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Neurology [ALERT®]

Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

No Evidence Supporting Coenzyme Q10 Use in Parkinson's Disease

By Claire Henchcliffe, MD

Associate Professor of Neurology and Neuroscience, Weill Cornell Medical College

Dr. Henchcliffe reports she is on the speakers bureau and advisory board for GE, Teva Pharmaceutical Industries, and UCB; advisory board for Allergan and USWorldmeds; receives grant/research support from Biogen and Kaneka; and does CME program development and presentation for MedIQ.

SYNOPSIS: This large, randomized Phase 3 clinical trial of high-dose coenzyme Q10 failed to show any neuroprotective benefit in early Parkinson's disease.

SOURCE: Parkinson Study Group QE3 Investigators. A randomized clinical trial of high-dosage coenzyme Q10 in early Parkinson disease: No evidence of benefit. *JAMA Neurol* 2014;71:543-552.

This Phase 3, double-blind, placebo-controlled trial, nicknamed QE3, was designed to test the hypothesis that high-dose coenzyme Q10 is neuroprotective in Parkinson's disease (PD). Individuals with early unmedicated PD (n = 600) were randomized to placebo, 1200 mg coenzyme Q10 (CoQ10) daily, or 2400 mg CoQ10 daily for 16 months or until there was a need for dopaminergic therapy. All received 1200 IU vitamin E in the combination wafers, thus reproducing the intervention in the preceding Phase 2 (QE2) study. Mean age at enrollment was 62.5 years, one-third were women, and 7.5% were minorities. There were no differences between groups when analyzed based on sex, age, or severity of PD. Mean baseline total Unified Parkinson's Disease Rating Scale (UPRDS) at baseline was 22.7, corresponding to a mild degree of symptomatology, and mean disease duration ranged between 2.0 ± 1.5 and 2.2 ± 1.9 years in the different treatment groups. At study completion, no statistically significant differences were found between groups in primary and secondary outcome variables. In fact, treatment groups had marginally worse changes from baseline to endpoint when

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compared with the placebo group. Change (worsening) in total UPDRS score from baseline to endpoint was: + 6.92 ± 0.63 points (placebo); + 7.50 ± 0.62 points (1200 mg CoQ10 daily); and + 8.01 ± 0.63 points (2400 mg CoQ10 daily). No imaging biomarkers were included. Although 72.5% of participants reported side effects, they were mild in 62.7% and did not markedly differ between the three groups. The most common adverse events reported were back pain, constipation, and insomnia. In the CoQ10 arms, 3% had treatment reduced and 8.3% had treatment suspended, compared with 1% and 6.4%, respectively, in the placebo arm. Serious adverse events were reported in 33 individuals: Of these, one event of severe gastrointestinal bleeding was considered possibly related to the study intervention (this was in association with angiodysplasia). There was one death from cardiac arrest 8 days after completing the study (1200 mg CoQ10 daily).

■ COMMENTARY

Despite a robust rationale for a potential neuroprotective effect of CoQ10 in PD, this large Phase 3 QE3 study has failed to demonstrate any benefit. The result is disappointing, to say the least. Several lines of evidence had supported CoQ10 as a promising candidate for neurprotection. CoQ10 is a potent antioxidant and is critical in the mitochondrial electron transport chain, and therefore was predicted to "correct" increased oxidative stress and mitochondrial dysfunction in PD. Robust preclinical data in cell culture and animal models have supported its neuroprotective activity. A Phase 2 study of doses of CoQ10 up to 1200 mg daily (nicknamed QE2) demonstrated safety and tolerability in 80 subjects with early PD, and importantly also suggested that it might slow PD progression. CoQ10 has also been studied in a futility design study, conducted by the NINDS Neuroprotection Exploratory Trials in PD (NET-PD) program. CoQ10 administered to 213 patients did not meet futility criteria and was deemed worthy of further study. On the other hand, MitoQ, a coenzyme Q10 derivative, failed to show benefit in a recent study in 128 early PD patients. Moreover, the NET-PD trial results noted above have been criticized, based on use of historical control subjects. Although a "failure," mitochondrial medicine may yet prove beneficial and the QE3 study highlights a number of critical issues in developing neuroprotective therapies. Potential reasons for a negative result include limitations of animal models as predictors of success for neuroprotective strategies in humans, heterogeneity of PD etiopathogenesis, and limited readouts available for use in clinical trials. The study should therefore encourage ongoing efforts in the field to 1) improve disease modeling, for example using genetic animal models and iPS cells; 2) determine the "best" study population for an intervention; and 3) identify objective biomarkers that will measure disease progression as well as demonstrate target engagement. ■

ABSTRACT & COMMENTARY

The Relationship Between REM Sleep Behavioral Events and Parkinson's Disease

By Matthew R. Ebben, PhD

Assistant Professor of Psychology in Clinical Neurology, Center for Sleep Medicine, Weill Medical College of Cornell University

Dr. Ebben reports no financial relationships relevant to this field of study.

SYNOPSIS: This large-scale polysomnographic study demonstrated that the prevalence of REM sleep behavioral events in unmedicated patients with newly diagnosed Parkinson's disease is higher than in healthy controls.

SOURCE: Sixel-Doring F, et al. Rapid eye movement sleep behavioral events: A new marker for neurodegeneration in early Parkinson disease? *Sleep* 2014;37:431-438.

REM sleep behavior disorder (RBD) was first proposed as a clinical sleep disorder in the mid-1980s by Schenck, who described patients acting out dreams in the context of REM sleep. This condition is most common in males over the age of 50, particularly in the sixth and seventh decade of life. It is now well known that α-synucleinopathies, such as multiple systems atrophy, Lewy body dementia, and Parkinson's disease (PD), have a strong association with RDB. In fact, 50-80% of idiopathic RBD patients will develop an α-synucleinopathy within 10-15 years. However, few large-scale polysomnographic (PSG) studies have investigated the prevalence of RBD in newly diagnosed and unmedicated PD cases, which is the focus of this study. Moreover, most previous investigations have concentrated on violent dream enactment, whereas the Sixel-Doring study includes subtle purposeful movements in REM sleep as well as REM sleep without atonia (RWA) in their investigation.

Subjects included men and women between the ages of 40-85 years with a diagnosis of PD based on the UK Brain Bank Criteria. PD subjects were compared to neurologically healthy controls (HC) matched by age, sex, and educational level. Exclusion from the PD group included severe vascular encephalopathy or normal pressure hydrocephalus on MRI, multiple system atrophy, progressive supranuclear palsy, medication-induced PD, and/or past treatment with antipsychotic drugs. Exclusion from the HC group included a history of a central nervous system disorder in self or a close relative, evidence of cognitive decline (Mini-Mental State Examination [MMSE] < 26), and/or a current sleep disorder.

Both HC and PD groups were given two PSGs; when possible, the second recording was used for analysis. Investigators reviewed and documented videos from the subjects for visible movements and vocalizations. All purposeful movements and noises were classified as REM sleep behavioral events (RBE). Surface electrodes on the mentalis muscle quantified RWA. The number of 3-second groups with elevated muscle tone within a 30-second epoch of sleep was used to gauge the degree of RWA in each subject. An RBD screening questionnaire was used to assess history of RBD.

In addition to PSG, each subject also had a neuropsychological assessment that included tests of executive function, attention, speech, verbal fluency, memory, and visual spatial function.

A total of 159 subjects with PD and 110 HC were used for analysis. In the PD group, 25% had purposeful movements and/or vocalizations as well as increased mentalis activity in REM sleep qualifying them as definite RBD, compared to 2% of HC. This finding was not statistically significant. In subjects without behaviors during REM sleep, 4% in the PD group and 2% of the HC showed RWA (not significant). On the measure of RBE, 51% of PD subjects and 15% of HC were found to be positive ($P < 0.001$). REM latency was significantly longer in the PD vs HC groups ($P = 0.003$). However, no other sleep parameters were significantly different between groups.

MMSE, clock drawing, and odor identification scores were significantly worse in the PD with RBE vs PD without RBE groups. Tremor, UPDRS (subscale 3), postural instability/gait disorder, and Hoehn and Yahr stage were not significantly different between groups.

Neuropsychological assessments revealed that PD + RBE group had significantly worse verbal fluency (both semantic and lexical) and memory, as well as spatial ability, similarity discrimination, and Stroop interference compared to the HC-RBE group.

■ COMMENTARY

This study found that a higher number of PD subjects had RBE events (51%) compared to definite RBD (25%). Neuropsychological assessment of the PD with RBE group showed a broad decrement in function over the HC without RBE group. However, a higher number of HC subjects were also found to have RBE (15%) compared to definite RBD (2%). The authors of this paper had no explanation for the high percentage of normal controls with RBE. It will be important to follow these subjects prospectively to see if they convert to PD. Nonetheless, this suggests that RBE events can be used as part of an assessment for PD, but should not be used independently as a diagnostic tool for PD. More importantly, this study suggests that patients found during polysomnographic testing to have purposeful movements during REM sleep, not quite rising to the level of definite RBD, should be evaluated for PD. ■

ABSTRACT & COMMENTARY

Electrodiagnosis of Thoracic Outlet Syndrome

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Rubin reports no financial relationships relevant to this field of study.

SYNOPSIS: Thoracic outlet syndrome is difficult to accurately diagnosis and requires adherence to rigorous clinical and electrophysiological criteria to avoid errors and unnecessary surgery.

SOURCE: Tsao BE, et al. Electrodiagnostic features of true neurogenic thoracic outlet syndrome. *Muscle Nerve* 2014;49:724-727.

Thoracic outlet syndrome (TOS) refers to disorders attributed to compromise of the neurovascular structures in that area, including arterial TOS, venous TOS, true neurogenic TOS (TN-TOS), or combinations of the above. TN-TOS, also known as Gilliat-Sumner hand, involves motor and sensory loss in the arm and hand due to stretching of the lower trunk of the brachial plexus over a fibrous band, arising from the end of a rudimentary cervical rib and attaching to the upper surface of the normal first thoracic rib. Anterior scalene muscle compression of the lower trunk may also be causative. Electrodiagnostic studies are required in all patients in whom this diagnosis is considered, and a specific set of findings should be sought. What are they?

To determine the electrodiagnostic features of TN-TOS, retrospective review of the Cleveland Clinic Electrodiagnostic Laboratory database was undertaken for the years 1975-2008, and all patients with surgical verification of TN-TOS and preoperative electrodiagnostic studies were included for study. Nerve conduction studies were performed using standard techniques and distances, limbs were warmed and kept at a minimum surface temperature of 34° C, needle electromyography (EMG) was performed using concentric needle electrodes, and all examiners had completed fellowship training at the Cleveland Clinic.

Among 32 patients who met inclusion criteria, all were referred for nonspecific hand weakness and atrophy, with symptoms on the dominant side in 81% (n = 26). Age ranged from 17-77 years, and symptom duration from 2 months to 20 years (mean = 61 months). Handgrip or fine distal motor weakness was described in 97% (n = 31), and intrinsic hand muscle atrophy, particularly of the thenar muscles, was present in all. Pain, paresthesiae, or numbness of the medial forearm or hand was noted in 97% (n = 31). Cervical spine radiographs, performed in 29 patients, identified a cervical rib or elongated C7 transverse process in 83% (24 of 29), which was bilateral in 66% (n = 19) and on the asymptomatic side in a single patient. Surgical exploration revealed a tendonous band in all patients, which was resected, with concomitant first thoracic rib resection in 10 patients.

Nerve conduction studies revealed that the median compound motor action potential (CMAP) amplitude recording from abductor pollicis brevis was decreased for age in 91% and by side-to-side comparison in 97%. Ulnar CMAP values, recording from abductor digiti minimi, were decreased in 3.1% and by side-to-side comparison in 38%. Among sensory nerves, the medial antebrachial cutaneous sensory nerve action potential (SNAP) amplitude was the most sensitive, being low for age in 84% and by side-to-side comparison in 95%, with ulnar SNAP amplitude decreased in 6.3% and 78%, respectively. Chronic motor axon loss was evident on needle EMG, particularly in T1/median nerve innervated intrinsic hand muscles, and less so in C8 median or ulnar innervated hand and forearm muscles, with spontaneous activity in the form of fibrillation potentials noted in 50% in the former and in 33% in C8/ulnar intrinsic hand muscles. TN-TOS affects T1 > C8 fibers, and comparison to the unaffected side is critical for accurate diagnosis.

■ COMMENTARY

One of the most controversial diagnoses in medicine, and frequently over diagnosed, TOS is often diagnosed and treated surgically with poor results. Careful adherence to objective clinical criteria is necessary to avoid this pitfall, as patients with nonspecific arm numbness, tingling, and pain are often given this label. Electrodiagnostic studies are crucial to accurate diagnosis, and the authors are to be commended for outlining their findings in this retrospective study. Physicians would be well advised to rigorously adhere to these criteria before referring such patients for surgery. ■

ABSTRACT & COMMENTARY

Copper and AD – New Information

By Richard S. Isaacson, MD

Associate Professor of Neurology (Education), Weill Cornell Medical College

Dr. Isaacson reports he is a retained consultant and on the speakers bureau for Novartis, and is a retained consultant for and receives grant/research support from Accera.

SYNOPSIS: Patients with mild cognitive impairment with elevated free serum copper levels may have a higher rate of conversion to Alzheimer's disease compared to those with normal free serum copper levels.

SOURCE: Squitti R, et al. Value of serum nonceruloplasmin copper for prediction of mild cognitive impairment conversion to Alzheimer disease. *Ann Neurol* 2014;75:574-580.

While there are many uncertainties as to the exact cause of Alzheimer's disease (AD), recent research has started to clarify the relationship between a variety of metals, or more specifically the heavy metals, and development of AD.[1] While heavy metals are found naturally in the environment and several are essential for optimal health, high concentrations have been associated with a variety of diseases. Aside from being contained in dietary sources, heavy metals may also enter the body through air inhalation or handling manually. In the landscape of AD, controversy has surrounded the potential influence of several essential heavy metals, including copper, zinc, and iron, as well as the nonessential metal aluminum. Further, the potential clinical efficacy of chelating agents to remove these metals has also been controversial, and evidence is insufficient to warrant its use.

A new longitudinal study helps to clarify this controversy by demonstrating that higher levels of nonbound ceruloplasmin (non-Cp) copper, also called "free copper," in the earliest stages of mild cognitive impairment (MCI) could account for a faster rate of progression to dementia due to AD. This study follows meta-analyses demonstrating that free copper levels are higher in AD patients. This study by Squitti and colleagues included 42 MCI converters and 99 stable MCI patients. Levels of copper, ceruloplasmin, and non-Cp copper, as well as a host of other biomarkers (iron, transferrin, ferritin, APOE genotype, MMSE scores) and potential risk factors (age, sex, hypercholesterolemia, blood pressure) were assessed. Of these, the only significant predictor of conversion from MCI to AD was non-Cp copper ($P = 0.022$). Of note, conversion rates were independent of APOE4 genotype. Based on these findings, the authors suggested healthy lifestyle choices and potential dietary modification to mitigate this risk.

■ COMMENTARY

While the body needs copper, there is the potential that high amounts from either food or the environment over a long period of time could lead to increased beta-amyloid deposition or decreased clearance in the brain, as well as inflammation. Additionally, copper metabolic dysfunction (as evidenced by increased serum-free copper levels) is a condition exhibited only by a subset of AD patients (about 60% of AD patients and 50% of MCI). This "copper phenotype" is recognizable early in the disease course, and defining this group further may provide more targeted interventions while also preventing ineffective and even potentially dangerous adverse events derived from chelating agents (e.g., D-penicillamine) or the use of zinc therapy in AD patients not exhibiting this phenotype.

Preliminary evidence supports the idea that changes toward a safer diet in patients with copper dysfunction should carefully follow the RDA for copper. In this regard, copper enters the body mainly through dietary intake (food ~75%, drinking water ~25%). RDA for copper is 0.9 mg/day, whereas the tolerable upper intake level has been set at 10 mg/day.[2] Scientific and medical consensus will only be reached after further research proves that reducing copper absorption can change the clinical history of cognitive decline. Some of the foods that may have the highest amounts of copper include canned clams, liver, and oysters. Other surprising high sources of copper include mushrooms and sesame seeds.

The body of evidence toward dietary interventions in AD is growing, and progress continues to be made in determining modifiable and non-modifiable risk factors involved in the development of AD, as well as pharmacogenomics and nutrigenomic considerations for AD management.[3] While further studies are warranted regarding the association of non-Cp copper with cognitive dysfunction and AD, minimizing chronic high exposure and/or copper reduction strategies may be one of the myriad of potentially useful strategies in the multi-modal AD risk-reducing armamentarium. ■

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ABSTRACT & COMMENTARY

Predictors of Seizures After Trauma

By Nitin K Sethi, MD

Assistant Professor of Neurology, Weill Cornell Medical College

Dr. Sethi reports no financial disclosures relevant to this field of study.

SYNOPSIS: In this large prospective study of trauma patients, the most important factor associated with post-traumatic seizures was the presence of alcohol intoxication.

SOURCE: Vaaramo K, et al. Predictors of new-onset seizures: A 10-year follow-up of head trauma subjects with and without traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2014;85:598-602.

Recent reports indicate that both civilian and military cases of traumatic brain injury (TBI) are on the rise. An estimated 1.5-2.5 million civilian TBI cases occur per year in the United States. Mild TBI has also been recognized as the "signature injury" of America's global war on terrorism in Iraq and Afghanistan. Seizures are a long-recognized sequela of head injury, especially when complicated by moderate-to-severe TBI. While seizures occur soon after head trauma in immediate and early post-traumatic epilepsy (PTE), epilepsy can be a delayed consequence with seizures occurring as far out as 5-20 years. Penetrating head trauma, brain contusion, subdural hematoma, epidural hematoma, intracranial hemorrhage, and depressed skull fracture all increase the risk of PTE. Other predictors include age 65 years or older, Glasgow Coma Scale (GCS) of 3-8, loss of consciousness (LOC) > 30 minutes, and post-traumatic amnesia (PTA) lasting more than 24 hours.

The authors investigated risk factors for new-onset seizures in a cohort of 739 trauma patients. There were 362 trauma patients without TBI (GCS score of 15, no LOC, no PTA), 297 with mild TBI (GCS scores of 13-15, LOC < 30 min or PTA < 1 hr, no traumatic intracranial findings on CT/MRI) and 80 with moderate-to-severe TBI (GCS < 13, patients with evidence of TBI on CT/MRI). Those with a prior history of seizures, dementia, stroke, and other neurological disease were excluded. Out of 42 patients who developed new-onset seizure(s), alcohol-related seizures occurred in 19 (45.2%), most commonly among those with no TBI. Seventeen of these patients (85.2%) were intoxicated at the time of the index trauma. Moderate-to-severe TBI patients had higher mortality and were more likely to develop PTE. Alcohol-related head injury, moderate-to-severe TBI, and preceding psychiatric disease were all found to be independent predictors of new-onset seizure.

■ COMMENTARY

One of the sequelae of trauma with TBI, in both the civilian and military setting, is the emergence of seizures and development of PTE, which may occur as far out as 5 years following head injury. While the severity of head trauma is the main predictor for the emergence of PTE, active alcohol and drug abuse at the time of the index injury predisposes to new onset seizures via a complex and multifaceted interaction. Alcohol impairs reaction time, hand-eye coordination, judgment, and driving skills predisposing one to trauma and TBI. It further lowers the seizure threshold via its effects on glutamate NMDA and GABA receptors.[1] Chronic alcoholics are prone to electrolyte and glucose imbalance and seizures may occur both in the setting of binge drinking (rum fits) as well as abrupt cessation (alcohol withdrawal seizures and delirium tremens). Patients may at times present with new onset status epilepticus. All patients with head trauma should be screened for alcohol and drug abuse and effective intervention strategies should be implemented if abuse is identified. These patients remain at risk for post-traumatic seizures and should be kept under observation. While benzodiazepines (lorazepam) are efficacious for primary and secondary prevention of recurrent seizures in the alcoholic patient, long-term anticonvulsant therapy may not be needed in abstinent patients or those with mild TBI.[2,3] ■

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STROKE ALERT

By Matthew E. Fink, MD

Professor and Chairman, Department of Neurology, Weill Cornell Medical College, and Neurologist-in-Chief, New York Presbyterian Hospital

Smoking is a Risk Factor for Perimesencephalic Subarachnoid Hemorrhage

SOURCE: Mensing LA, et al. Risk factors in patients with perimesencephalic subarachnoid hemorrhage. *Eur J Neurol* 2014;21:816-819.

Smoking and hypertension are well-documented risk factors for aneurysmal subarachnoid hemorrhage (aSAH), while excessive alcohol consumption is less well documented. The cause of benign perimesencephalic subarachnoid hemorrhage (PMH) is unknown, and this study was undertaken to elucidate the risk factors for PMH.

Seventy-nine patients with PMH, admitted to the University Medical Center Utrecht, were studied and compared to 574 control patients admitted from general medical practices. All participants filled out questionnaires regarding smoking habits, history of hypertension, and alcohol consumption, and odds ratios (ORs) were calculated to assess the association of risk factors and PMH. Adjusted ORs for the occurrence of PMH were 1.7 (95% confidence interval [CI], 1.0-2.8) for smoking cigarettes, cigars, pipes, or any combination of these; 1.1 (95% CI, 0.6-2.0) for hypertension; and 1.1 (95% CI, 0.5-2.1) for excessive alcohol consumption. Similar to aSAH, smoking is a risk factor for PMH, but hypertension and excessive alcohol consumption were not, suggesting a different pathophysiology for PMH compared to aSAH. ■

Early Intensive Hemodynamic Management May be Beneficial in Poor-Grade Patients with Aneurysmal Subarachnoid Hemorrhage

SOURCE: Mutoh T, et al. Early intensive versus minimally invasive approach to postoperative hemodynamic management after subarachnoid hemorrhage. *Stroke* 2014;45:1280-1284.

After aneurysmal subarachnoid hemorrhage (aSAH), and following obliteration of the offending aneurysm, one of the main remaining causes of severe disability and death is delayed cerebral ischemia (DCI). The pathogenesis of cerebral ischemia in this setting is multifactorial and includes vasospasm, microcirculatory dysfunction, microembolism, and cortical spreading depolarization. Systemic hemodynamic insufficiency and low intravascular volume seem to contribute to the development of DCI. Controversy has existed for decades regarding the benefits and risks of invasive hemodynamic monitoring for administration of hemodynamic therapies, and proof of its benefit is lacking from randomized trials. Mutoh et al now present new evidence in a randomized, clinical trial of invasive monitoring and early goal-directed fluid therapy (EGDT) vs standard hemodynamic therapy.

One hundred sixty patients with aSAH, who had their aneurysm obliterated with surgery or endovascular coiling, were randomized to receive early (within 24 hours) EGDT guided by cardiac output monitoring with a transpulmonary thermodilution catheter method (PiCCO) or standard therapy guided by measurements of fluid balance or central venous pressure during hemodynamic therapy in patients with clinical and radiographic indications of DCI. The groups were then compared for the frequency of DCI and outcomes were measured by modified-Rankin score at 3 months.

For all clinical grades combined, there were no significant differences in the rates of DCI between the two groups (33% intensive vs 42% standard; $P = 0.33$) or in the modified-Rankin score at 3 months (67% intensive vs 57% standard; $P = 0.22$). However, in patients with poor clinical grade, those who received early intensive therapy had a significantly lower rate of DCI compared to those who received standard therapy (5% vs 14%; $P = 0.036$), a higher modified-Rankin score at three months (52% vs 36%; $P = 0.026$), and a shorter length of stay in the intensive care unit (14 days vs 17 days; $P = 0.043$). Poor grade patients fared better with intensive fluid therapy and monitoring compared to standard therapy. ■

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CME QUESTIONS

1. **Which of the following is correct regarding neuroprotection in Parkinson's disease?**
   a. Success in animal models has been strongly predictive of success in clinical trials.
   b. The recent Phase 3 trial of high-dose coenzyme Q10 failed due to lack of tolerability.
   c. Clinical trial testing is limited by lack of objective markers that measure underlying disease progression.
   d. The failure of coenzyme Q10 to halt progression of Parkinson's disease disproves a role for oxidative stress in neurodegeneration.

2. **The Sixel-Doring et al study showed the following in regards to how REM sleep behavioral events (RBE) should be used to screen for Parkinson's disease?**
   a. RBE is diagnostic for Parkinson's disease.
   b. RBE can be helpful in the assessment of Parkinson's disease, but alone is not diagnostic.
   c. RBE is not an indicator Parkinson's disease.
   d. RBE has both high sensitivity and specificity for Parkinson's disease.

3. **Electrodiagnostic features of true neurogenic thoracic outlet syndrome include:**
   a. chronic motor axon loss on needle EMG, particularly in T1/median nerve innervated intrinsic hand muscles.
   b. decreased median compound motor action potential amplitude recording from abductor pollicis brevis.
   c. decreased ulnar compound motor action potential amplitude values recording from abductor digiti minimi.
   d. low medial antebrachial cutaneous sensory nerve action potential amplitude.
   e. All of the above

4. **Which of the following statements regarding predictors of new-onset seizures in head trauma patients is most accurate?**
   a. Mild TBI is a predictor of new-onset seizures.
   b. Moderate-to-severe TBI, age 65 years or older, alcohol and drug abuse as the cause of the index injury, and preceding psychiatric disease are all predictors of new-onset seizures in head trauma patients.
   c. Moderate-to-severe TBI is a predictor of new-onset seizures.
   d. Head trauma does not predispose to new-onset seizures.

5. **While metals are found naturally in the environment and several are essential for optimal health, high concentrations have been associated with a variety of diseases. All of the following have been found to have a potential association with the pathogenesis of Alzheimer's disease *except*:**
   a. zinc.
   b. copper.
   c. iron.
   d. lead.
   e. aluminum.

6. **Hypertension is a risk factor for perimesencephalic subarachnoid hemorrhage.**
   a. True
   b. False

7. **Intensive fluid therapy with invasive monitoring confers no benefit for patients who have sustained aneurysmal subarachnoid hemorrhage.**
   a. True
   b. False

[IN FUTURE ISSUES]

More on Migraine

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