypothesized that an excess frequency of OSA in African-American women may explain the higher prevalence of GHTN in this population.

Method: As part of a larger, prospective study, third-trimester pregnant women ≥18 years old were recruited from obstetric clinics and invited to complete several sleep questionnaires. For the present study, women who were normotensive at study entry were included and their risk of OSA was determined from a validated screening tool. High OSA risk was defined as habitual snoring ≥3 nights/week. Diagnoses of GHTN/pre-eclampsia were obtained from medical records following delivery.

Results: Among 1171 participants (mean age 29.6±5.6 years, mean BMI 26.1±8.6kg/m²), 194 (17%) were African-American, 241 (21%) had GHTN, and 403 (34%) had high OSA risk. The prevalence of GHTN was similar in African-American and Caucasian participants (23% vs. 20%, p=0.42), as was the prevalence of OSA risk (37.5% vs. 35.5%, p=0.14). OSA was significantly more common in women with GHTN than in those without (48% vs. 34%, p<0.001). The prevalence of GHTN was greater in women with high OSA risk than in those without high risk (27% vs. 17%), and the odds ratio (OR) for GHTN and high OSA risk was 1.8. The OR for GHTN and OSA risk in Caucasian women was slightly higher than in African American women (OR 1.9, vs. OR 1.4). In a logistic regression model including race, body mass index (BMI), age, and parity, OSA status was independently associated with GHTN (OR=1.3, 95%CI 1.01-1.75). Race was not independently associated with GHTN.

Conclusions: This study found that a significant proportion of pregnant women are at risk for OSA regardless of racial background, and that the presence of high OSA risk is associated with gestational hypertension. Nearly half of all women with gestational hypertension had high risk for OSA. Neither OSA risk nor gestational hypertension proved to be more common in African-American women than in other subjects. These findings require confirmation by objective measures, but suggest that all pregnant women should be screened in some manner for OSA, especially in the setting of gestational hypertension.

Lindsey De Lott - Occult Macular Dystrophy As A Cause Of Unexplained Vision Loss

Purpose: Reduced visual acuity or visual field abnormalities in the setting of a normal pupillary and funduscopic examination frequently leads to a diagnosis of functional vision loss. However, with mfERG and OCT testing showing foveal photoreceptor loss or dysfunction, occult macular dystrophy (OMD) has been identified as an organic cause of vision loss. We present 11 cases of OMD and describe the clinical, electrophysiological and OCT characteristics of this rare disorder.

Methods: Eleven patients (21 eyes) ages 16 to 62 years with complaints of visual loss were examined. Visual acuity, color vision, Goldmann and Humphrey visual fields, mfERG, full-field ERG, fundus examination, fundus photos, and OCT were obtained. mfERG was recorded as a scaled array of 103 hexagons. Amplitude and implicit time of six eccentric rings were compared to normal controls (n=15). Linear regression was used to determine correlation between foveal thinning or mfERG P1 amplitude and visual acuity.

Results: Visual acuity ranged from 20/20 to 20/400. Color vision was normal to severely affected. Visual fields were normal in 6 patients and 5 patients had central or paracentral scotomas. Full field ERGs were normal in all patients. Fundus examinations revealed normal optic nerve appearance without macular or peripheral retinal changes in all eyes. In some patients, OCTs showed thinning of the fovea. mfERGs showed significant amplitude reduction centrally (P<0.0001) and prolongation of implicit times (p<0.0001). There was no correlation between foveal thinning or mfERG P1 amplitude and visual acuity.

Conclusions: OMD is characterized by subnormal acuity, central scotoma, variable decrease in color vision, normal funduscopic appearance, and variable progression over time. Full field ERG is normal, but mfERG is abnormal in all patients. OCT may show thinning of the fovea. The severity of foveal thinning and mfERG amplitude loss does not correlate with visual acuity. Foveal dysfunction and/or photoreceptor loss are likely causes of vision loss in OMD.

Matthew Hastings –
Electromyography (EMG) is a useful diagnostic test in the diagnosis of neurological disorders. Studies have examined the predictors of patient's pain during EMG, physicians' ability to judge a patients' pain, and methods of controlling pain during EMG. While most authors cite pain as the cause of early termination or alteration of EMG studies leading to incomplete or inconclusive results, it remains unclear how often an electromyographer's perception of a patient's pain actually leads to alteration of the electromyographer's standard needle EMG practices.

**Primary objective:** To determine the frequency in which an electromyographer's perception of a patient's pain leads to an alteration of standard needle EMG practices.

**Secondary objective:** To determine the frequency of use of various methods of pain control used during needle EMG examination.

**Methods:** An electronic survey consisting of 12 questions will be sent to [4700-5000?] members of the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM). Six questions pertain to demographic information (gender, level of training, frequency of EMG performance, years of experience, American Board of Electrodiagnostic Medicine (ABEM) certification, and medical specialty). One three-part question pertains to frequency and ways of altering an EMG study due to an electromyographer's perception of a patient's pain. Two questions pertain to needle type used during EMG. One 17-part question pertains to methods of pain control during EMG. The results will be collected by the AANEM and analyzed by the resident investigator in a method to be determined.

**Results:** To be determined.

**Conclusions:** To be determined.

**Meena Murti** - Mallampati Grade and Snoring in Pregnancy

**Introduction:** Emerging data suggest that pregnancy is associated with an increased frequency of habitual snoring (HS) and sleep-disordered breathing (SDB) which may promote maternal hypertension. In sleep clinics, Mallampati grade (MP) is used to screen for SDB risk, but this assessment has not been widely used in the context of pregnancy. The goal of this study was to examine the relationship between HS, MP, and gestational hypertension.

**Methods:** Within a larger study of sleep in pregnancy, we obtained prospective data on women surveyed in the third trimester using validated instruments. HS was defined as snoring ≥3 nights/week. MP was obtained from medical records and dichotomized into grade I/II (low) or III/IV (high). Development of gestational hypertension was ascertained from the medical records after delivery.

**Results:** Data were obtained from 952 subjects (mean age 29.7±5.7 years, mean BMI 30.7±7.6kg/m²). HS was present in 36% of women and was more frequent in obese women (BMI≥30kg/m²) than non-obese women (55% vs. 29%; p<0.001). Women with high MP were more likely to have HS as compared to those with lower MP (51% vs. 34%; p=0.001). In a logistic regression with maternal age, gestational age, race, BMI, parity, smoking status, and the presence of diabetes taken into account, a high MP showed independent association with gestational hypertension (O.R. 2.0, 95%CI[1.1-4.2]; p<0.04). Addition of HS to the model made the relationship non-significant (O.R. 1.3, 95%CI[0.7-2.6]; p=0.38).

**Conclusion:** A substantial proportion of pregnant women have HS, and this key risk factor for SDB is associated with a simple measure of oropharyngeal crowding. The independent association of high MP with gestational hypertension is likely mediated by SDB, as addition of HS to the model removed the association. Use of this non-invasive, cost effective, oral assessment during routine physical examination may have clinical utility in pregnant women.

**Meredith Peters** - Changes in Polysomnography Following Cognitive-Behavioral Therapy for Insomnia in Patients with Major Depressive Disorder.

**Introduction:** Insomnia is pervasive in Major Depressive Disorder (MDD) and may contribute to relapse and recurrence. Studies of sleep using polysomnography (PSG) in MDD patients have consistently shown abnormalities in both sleep continuity and architecture. In this study, we examined whether changes in polysomnography were evident following a nonpharmacological treatment for insomnia in MDD patients.

**Methods:** Thirteen participants with MDD and chronic insomnia (mean age 43.4 ± 12.3 years, 11 women) were randomized to 6 sessions of group cognitive-behavioral therapy for insomnia (CBT-I, n=8) or to wait-list control (WLC, n=5). Daily sleep diaries were completed throughout treatment. The Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), self- and clinician-rated Quick Inventory of Depressive Symptomatology (QIDS-SR16), and clinician-rated Hamilton Rating Scale of Depression (HRSD-17) and Clinical Global Impressions (CGI) were completed pre- and post-treatment. Before and after treatment, participants underwent two nights of PSG.

**Results:** No changes in sleep or mood (self- and clinician-rated) were evident for the WLC before starting treatment (all p>0.05). Daily diaries indicated post-CBT-I improvements in total wake time (58.9 ± 24.4 vs. 117.8 ± 57.0 mins, p<0.001) and sleep efficiency (86.6 ± 5.6% vs. 76.8 ± 10.8%, p<0.001) but not total sleep time. PSQI and ISI scores decreased from, respectively, 11.3 ± 4.1 to 7.5 ± 1.2 (p=0.001) and 16.8 ± 4.5 to 10.9 ± 4.8 (p<0.001). Clinician ratings of mood on the HRSD-17 and CGI improved following CBT-I (p<0.05) with a trend for improvement on the self-rated QIDS-SR16 (p=0.059) and clinician-rated QIDS-SR16 (p=0.064). Only Stage 2 increased significantly (54.7 ± 8.0 vs. 48.0 ± 9.4%, p<0.05) on PSG after CBT-I.

**Conclusions:** Self- and clinician-rated mood and sleep improvements following CBT-I were not reflected in most objective sleep continuity and architecture changes. We will evaluate whether sleep changes may be evident using quantitative sleep EEG measures.

**Mudassar Asghar** - Epilepsy and Aicardi syndrome: A case of Hemi-hypsarrythmia

This is a case of an 8 month old female with medically-refractory epilepsy who was found to have agenesis of the corpus callosum, right sided coloboma, and infantile spasms. Clinically, she met the criteria for Aicardi syndrome, an X-linked chromosomal abnormality consisting of the classic triad of callosal agenesis, infantile spasms, and congenital defects of the eye. This presentation will review the incidence of hypsarrythmia in Aicardi syndrome and specifically look at whether hemi-hypsarrythmia has been reported in the literature.

**Nadir Osman** - Menin- is an anti-incretin and anti-orexin factor modulated by food-intake and diet.
Background & Aims: Ingestion of food initiates a complex network of hormonal and neural signals that ensures the proper absorption and storage of nutrients. A defect in any signaling pathway within the network results in pathologies associated with dys-regulated nutrient utilization such as obesity and type-2 diabetes. Incretins are expressed in the brain and gut and stimulate insulin secretion in response to oral nutrient intake to regulate glucose production and utilization. Orexins, expressed in brain and gut are appetite-stimulating peptides stimulated by hypoglycemia. Menin is the 67kDa product of the MEN1 gene, a tumor suppressor gene responsible for an autosomal-dominant cancer syndrome, and expressed ubiquitously. This study identifies cells expressing menin specifically in the brain and gut, and describes an association of menin with incretins and orexins. Methods: A) We fasted/refed C57BL/6 wild type (WT) and diabetic mice at 4 and 7hrs and B) fed these animals a high-fat or high fat high carbohydrate diet for 2 and 3 months. Tissue was collected and mRNA expression was analyzed by RT-PCR. Immunofluorescence was used to analyze co-localization of menin with incretins and orexins. Promoter activity was determined by dual-luciferase and protein expression by western blot analysis. Results: We demonstrate that menin is expressed in specific regions of the hypothalamus and in the K and L cells, and that fasting and re-feeding or chronic high fat diet modulates menin levels, in correlation with changes in incretin and orexin levels. Conclusion: Menin is an anti-incretin, anti-orexin factor modulated by feeding and high fat diet.

Olga McBabee - IVIG-related complications with long-term use IVIG treatment (> 1 year) in patients with neuromuscular disorders (chronic inflammatory demyelinating polyneuropathy (CIDP), myasthenia gravis (MG), multifocal motor neuropathy (MMN), etc)

Retrospective assessment of IVIG-related adverse events in 97 patients from neuromuscular clinic of University of Michigan treated with IVIG for different neuromuscular disorders (CIDP, MG, MMN, etc) since 2005.

Preeti Gupta - Title: Predictors of Outcome of Intensive Care Unit patients monitored with Status Epilepticus

Status epilepticus (SE) is a common neurological emergency with an estimated 150,000 cases and 55,000 deaths annually in the United States. SE includes generalized SE (including generalized convulsive SE and myoclonic SE), nonconvulsive SE, and complex partial SE. Generalized convulsive status epilepticus (GCSE) is defined as a single epileptic seizure of greater than thirty minutes duration or a series of epileptic seizures greater than thirty minutes during which function is not regained. Generalized seizures typically last ninety seconds and if there is evidence for ongoing motor activity greater than 5-15 minutes, treatment is indicated. (Lowenstein 99). Studies show that the current treatment of GCSE includes intravenous administration of 4mg of lorazepam followed by loading with 20mg/kg of fosphenytoin. Lorazepam and may be repeated if necessary. Refractory status epilepticus is defined as not responding to first line anti-epileptic therapy and is treated with midazolam, propofol, or barbiturates (phenobarbital and/or phenobarbital) usually to achieve burst suppression for at least 24 hours. Status epilepticus which can lead to significant morbidity and even mortality. Outcome from even aggressive treatment (defined as treatment of refractory SE for at least 24-48 hours) can be quite variable among different patient populations. The exact predictors of outcome and the effects of systemic disease are less defined in the literature.

We investigated all intensive care unit patients who underwent continuous EEG monitoring in 2008 and 2009. We studied their EEG, admission anti-epileptic therapy if present, treatment of status epilepticus, discharge anti-epileptic therapy, comorbidities, systemic illnesses at the time of diagnosis, and outcome. We used the Karnosky performance scale to define outcome; death (KPS 0), poor outcome (KPS 10-50), intermediate outcome (KPS 60-70) and good outcome (KPS 80-100).

Rani Singh - SEIZURE INCIDENCE, EEG CHARACTERISTICS, AND SHORT-TERM OUTCOME IN THE PEDIATRIC STROKE POPULATION

Rationale: The incidence of childhood stroke ranges from 2 to 8 in 100,000 per year in North America. The EEG in the acute setting of pediatric stroke is poorly characterized. In this study, we identify the incidence of seizures, EEG characteristics, and short-term outcome in patients presenting with an acute stroke at a tertiary care children's hospital.

Methods: Data was prospectively collected and retrospectively reviewed of patients presenting to a tertiary care children's hospital with an acute ischemic stroke (AIS), hemorrhagic stroke (HS), or cerebral sinus venous thrombosis (CSV). Over a 3.5-year period, 77 patients were identified and charts were queried for demographics, stroke type, witnessed clinical seizure activity, and EEG characteristics.

Results: The median age at presentation was 8.3 years (range: 2 months-18 years). 21% presented with clinical seizure activity, and an additional 10% had a clinical seizure during the acute hospitalization. 25% had a clinical seizure within the first 24 hours of presentation. Seizure incidence varied significantly among age, greatest in the 1 year – 5 years age group (p = 0.001), but did not vary among sex or stroke subtype. Those with a clinical seizure had higher rates of focal epileptiform discharges, focal slowing, generalized slowing, and electrographic seizures on EEG than those without (p = 0.001). Status epilepticus was common in those with an EEG (17%), and was more common in infants. NCSE was captured only in patients with prolonged EEG monitoring, always starting within 24 hours of monitoring. Seizure incidence and NCSE did not vary among stroke subtype. 24% of children had recurrent seizures six months after their stroke.

Conclusions: Pediatric stroke patients represent a population that is at high risk of seizure and encephalopathy. Patients are at greatest risk of a clinical seizure within the first 24 hours of presentation, and NCSE is common. Children with seizures in the first 24 hours of stroke onset are more likely to develop epilepsy.

Samir Karia - Myoclonic epilepsy of late onset in Down\'s syndrome (LOMED) – a late manifestation of neurodegenerative process in Down\'s syndrome

Late onset myoclonic epilepsy in Down\'s syndrome (LOMED) has been described in a very few adult patients with Down\'s syndrome, Alzheimer-type abnormalities have been described in more than half of adult Down\'s syndrome patients above 50 years of age. Both these feature together has been reported as Senile myoclonic epilepsy of Gentiloni. We report a 47 year old female patient with Down\'s syndrome who had cognitive as well as neurological decline over few years and later was diagnosed with Alzheimer\'s disease. Patient had one episode of generalized seizure around the time of diagnosis of Alzheimer\'s disease, but developed myoclonic seizures later in the course of Alzheimer\'s disease and was associated with rapid cognitive decline. The characteristic electrographic changes of fast spike-waves or polyspikes-wave were noticed later in the course of myoclonic epilepsy.

Samuel Taylor - EEG Power as a Metric of Drowsy Driving Behaviors

Introduction: Drowsy driving is a significant cause of motor vehicle accidents. It is critically important to identify drowsiness before it contributes to driver error, but no valid methods exist. We previously failed to identify drowsiness using visual scoring of EEG. In this study, we identify the incidence of seizures, EEG characteristics, and short-term outcome in the pediatric stroke population.

Methods: Ten healthy male subjects (Mean Age = 21.9, SD ± 2.1 years) maintained a 5-hour sleep schedule for 5 consecutive days, confirmed by sleep diary, actigraphic monitoring, and polysomnography. They drove on a closed 4.43 km course until they were either too sleepy to continue or 2 hours had elapsed. The cars were instrumented to collect performance data and simultaneous 16-lead EEG was acquired using standard polysomnography software. Drowsy driving episodes were identified via video profiling. Two of the 10 subjects neither exhibited drowsy driving behaviors nor experienced scorable sleep. The alpha, theta, and delta frequencies (left head region) from three of these subjects, for the 30 seconds preceding these episodes, were subjected to power analysis. Data from these drowsy episodes were compared to the first 5 minutes of the driving task when there was no video evidence of drowsy driving.


**Results:** No significant differences in EEG power between the control and drowsy episodes were evident for most electrode sites, though differences in theta power (Mean: 10.2 ± 2.0 vs. 10.9 ± 1.8, p=0.053) and the ratio of theta to alpha power (Mean: 1.24 ± 0.31 vs. 1.64 ± 0.25, p=0.029) were statistically significant in the left parietal and central head regions respectively.

**Conclusion:** Preliminary findings indicate nearly no differences in EEG power between control and drowsy episodes. We will continue to evaluate the efficacy of this method with the additional 5 subjects and compare quantitative measures with driving behaviors.

Sarah Berini - MRI parameters as prognosticators of the clinical course in multiple sclerosis

Introduction:

T2/Flair lesion burden and contrast enhancing lesions in multiple sclerosis have traditionally been utilized to track disease progression and to assess response to disease modifying therapies, but this approach has been more successful in relapsing remitting multiple sclerosis than it has been for secondary progressive multiple sclerosis. Diffusion tensor imaging may be a more accurate method for detecting clinically significant changes in secondary progressive MS.

Objective:

To conduct a retrospective study comparing DTI images from both relapsing remitting and secondary progressive MS patients at 12-36 month intervals with normal controls. The genu, splenium and body of the corpus callosum will be assessed in order to determine which areas have change in mean diffusivity, fractional anisotropy or perfusion parameters and if these changes are predictive of future lesion accumulation and clinical disease progression in RRMS and in SPMS. This study will provide a foundation for a future prospective study.

Methods:

Study subjects: 20 patients with RRMS and SPMS who receive clinical care at the University of Michigan Multiple Sclerosis Center with 2 Brain MRI scans performed between 2006 and 2010. Controls are any adult patient with a brain MRI at the University of Michigan that included diffusion and perfusion sequences.

Study Design:

The study is a retrospective study comparing at least 2 MRI brain scans, at least 12 months apart on 20 patients with RRMS and 20 patients with SPMS to be compared with normal controls. Measurements are taken from the genu, splenium and body of the corpus callosum as well as from the periventricular white matter. Clinical data including disease modifying therapies and reason why the scans were obtained was also gathered. T-test will be used to compare controls and normals. We will also be attempting to determine if mean diffusivity and fractional anisotropy are predictive of future lesion accumulation and clinical disease progression. Logistic regression will be used for this purpose.

Conclusion:

Currently all study patients have been selected, clinical data has been gathered and measurements are being drawn and compared by three separate radiologists.

Shawn Hervey-Jumper - Torticollis associated with Neonatal Brachial Plexus Palsy

**Background:** Torticollis occurs in the context of neonatal brachial plexus palsy, but literature review revealed little information regarding the incidence, natural history or factors associated with recovery of the condition. Consequently, clinicians encounter difficulties counseling patients and recommending treatments because neither clinical outcomes nor definitive treatment guidelines have been reported for torticollis associated with neonatal brachial plexus palsy.

**Methods:** We retrospectively reviewed 128 patients with neonatal brachial plexus palsy at the University of Michigan from 2005 to 2009. All patients were followed for at least 3 months in the Brachial Plexus Program with detailed examinations at regular intervals.

**Results:** Of 128 patients diagnosed with neonatal brachial plexus palsy, 43% presented concurrently with torticollis. Ninety-eight percent had torticollis ipsilateral to the side of the brachial plexus palsy. Statistically significant differences (p<0.05) were found between torticollis and non-torticollis groups with regards to recovery of brachial plexus palsy as indicated by biceps recovery by 6 months of age (p=0.038). Associations were seen with concurrent phrenic nerve palsy (5.4% in torticollis group vs. 1.4% in non-torticollis group, p=0.189), the use of birthing aids such as vacuum and forceps extraction (27% in torticollis group compared with 16% in non-torticollis patients, p=0.137), the use of episiotomy during delivery (56% compared with 44% in non-torticollis patients, p=0.160), need for nerve repair/reconstruction (22% torticollis patients vs. 11% non-torticollis patients, p=0.094), and maternal diabetes (13% compared with 22% in non-torticollis patients, p=0.180). No significant differences (p> 0.2) were found between the torticollis and non-torticollis groups with regard to affected side, gender, birth weight and length, gestational age, shoulder dystocia, ICU hospitalization, clavicle fracture, presentation at delivery (cephalic, breech), method of delivery, duration of labor, delivering clinician, use of birthing maneuvers, maternal hypertension during pregnancy, gravidity, maternal weight gain, maternal age at delivery, and severity of brachial plexus palsy (Narakas grade). No patients were found to have concurrent hip dysplasia on clinical examination. Recovery from torticollis was observed in 64% of patients by 23 weeks (standard deviation 12) with conservative management.

**Interpretation:** We observed a high incidence (43%) of torticollis associated with neonatal brachial plexus palsy. The presence of concurrent torticollis was associated with poorer recovery from the brachial plexus palsy (as indicated by biceps recovery) than those presenting without torticollis. Although the severity of brachial plexus palsy did not correlate with the presence of torticollis, concurrent phrenic nerve palsy may be associated with torticollis in the context of neonatal brachial plexus palsy. Much controversy surrounds the management of these patients, but our data suggests that conservative management with physical / occupational therapy yields a reasonable recovery.

Veronica Sesi - Use of Sleep Aides During Pregnancy

**Introduction:** Some sleep disruption is often considered a normal part of pregnancy and few women seek treatment for sleep problems. There are a number of sleep aides available but most are contraindicated during pregnancy. To our knowledge there are no published data on the use of sleep aides by pregnant women.
Methods: As part of a larger study of sleep during pregnancy, pregnant women in their last trimester were invited to complete validated questionnaires including the General Sleep Disturbance Scale. Sleep disturbance was considered present if the mean total score or any subscale score was 3. This scale includes questions regarding the use of alcohol, tobacco, herbal products, pain medications, prescription and over the counter sleeping pills to induce sleep. Frequent use of sleep aids was defined as use of any of these aids ≥3 nights/week.

Results: Surveys have been completed by 1396 women (mean age 29.7±5.7 years, gestational age 34.2±3.8 weeks, and 43% primiparous). In total, 71% of women reported poor sleep quality and 14% reported frequent use of ≥3 sleep aids. Frequent use of alcohol was reported in 0.4% of women, tobacco in 1.4%, herbal products in 0.6%, pain medications in 4.1%, prescription medications in 3.4%, and over-the-counter sleeping pills in 3.9%. A small proportion reported frequent use of multiple sleep aids (1.4%). Multiparous women were more likely to report frequent use of sleep aids (21% vs. 16%; p<0.016). In a logistic regression model accounting for age, race, BMI, and parity, both poor sleep quality and poor daytime function independently predicted frequent sleep aid use (O.R. 2.3, 95%CI 1.5-3.5 and O.R. 1.5, 95%CI 1.1-2.3; p<0.001 respectively).

Conclusion: Sleep disturbance is common in pregnant women and a large minority report frequent use of substances to induce sleep. Of concern, several of these sleep aids are contraindicated during pregnancy.

Vessela Giger-Mateeva - Transgenic expression of the FIG4(I41T) phosphatase: A mouse model of human leukodystrophy

Proper myelination of central nervous system (CNS) fibers ensures rapid propagation of action potentials. In addition, myelination regulates axon caliber, health, and stability. The myelinating glia of the CNS is the oligodendrocyte (OL). Defects in OL maturation or differentiation results in defects of CNS myelination. Lack (dysmyelination) or loss (demyelination) of myelination causes severe neurological deficits including tremor, seizures, and death.

The pale tremor mouse (plt) has a severe neurological phenotype that is caused by a spontaneous mutation of the FIG4 gene. Mice null for FIG4 show severe tremor and typically die before one month of age. The FIG4 gene encodes a PI(3,5)P(2) 5-phosphatase that regulates levels of membrane bound phosphoinositides on vesicles and thereby influences vesicle trafficking to lysosomes. Growing evidence suggests that loss of FIG4 causes defects in autophagy, a key pathway of protein turnover and organelle degradation. Interestingly, mutations in the human FIG4 gene have been described. A point mutation at amino acid 41 of FIG4 results in a new form of Charcot-Marie-Tooth disease, called CMT4J (Cow et al., 2007; Nature, 448(7149):68-72). Whether loss of FIG4 or mutation of FIG4 at amino acid 41 causes defects in CNS myelination has not yet been examined.

To examine whether the Fig4 gene is important for proper myelination of CNS axons, the optic nerve of wild-type and plt mice was analyzed at the light microscopic and ultra-structural level. Electron microscopy revealed a severe hypomyelination 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 hypomyelination phenotype, biochemical studies revealed that levels of myelin-associated glycoprotein (MAG), Oligodendrocyte myelin glycoprotein (OMgp), and myelin basic protein (MBP) are decreased by more than 50% in plt brain extracts compared to age-matched wild-type controls. Furthermore, the number of MAG-positive OLs is significantly decreased in the optic nerve of plt mice compared to wt controls. To assess whether axon hypomyelination observed in the optic nerve leads to functional impairments, the conduction velocity (CV) of action potentials in optic nerve explants was assessed in vitro. Consistent with the anatomical findings, CV studies showed that in plt optic nerve there is a profound shift toward slower conducting axons.

To examine whether the FIG4 mutation at amino acid 41 FIG4(I41T), previously described in human CMT4J patients, results in a CNS myelination defect, transgenic mice were generated that lack wild-type Fig4 but instead express the mutant FIG4(I41T). Our preliminary studies revealed that FIG4 (I41T) mice show a hypomyelination defect in the CNS. Thus, our findings suggest that FIG4 is important for proper myelination of CNS and PNS axons. Moreover, the FIG4 mutant I41T is not sufficient to rescue the plt phenotype and provides a potential explanation for why this mutation causes neurological defects in human patients. In future studies the plt mouse will be further characterized to determine the mechanism of how loss of the FIG4 gene product leads to hypomyelination.

Vikas Kotagal - REM sleep behavior disorder is associated with cortical cholinergic deficit in Parkinson’s disease without dementia

Objectives: To explore the neurochemical basis of REM sleep behavior disorder (RBD) in non-demented subjects with Parkinson’s disease (PD) using vesicular monoaminergic type 2 (VMAT2) (+)C-11)dihydrotetrabenazine (DTBZ) and acetylcholinesterase (AChE) [C-11]methyl-4-piperidyl- Transgenic expression of the FIG4(I41T) phosphatase: A mouse model of human leukodystrophy

Methods: RBD is a well-described phenomenon consisting of vivid dreams and incomplete muscle atonia leading to motor automatisms during REM sleep that may precede or occur with PD. RBD is now being recognized as a risk factor for the development of dementia in PD but it is unclear if the presence of RBD is associated with cortical or subcortical cholinergic denervation. We evaluated 45 patients with PD (mean age 64.7±5.8, Hoehn and Yahr stages I-III) using the Mayo Sleep Questionnaire to assess for symptoms of RBD as well as DTBZ and PMP brain PET imaging.

Results: 27 out of 42 subjects reported positive symptoms of RBD. Those individuals who reported RBD symptoms showed significantly decreased cortical AChE activity compared to subjects without RBD (0.0259±0.0023 vs. 0.0283±0.0029, t=2.91, P=0.006).

There were no significant differences in subcortical (thalamic) AChE activity (0.0558±0.0050 vs. 0.0580±0.0050, t=1.35, P=0.19) or striatal VMAT binding (1.92±0.25 vs. 2.04±0.40, t=1.24, P=0.22).

Conclusions: The presence of RBD in PD correlates with cortical cholinergic denervation and may predict the ultimate development of Parkinson’s disease with dementia.