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Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Prevalence of Refractory Juvenile Myoclonic Epilepsy

By Pegah Afra, MD

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Dr. Afra reports she is on the speakers bureau and is a consultant for UCB and Sunovion, and is a consultant for GW Pharmaceuticals and SK-Pharma.

SYNOPSIS: Juvenile myoclonic epilepsy (JME) is a common form of generalized epilepsy. Although the prognosis of JME is not clear, it is assumed to have a good response to treatment. The authors of this meta-analysis found a higher than expected prevalence of refractoriness in JME, which will affect how neurologists counsel patients with JME.

SOURCE: Stevelink R, Koeleman BPC, Sander JW, et al. Refractory juvenile myoclonic epilepsy: A meta-analysis of prevalence and risk factors. *Eur J Neurol* 2019;26:856-864.

Juvenile myoclonic epilepsy (JME) is the most common form of genetic generalized epilepsy and affects 5-10% of all people with epilepsy. Generally, it is assumed that treatment response in JME is good. This assumption is reflected in the 1989 International League Against Epilepsy proposal for revised classification of epilepsies as "response to appropriate drug is good."[1] Stevelink et al sought to determine the prevalence and prognostic factors for refractory JME via a meta-analysis of existing literature in accordance with PRISMA guidelines.

The authors performed a literature search in PubMed and EMBASE and identified 1,362 articles that reported treatment outcomes in people with JME (either with retrospective or prospective studies). They removed duplicates, applied inclusion/exclusion criteria (i.e., including articles describing seizure freedom from all seizure types and excluding articles that specifically recruited refractory individuals or those in remission), and selected 43 articles for inclusion. Using a random-effects meta-analysis, they assessed three areas: 1) prevalence of refractory

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JME, 2) seizure recurrence after antiepileptic drug (AED) withdrawal, and 3) risk factors for refractory JME.

For the meta-analysis of prevalence of refractory JME, the authors used 43 articles describing treatment outcomes for 3,311 subjects. Refractory JME was defined as the persistence of any seizure (i.e., myoclonic, absence, or generalized tonic-clonic) despite AED treatment and regardless of the length of seizure-free follow-up period. Subjects with "pseudorefractory epilepsy" were excluded. The meta-analysis of 43/43 articles (with 3,311 subjects) yielded that 35% (95% confidence interval [CI], 29-41%) of individuals with JME were refractory to treatment. There was wide heterogeneity between studies; however, the proportion of refractoriness was comparable between prospective (36%; 95% CI, 18-56%) and retrospective (35%; 95% CI, 29-42%) studies. The estimates of refractoriness also were comparable when assessing one-, two-, and five-year seizure freedom, suggesting that people who are seizure free at one year are likely to remain so. Additionally, the proportion of seizure-free individuals did not change over time (i.e., with publication year).

For the random-effects meta-analysis of potential risk factors of refractory JME, 21/43 articles that reported seizure outcome in relation to potential risk factors were used. Univariate meta-analysis was performed on 10 risk factors. Six risk factors were determined as significant: 1) having all three seizure types (myoclonic, generalized tonic-clonic, and absence); 2) psychiatric comorbidities; 3) having absence seizures; 4) history of childhood absence epilepsy progressing to JME; 5) early age at epilepsy onset; and 6) praxis-induced seizures (seizures and epileptiform discharges in the EEG induced by complex cognition-guided tasks, such as playing chess, writing, or drawing). Four risk factors were determined as not significant: 1) female gender, 2) epileptiform asymmetry in the EEG, 3) photoparoxysmal response, and 4) family history of epilepsy.

For the meta-analysis of seizure recurrence after AED withdrawal, the authors used 11/43 articles that described seizure outcomes for patients who withdrew from treatment. They included a subset of 246 subjects. The meta-analysis yielded seizure recurrence in 78% (95% CI, 58-94%) of subjects after withdrawal (with wide variation in estimates and high heterogeneity).

■ COMMENTARY

JME is a heterogenous disorder in which the prognoses have not been entirely clear.[2] Overall, it has been assumed that JME responds well to AEDs.[1] Stevelink et al found an unexpectedly high prevalence of refractoriness in JME (35%) based on all seizure types (i.e., absence, myoclonic, and generalized tonic-clonic seizures). This prevalence of refractoriness affecting one-third of people with JME is comparable to other forms of epilepsy (including partial onset epilepsies). The authors reported heterogeneity between studies, possibly because of an overestimation of refractoriness (due to articles from tertiary care centers and selection bias) and underestimation of refractoriness for myoclonic seizures. All these suggest that when counseling patients, clinicians should consider that the commonly held assumption that JME responds well to AEDs may not hold true and that prospective large-scale studies in JME are needed to clarify this matter further.

The authors found that refractoriness was comparable at one, two, and five years. This suggests that people who are seizure-free for at least one year are likely to remain seizure free (i.e., the patients who are not refractory indeed have a good and sustained response to an appropriately chosen AED). Six risk factors for refractoriness, as noted above, should be considered when counseling patients with JME and may be helpful in identifying a subset of refractory patients.

Regarding withdrawal of AEDs after seizure freedom, this study confirmed that there is high probability of seizure recurrence (78%) after AED withdrawal.

Another important finding was there was no decrease in the proportion of refractoriness over the last decade. This highlights the well-known fact that the newer AEDs do not have higher efficacy compared to the standard, sodium valproate. There

continues to be a need to develop AEDs and nonpharmacologic treatment modalities with higher efficacy for effective treatment of JME. ■

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ABSTRACT & COMMENTARY

Neuropathy After Total Knee Arthroplasty

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Rubin reports he is a consultant for Merck Sharp & Dohme Corp.

SYNOPSIS: In a large series of cases from the Mayo Clinic, 54 cases of new neuropathy occurred in 14,450 total knee arthroplasties. Most were isolated peroneal neuropathies. No specific risk factors were identified in this series.

SOURCE: Speelziek SJA, Staff NP, Johnson RL, et al. Clinical spectrum of neuropathy after primary total knee arthroplasty: A series of 54 cases. *Muscle Nerve* 2019;59:679-682.

Total knee arthroplasty (TKA) is expected to reach 2,854 procedures per 100,000 population by 2050. Although it is considered safe and effective for end-stage arthritis of the knee, complications occur during and after TKA, including myocardial infarction, thromboembolism, tourniquet-related ischemic injury, arterial injury, and neuropathy, most commonly peroneal nerve palsy. What is the spectrum and frequency of neuropathy following TKA, what are their clinical and electrophysiological features, and what is their mechanism of injury (mechanical, inflammatory, or both)?

In a retrospective review, Speelziek et al identified all patients 18 years of age or older who underwent TKA at Mayo Clinic Rochester between Jan. 1, 1996, and Sept. 30, 2016, and developed neuropathy within eight weeks of surgery. Exclusionary criteria included patients with pre-existing neuropathy, active radiculopathy, or central nervous system issues, which precluded accurate examination and evaluation of the patient. The review encompassed anesthesia type; findings on clinical, electrophysiologic, and radiologic studies; tourniquet time; and time to motor recovery.

Among 14,450 TKAs performed during the study period, 54 instances of new neuropathy were identified in 53 patients, for a neuropathy incidence of 0.37%. Mean age was 65.2 years; 41 patients were female; postoperative day 2 was the mean time of neuropathy symptom onset, with a range of 0-28 days; and almost all were mononeuropathies of the ipsilateral limb, with one patient having both peroneal and tibial mononeuropathies. Over a mean of 10.1 months, but ranging from two to 136 months, complete or almost complete recovery occurred in all but one patient who appreciated no recovery whatsoever. Four patients were lost to follow-up.

Peroneal neuropathy, presenting as foot drop, nonfocal in eight of 10 patients studied electrodiagnostically, was the most common form of post-TKA neuropathy, seen in 37 (68.5%) patients, followed by sciatic neuropathy in 11 (20.4%), tibial or ulnar neuropathy in two patients each (3.7%), and sural or lumbosacral plexopathy in one patient each (1.9%). Sciatic neuropathy was localized proximal to the short head of biceps femoris in four studies and distally in three studies, with two studies limited to nerve conduction studies only, precluding localization, and one additional study that was normal. Tibial neuropathy presented with tingling or hyperesthesia of the sole or toes, with impaired Achilles reflex and ankle inversion weakness. Diffuse progressive neuropathic pain and weakness of the ipsilateral leg were the features of the single instance of post-TKA lumbosacral plexopathy in a 67-year-old woman who responded to intravenous methylprednisolone after being refractory to opiates, with significant improvement over the treatment period. Overall, for tourniquet time longer than 100 minutes, a time generally associated with an increased risk of complications, mean motor recovery time was 11.8 months, ranging from 7.9-15.7 months, whereas for tourniquet time less than 100 minutes, mean motor recovery time was 8.1 months, ranging from 5.1-11.0 months, a nonsignificant difference due to a large standard deviation in each group. No correlation with type of anesthesia was evident, and inflammatory origin of post-TKA neuropathy, as evidenced by the single instance of lumbosacral plexopathy, was extremely rare.

■ COMMENTARY

Combined general and spinal epidural anesthesia is commonly used for bilateral TKA, with accidental dural puncture occurring in 0.19-3.6%. Cranial nerve palsy is a rare complication of dural puncture, but both abducens nerve palsy and oculomotor nerve palsy have been reported following accidental dural puncture during bilateral total knee replacement. In either instance, reassurance of the patient is important as most cranial nerve palsies following dural puncture resolve within one to four weeks. Following total hip arthroplasty, foot drop also is the most common neurologic complication, but due to sciatic nerve injury, with the peroneal division more commonly and severely affected than the tibial. ■

ABSTRACT & COMMENTARY

Cognitive-Motor Dissociation in Patients Admitted to ICUs After Acute Brain Injuries

By Peter B. Forgacs, MD

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

SYNOPSIS: In a large, prospective, single-center study, more than one in six patients with acute brain injuries may have cognitive-motor dissociation (CMD) (e.g., they harbor capacity to modulate their brain activity in response to motor commands while remaining behaviorally unresponsive at the bedside). Some acute CMD patients were found to have a much higher chance for recovery of neurological functions and for reaching independent levels of activities of daily living by 12 months after brain injury.

SOURCE: Claassen J, Doyle K, Matory A, et al. Detection of brain activation in unresponsive patients with acute brain injury. *N Engl J Med* 2019;380:2497-2505.

Cognitive-motor dissociation (CMD), the uncoupling of behavioral ability to follow commands from evidence of brain activation in response to motor commands as detected by electroencephalography (EEG) or functional neuroimaging (e.g., "covert" command following), primarily has been described in patients with chronic brain injuries (months to years after a brain injury). In standard clinical practice, bedside responsiveness (e.g., motor activity following the verbal commands "open your eyes," "squeeze my hand," or "wiggle your toes") often is used as a proxy for detection of preserved consciousness. During the early ICU course following severe brain injury, a lack of responsiveness often is considered indicative of the severity of the brain injury (especially if sedative effects are ruled out) and weighed heavily in goals of care decisions (e.g., withdrawal of life-sustaining therapies [WLST]). However, the prevalence of CMD (covert responsiveness) in the setting of acute severe brain injuries as well as the importance of CMD in the prognosis of neurological and functional recovery is unknown.

Claassen et al prospectively assessed all consecutive patients admitted to the neurological ICU of the Columbia University Medical Center in New York. All patients with severe acute brain injuries of any etiology who were diagnosed to be in coma, vegetative state, or minimally conscious state-minus (presence of visual fixation, visual pursuit or localization to pain but no motor response to commands) based on the Coma Recovery Scale – Revised (CRS-R) while undergoing continuous EEG monitoring were considered. Recordings of alternating commands of "keep opening your right (or left) hand" and "stop opening …" were played to patients via headphones multiple times during their admission until they remained clinically unresponsive. Each EEG recording for each patient was trained individually using a machine learning approach (support vector machine) to differentiate between power spectral density across four frequency bands (δ, θ, α, β) during the periods following the alternating commands and used to assess command-related brain activation. Clinical outcomes included recovery of bedside command responsiveness, followed by the time of hospital discharge and a scored structured telephone interview (Glasgow Outcome Scale–Extended [GOS-E]) at 12 months after injury.

A total of 104 patients were enrolled in the study. Sixteen patients (15%) were found to have evidence of brain activation in response to a motor command while remaining unresponsive behaviorally (consistent with CMD) during at least one of their assessments, with a median of four days after ICU admission. Fifty percent of CMD patients (8/16) recovered bedside command by the time of hospital

discharge, with a median time of six days following first detection of CMD by EEG, compared to 26% of patients who did not have evidence of CMD. In addition, 44% of CMD patients (7/16) vs. 14% (12/84) of non-CMD patients scored above 4 on the GOS-E scale (indicative of the ability of function independently for at least eight hours daily) at 12 months after the brain injury. Of note, of the six CMD patients who died, four died after a WLST decision and two after progression to brain death, with all six cases following additional systemic and neurological complications after detection of CMD.

■ COMMENTARY

The results of this paper are alarming and suggest that a significant portion of patients who appear unresponsive at the bedside in the ICU may have measurable levels of preservation of cognitive functions for several days preceding the recovery of bedside responsiveness. Although the extent of this preservation is uncertain and there is no direct evidence based on this study if the detected signals are related to true language comprehension or recognition of the commands, the association between the detection of these signals and the clinical outcome is highly intriguing and warrants further clinical consideration. Patients with evidence of acute CMD likely have greater functional integrity of various brain areas similarly to patients with chronic CMD.

However, given the importance and clinical relevance of this study, some methodological limitations need to be emphasized. Furthermore, independent replication of the results is paramount before this approach can be generalized and considered in clinical practice. For example, the responses even within patients were highly inconsistent (e.g., of the four patients who had more than three assessments, only 1/8, 2/8, 1/5, and 2/5 EEG recording sessions showed positive results [S2 table of paper]). This could be the result of fluctuations in levels of consciousness commonly seen in ICU patients or variation in the level of sedation, but suggests that false-negative results cannot rule out the possibility of some preservation of cognitive functions. Additionally, while the authors, very appropriately, employed false discovery rate (FDR) correction, with the FDR level set at 5%, it is possible that up to five patients (from 104) were categorized falsely as positive for command following. It is important to emphasize that the risk of both false-negative or false-positive findings needs to be interpreted with precise understanding of the methodological details, especially if such considerations are factored into WLST discussions.

Nonetheless, this study represents a critical milestone and will generate several lines of study for patients admitted to ICUs after acute severe brain injuries. Such studies will further refine our understanding of the neural substrates of acute CMD and provide the possibility of early therapeutic interventions. Once these methods are validated and generalized, detection of preserved higher cognitive function as early as possible after acute severe brain injury may aid prognostic decisions that weigh on caregivers and families. Patients identified with such methods should receive continued aggressive care to ensure the best chances for their recovery. Looking forward, the ease of repeated measurements with methods using EEG signals with individualized machine learning approaches may lead to the development of automated or semi-automated methods in the future that could longitudinally trace recovery of cognition independently of recovery of motor functions. ■

ABSTRACT & COMMENTARY

Amyloid, Tau, Neurodegeneration Diagnostic Framework to Predict Memory Decline Before the Onset of Dementia

By Makoto Ishii, MD, PhD

Assistant Professor of Neuroscience and Neurology, Feil Family Brain and Mind Research Institute, Department of Neurology, Weill Cornell Medical College

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

SYNOPSIS: In a population-based longitudinal study of older individuals without dementia, the inclusion of imaging biomarkers for amyloid, tau, and neurodegeneration modestly improved the ability to predict memory decline compared to a model that only used clinical data and APOE genotype.

SOURCE: Jack CR Jr, Wiste HJ, Therneau TM, et al. Association of amyloid, tau, and neurodegeneration biomarker profiles with rates of memory decline among individuals without dementia. *JAMA* 2019;321:2316-2325.

For more than 100 years, Alzheimer's disease (AD) could be diagnosed definitively only by postmortem histopathological confirmation of amyloid-beta plaques and tau neurofibrillary tangles. With the recent development of cerebrospinal fluid (CSF) immunoassays and positron emission tomography (PET) tracers specific for amyloid-beta and tau, it is possible to detect these neuropathological hallmarks in vivo before the onset of dementia. By using specific cutpoints, an individual can be classified as abnormal (+) or normal (-) for amyloid (A), tau (T), or neurodegeneration (N). A diagnostic framework based on the AT(N) biomarker profile has been constructed that biologically defines AD by pathological changes in A, T, and N. However, it is not known if the biological information obtained by the AT(N) profile would be clinically meaningful. For example, in predementia individuals, it is not clear if memory decline varies by the AT(N) profiles or if the use of AT(N) profiles would improve the ability to predict memory decline.

Some of the originators of the AT(N) framework sought to address these questions by examining 480 nondemented subjects enrolled in the Mayo Clinic Study of Aging, a population-based study of cognitive aging in a geographically defined population of Olmsted County, MN, with a median follow-up of 4.8 years (interquartile range [IQR], 3.8-5.1). Amyloid PET, tau PET, and MRI measures of cortical thickness were obtained at baseline to evaluate for A, T, and N, respectively. The primary outcome was a numeric memory composite score based on three delayed recall memory tests. Age, sex, education, APOE genotype, and a composite cardiovascular and metabolic conditions (CMC) score were used as variables for the clinical prediction model.

Of 480 subjects, 99% of study participants were self-reported white, and 44% were women. For the AD biomarker profiles, there were 140 (29%) A-T-(N)-, 33 (7%) A-T+(N)-, 81 (17%) A-T-(N)+, 22 (5%) A-T+(N)+, 54 (11%) A+T-(N)-, 24 (5%) A+T+(N)-, 69 (14%) A+T-(N)+, and 57 (12%) A+T+(N+) subjects. The A+T+(N)+ group was older, with a median age of 83 years (IQR, 76-87) compared to the median age of 67 years (IQR, 65-73) for the A-T-(N)- group. Ninety-two percent of study participants were cognitively unimpaired, with the A+T+(N)+ group having the largest proportion of mild cognitive impairment (30%). The proportion of APOE E4 carrier was greater among the four A+ groups compared to the four A- groups (40% vs. 21%; $P < 0.001$).

In the clinical prediction model, age and APOE E4 status were significantly associated with a faster rate of memory decline, but sex, education, and CMC score were not. Adding the AT(N) biomarker model to the clinical prediction model led to a relatively small but statistically significant improvement in predicting memory decline (likelihood ratio test $P < 0.001$ with R2 increasing from 0.26 to 0.31). Furthermore, the A+T+(N)+, A+T+(N)-, and A+T-(N)+ groups had the fastest rates of memory decline compared to the other five groups ($P = 0.002$). Finally, an estimated 46% of memory decline in older predementia individuals was associated with abnormal AT(N) biomarker profile.

■ COMMENTARY

Despite the increasing use of AD biomarkers in research, the AT(N) classification remains a research construct that requires clinical validation. This important study by Jack et al is the first to use longitudinal clinical outcomes to examine the association of the AT(N) classification system with memory decline in a relatively large number of predementia individuals. As predicted, the A+T+(N+) group had the highest proportion of mild cognitive impairment, and those groups with the worst pathological changes A+T+(N+), A+T+(N-), A+T-N(+) had the fastest rate of memory decline. These results appear to validate the AT(N) profile as an appropriate framework for classifying and risk-stratifying predementia individuals. However, adding AT(N) profiles led to only a modest improvement in the ability to predict memory decline, which as the study authors noted is of uncertain clinical importance.

Additional study limitations are worth noting. First, the AT(N) profile used strict cutpoints, which may be challenging to define as these measures are part of a natural continuum. Second, the clinical prediction model that was used did not incorporate cognitive measures. It is not clear if the modest gains in predicting memory decline made with the addition of AT(N) biomarkers would be further reduced with the use of cognitive measures, which are common in clinical practice and significantly less expensive than imaging biomarkers. Third, it is not known whether the findings from this study can be generalized to other biomarkers (e.g., CSF) or to more diverse populations.

Despite these limitations, the findings from this study not only advance our fundamental understanding of AD but suggest an important role that AT(N) biomarker profiles could have in future clinical trials. A major limitation of past trials was the inability to identify those individuals with mild or no cognitive symptoms who had the highest risk for memory decline. It is plausible that past clinical trials failed in part because of the inclusion of subjects who ended up having very modest decline in memory during the short study period. This would make it difficult to discern any significant benefit from an intervention.

By stratifying individuals to the different AT(N) biomarker profiles, investigators conceivably could better prognosticate and target cognitively intact or mildly impaired subjects with the highest risk for memory decline, which would significantly increase the chance for successfully finding an effective therapy for AD. ■

ABSTRACT & COMMENTARY

Carpal Tunnel Syndrome in the Extreme Elderly

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Rubin reports he is a consultant for Merck Sharp & Dohme Corp.

SYNOPSIS: Carpal tunnel syndrome (CTS), when seen in the very elderly, is usually severe and is not reliably diagnosed by ultrasound. Nerve conduction studies and electromyography are the most sensitive and specific tests to make accurate diagnosis of CTS.

SOURCE: Mulroy E, Pelosi L. Carpal tunnel syndrome in advanced age: A sonographic and electrodiagnostic study. *Muscle Nerve* 2019; Apr. 26. doi: 10.1002/mus.26496. [Epub ahead of print].

Affecting 1-5% of the population, with a 3:1 female:male ratio, carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, occurring most often in obese women, and least so in thin men. Diabetes, hypothyroidism, and rheumatoid arthritis, as well as pregnancy and aromatase inhibitors, are associated with CTS, but evidence that age plays a factor is controversial. Diagnosis usually is confirmed by electrodiagnostic studies, with ultrasonography showing a significantly increased cross-sectional area of the median nerve compared to controls, offering a painless way of making the diagnosis. However, ultrasound may not be reliable in the very elderly.

Data from all patients referred to the Department of Clinical Neurophysiology, Auckland, New Zealand, between May 2014 and May 2015, who had undergone both electrodiagnostic and ultrasonographic studies of the median nerve, were reviewed retrospectively and divided selectively into two age groups, 40-65 years and 80-95 years. Electrodiagnostic studies conformed to recommendations of the American Association of Neuromuscular and Electrodiagnostic Medicine, and, to minimize operator bias, in all instances were preceded by ultrasound evaluation of the median nerve, performed by the same operator, consisting of evaluating the maximum median nerve cross-sectional area at the wrist as well as wrist-to-forearm ratio. Statistical analysis comprised Pearson's correlation coefficient and Shapiro-Wilk and Student t-tests.

Among a total of 92 patients and 110 hands included in the study, 59 were 40-65 years of age and 33 were 80-95 years of age. CTS was more severe, both clinically and electrodiagnostically, in the very elderly, whereas, paradoxically, maximal median nerve cross-sectional area at the wrist was significantly larger in the younger group.

Additionally, as CTS severity worsened in the younger group, so too did maximal median nerve cross-sectional area increase at the wrist, whereas this correlation was not seen in the elderly group. Mid-forearm median nerve cross-sectional area was similar in both age groups. Sensitivity of nerve ultrasound was significantly lower in the elderly group, with 46% of clinically abnormal hands and 39% of electrodiagnostically abnormal hands having normal ultrasound median nerve cross-sectional area measurements. No correlation was found in the elderly group between ultrasound and electrodiagnostic measurements. Electrodiagnostic testing was 100% sensitive in both groups with clinically moderate or severe CTS.

■ COMMENTARY

Despite a high prevalence, the etiology of CTS often remains uncertain. In 2002, a twin study in the United Kingdom suggested that the strongest risk factors for CTS in women were genetic.[1] Recently, the authors of a genome-wide association study, using 12,312 CTS cases and 389,344 controls from in the UK Biobank resource, identified 16 novel susceptibility loci for CTS, suggesting that genetic variants implicated in skeletal growth and extracellular matrix architecture alter the environment through which the median nerve traverses, thus predisposing to CTS. Mendelian randomization analysis revealed a causal association between short stature and a higher risk for CTS, with CTS patients, on the average, 2 cm shorter than controls. Connective tissue abnormalities appear causally connected to carpal tunnel syndrome.[2] ■

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CME QUESTIONS

1. **Juvenile myoclonic epilepsy is characterized by which of the following features?**
   a. Focal brain lesion as a cause for epilepsy
   b. Onset in early childhood and disappears by adulthood
   c. May present with myoclonic, absence, or tonic-clonic seizures
   d. Easily treated with sustained seizure-free period
2. **Which of the following statements is true regarding total knee arthroplasty (TKA)?**
   a. Certain forms of anesthesia are more prone to be associated with post-TKA neuropathy.
   b. An inflammatory origin of post-TKA neuropathy is common.
   c. Peroneal neuropathy, presenting as foot drop, is the most common form of post-TKA neuropathy.
   d. Sciatic neuropathy is the most common form of post-TKA neuropathy.
3. **Cognitive-motor dissociation describes a state best characterized by which of the following?**
   a. Lack of motor responsiveness at the bedside to verbal commands
   b. Inappropriate response to a verbal command
   c. EEG response to a verbal command without any discernible motor response
   d. Refusal to cooperate or malingering by a patient
4. **Which of the following statements about carpal tunnel syndrome (CTS) is true?**
   a. Ultrasonographic studies of the median nerve are the most sensitive way to make a diagnosis of CTS in any age group.
   b. Ultrasonographic studies of the median nerve are the most sensitive way to make a diagnosis of CTS in patients older than 80 years of age.
   c. Electrodiagnostic studies of the median nerve are the most sensitive way to make a diagnosis of CTS.
   d. Ultrasonographic studies or electrodiagnostic studies of the median nerve are equally sensitive to make a diagnosis of CTS.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss current scientific data regarding the diagnosis and treatment of neurological disease;
- discuss the pathogenesis and treatment of pain;
- describe the basic science of brain function;
- discuss new information regarding new drugs for commonly diagnosed neurological conditions and new uses for traditional drugs;
- identify nonclinical issues of importance for the neurologist.

[IN FUTURE ISSUES]

Update on Multiple Sclerosis