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Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

MRI Changes and Functional Outcomes Among Adults with Severe HSV Encephalitis

By Hai H. Hoang, MD

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SYNOPSIS: Herpes simplex virus is a common cause of encephalitis worldwide. When treated promptly, the mortality rate decreases from 70% to 15%, but many patients remain disabled. This multicenter cohort study analyzed magnetic resonance imaging in patients diagnosed with herpes simplex encephalitis admitted to the intensive care unit to identify factors associated with poor outcome at 90 days.

SOURCE: Sarton B, Jaquet P, Belkacemi D, et al. Assessment of magnetic resonance imaging changes and functional outcomes among adults with severe herpes simplex encephalitis. *JAMA Netw Open* 2021;4:e2114328.

Herpes simplex virus (HSV) is a common cause of encephalitis worldwide. Although treatment is available, the mortality rate remains at 15%, but many patients are left with disabling symptoms. The diagnosis of HSV encephalitis is confirmed with cerebrospinal fluid (CSF) detection of HSV polymerase chain reaction (PCR). Other supportive tests include brain magnetic resonance imaging (MRI) to rule out mimics. Typical radiological MRI findings include the presence of asymmetric changes in signal intensities in the mesial temporal lobes, inferior frontal lobes, and insula. Despite advancements in diagnostics, there has been less research on prognostic markers for patients with HSV encephalitis. To address this question, a multicenter cohort study of patients diagnosed with HSV encephalitis was conducted in France. The study looked at brain MRI data and patients' functional outcomes at 90 days after intensive care unit (ICU) admission.

Observational data were retrospectively collected from the electronic medical record between 2007 and 2019 for patients diagnosed with HSV encephalitis at 34 ICUs in France. Patients were included if they were admitted to the ICU, had CSF positivity for HSV PCR, completed brain MRI, and had follow-up data at 90 days. Data extracted from the

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chart included patient demographics, patient history, and clinical, laboratory, and brain electrophysiologic data. In addition, baseline health status was graded by Knaus score. Disease severity was denoted with Simplified Acute Physiology Score II and the Sequential Organ Failure Assessment score. Glasgow Coma Scale (GCS) score also was calculated at the time of ICU admission. Patients were included if they had a brain MRI within the first month of ICU admission. The extent of brain lesions was scored on fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) sequences. Functional outcomes were graded at 90 days after ICU admission using the Modified Rankin Scale (mRS). The cohort was broken down into poor functional outcome (mRS 3 to 6) vs. good functional outcome (mRS 0 to 2).

Between 2007 and 2019, 138 patients met study inclusion criteria, with a median age of 62.6 years. Functional status before ICU admission was good (Knaus class A or B) in 96.4% of cases. Median time to MRI acquisition was one day. Abnormal FLAIR hyperintensities were seen in 97.8% of cases. FLAIR lesions extending into more than three lobes were identified in 38.4% of patients. DWI abnormalities detected in more than three lobes were identified in 26.9% of patients. Thalamic involvement was noted in 46.3% of patients.

At 90 days, 68.8% of patients had a poor outcome, including death in 11.6%. The odds of an unfavorable outcome at 90 days were higher in patients with extensive brain lesions, both on FLAIR and DWI sequences. Multivariate analysis found that FLAIR sequence signal on more than three brain lobes (odds ratio [OR], 25.71; 95% confidence interval [CI], 1.21-554.42), age older than 60 years (OR, 7.62; 95% CI, 2.02-28.91), extensive bilateral parenchymal restricted diffusion patterns (OR, 3.17; 95% CI, 0.64-17.65), and focal diffusion signal abnormalities in the left thalamus (OR, 6.90; 95% CI, 1.12-43.00) were associated with increased odds of unfavorable outcome.

With predictive modeling machine learning methods, the detection of bilateral DWI abnormalities was associated with worse functional prognosis (87.2% of patients). Among patients without bilateral diffusion abnormalities (absence of abnormality or unilateral hypersignal), DWI hyperintensities in the left thalamus were associated with poor outcome, particularly in older patients (100% of patients aged > 60 years). Brain hemorrhages and blood-brain barrier disruption (detected by T2*-weighted and contrast-enhanced T1-weighted sequences, respectively), were not associated with poor functional outcomes.

■ COMMENTARY

This is the largest study to date that evaluated functional outcomes in patients with HSV encephalitis based on brain MRI data. A strength of this study is the ability for clinicians to provide a general predictive outcome for their patients by identifying the number of involved lobes on brain MRI, with more than three lobes portending to a poor prognosis. However, there are limitations. Specifically, the study's retrospective design and lengthy study inclusion period, which do not allow for consistency of neuroimaging procedures or clinical care across this long period of time. ■

ABSTRACT & COMMENTARY

What Is Focal CIDP?

By Michael Rubin, MD

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SYNOPSIS: Chronic inflammatory demyelinating polyneuropathy (CIDP) usually is diagnosed in patients who have a generalized disorder. However, there are focal syndromes that have been observed and diagnosed under different names that meet many of the clinical and electrodiagnostic criteria of CIDP and may be referred to as "focal" CIDP.

SOURCE: Benoit C, Svahn J, Debs R, et al. Focal chronic inflammatory demyelinating polyradiculoneuropathy: Onset, course, and distinct features. *J Peripher Nerv Syst* 2021;26:193-201.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired, immune-mediated, inflammatory demyelinating neuropathy. CIDP typically manifests as a symmetric, motor-predominant neuropathy with proximal and distal weakness, but may begin focally and remain so (referred to as focal CIDP), affecting either the brachial or lumbosacral plexus, or a nerve or several nerves in a single limb. Autoimmune neuropathies, such as multifocal motor neuropathy with conduction block (MMNCB) or multifocal acquired demyelinating sensory and motor neuropathy (MADSAM or Lewis-Sumner syndrome), are asymmetric variants of CIDP. These types also may have a focal onset, and remain so for years or decades, and may or may not be focal CIDP. Cases of idiopathic chronic brachial or lumbosacral plexopathy, with nerve root thickening on magnetic resonance imaging (MRI) and responding to intravenous immunoglobulin (IVIG), also may represent focal CIDP. Can these entities be teased apart from focal CIDP, or is focal CIDP an autoimmune neuropathy with a focal onset?

Patients with focal CIDP, limited to a single limb for two years or more, were selected from the CIDP database of the Pitie-Salpetriere Hospital, Paris, (2005-2018) and the Pierre Wertheimer Hospital, Lyon, (2010-2017) if they fulfilled European Federation of Neurology Society-Peripheral Nervous System (EFNS-PNS) clinical and electrodiagnostic criteria for CIDP. Absent electrodiagnostic criteria, they were diagnosed with focal CIDP if they fulfilled at least two supportive clinical criteria.

Patients were excluded if they demonstrated clinical characteristics consistent with Parsonage-Turner syndrome, electrodiagnostic findings suggestive of hereditary neuropathy with pressure palsies (HNPP), imaging findings suggestive of neoplastic disease, autoimmune conditions other than CIDP, or findings suggestive of motor neuron disease. Electrodiagnostic studies were performed using standard procedures, and somatosensory evoked potential (SSEP) studies were performed when warranted to evaluate proximal demyelination.

Patients were categorized as focal brachial or lumbosacral inflammatory demyelinating plexus neuropathy (F-PN), focal demyelinating sensory and motor neuropathy (F-SMN), or focal demyelinating motor neuropathy (F-MN). The latter two categories required involvement of a single nerve or multiple peripheral nerves, respectively. IVIG or oral steroids were used for treatment, with response defined as improvement of two or more Medical Research Council (MRC) grades. Statistical analysis comprised the chi-square and Kruskal-Wallis tests, with $P < 0.05$ defined as significant.

Among 30 focal CIDP patients, 18 had F-PN, seven had F-SMN, and five had F-MN. F-PN patients had motor nerve conduction abnormalities in 39%, but 80% demonstrated proximal demyelination based on SSEP study. All had focal hypertrophy or increased short tau-inversion recovery image signal intensity on plexus MRI. Abnormalities remained monomelic in 94% of F-PN patients but spread to other limbs in 57% and 40% of F-SMN and F-MN patients, respectively. Overall, Neuropathy Limitations Scale (ONLS) was best for F-PN, with none having a score > 2 at the final visit, compared to 43% and 40% for F-SMN and F-MN, respectively. Focal CIDP appears to encompass at least three entities, and F-SMN and F-MN are more likely to progress to a multi-limb MADSAM or MMNCB phenotype.

[Chronic inflammatory demyelinating polyneuropathy typically manifests as a symmetric, motor-predominant neuropathy with proximal and distal weakness, but may begin focally and remain so, affecting either the brachial or lumbosacral plexus, or a nerve or several nerves in a single limb.]

■ COMMENTARY

Atypical forms of CIDP vary, not only in phenotype but also in response to immunotherapy. Distal acquired demyelinating symmetric polyneuropathy (DADS), characterized by symmetric, demyelinating, sensory, length-dependent polyneuropathy, typically is more responsive to rituximab than IVIG, whereas MADSAM, a chronic, progressive, demyelinating mononeuropathy multiplex, responds to IVIG, but less favorably than does CIDP. IVIG is the treatment of choice for pure motor CIDP, as well as for focal CIDP and pure sensory CIDP, although the latter often requires maintenance therapy.[1] ■

REFERENCE

1. Menon D, Katzberg HD, Bril V. Treatment approaches for atypical CIDP. *Front Neurol* 2021;12:653734.

ABSTRACT & COMMENTARY

Proteomics: A New Method to Understand the Influence of Genetic Variation on Disease Pathogenesis

By M. Elizabeth Ross, MD, PhD

Nathan Cummings Professor and Head, Laboratory of Neurogenetics and Development; Director, Center for Neurogenetics; Chair, Neuroscience Graduate Program; Weill Cornell Medical College

SYNOPSIS: The combination of genome-wide association studies with the analysis of messenger ribonucleic acid and unique proteins in the brain, cerebrospinal fluid, and plasma can shed new light on our understanding of the genetic risks for the development of various neurological diseases.

SOURCE: Yang C, Farias FHG, Ibanez L, et al. Genomic atlas of the proteome from brain, CSF and plasma prioritizes proteins implicated in neurological disorders. *Nat Neurosci* 2021; Jul 8. doi: 10.1038/s41593-021-00886-6. [Online ahead of print].

A number of genome-wide association studies (GWAS) have used populations to identify genome regions (loci) associated with complex traits in various common medical diseases, including diabetes, cardiovascular disease, Alzheimer's disease, and other neurodegenerative disorders. When combined with ribonucleic acid (RNA) sequence data, typically from blood mononuclear cells, it has been possible to generate expression quantitative trait loci, or eQTLs, to help identify the genetic variants that drive phenotypic manifestations of disease. The report by Yang and colleagues at Washington University provides a next critical step in the process by using protein expression combined with genetic loci to identify protein QTLs, or pQTLs, to find biologically meaningful associations, new biomarkers, and promising drug targets for treating neurological disease.

Since deoxyribonucleic acid (DNA) sequence alterations may lead to altered protein levels without affecting levels of messenger RNA, pQTLs have the potential to reveal important disease associations that otherwise would not be detected using eQTLs. This report is of special interest since it examines protein levels not only in plasma but also in parietal brain tissue and cerebrospinal fluid (CSF) as well.

Starting with a cohort of 1,537 participants of European ancestry, groups broke down into 971 CSF samples from participants (249 with Alzheimer's disease, 717 cognitively normal); 636 plasma samples (230 patients with Alzheimer's disease, 401 cognitively normal); 458 parietal brain samples (297 patients, 27 normal controls, and 134 with unknown status [e.g., frontotemporal dementia and other neurological disorders]). Although other studies have examined the proteome using mass spectrometry, this project employed the capture of proteins using an aptamer-based platform consisting of modified, fluorescently tagged, single-strand DNA molecules that individually bind to specific proteins. Relative protein concentrations were measured by fluorescence intensity, which allowed for high throughput evaluation of 1,305 proteins.

The differential expression of proteins between patients and controls was compared to DNA genome sequence, single nucleotide polymorphisms (SNPs) that were defined as in "cis" (within 1 Mb upstream or downstream of the differentially expressed protein) or in "trans" (an SNP more than 2 Mb away from the gene encoding a particular protein differentially expressed).

Investigators found 274 significant pQTLs in CSF (223 of them novel), 127 in plasma (17 novel), and 32 in brain samples (27 of them novel). Several take-home points emerged. The majority of pQTLs (76% to 94%) were in cis, with SNPs close by to the gene encoding a differentially expressed protein. This likely accounts for the observed 42% to 53% of cis-pQTLs relating to a protein-coding SNP, contrasted with only 2% to 5% of RNA-based eQTLs, explained by protein-coding SNPs. Of those pQTLs in trans, more than 90% were on a different chromosome than the gene encoding the protein in question, suggesting an indirect, downstream effect of that genetic locus on the target protein.

Compared with other types of QTLs, 48% of brain pQTLs and 76.6% of CSF pQTLs in this study had no overlap with RNA expression, RNA splicing, DNA methylation, or histone acetylation. The authors interpreted this as indicating that protein level expression may provide some of the missing heritability of neurological disease, especially when

combined with other molecular traits. They also analyzed proteins implicated in these pQTLs to statistically identify proteins associated with disease risk (an approach called Mendelian randomization, or MR).

Relating to Alzheimer's disease risk, the researchers found three proteins in CSF, 13 in plasma, and seven in brain samples. For example, variants in CD33 — a microglia-specific gene — emerged as a signal for Alzheimer's disease risk. A clinical trial for anti-CD33 antibody as a therapeutic for Alzheimer's disease currently is underway.

■ COMMENTARY

This report is significant as an advance in the availability of large-scale proteomic information in multitissue datasets that may be applied to pQTLs using existing GWAS data for these and other neurological disorders. The report constitutes a unique resource for expanding MR analyses of complex traits contributing to neurological disorders. Through integration with other QTL and omic data analyses, this approach has the potential to fill a substantial gap in understanding the contribution of genetic variation — in combination with environmental influences — to brain disease. ■

ABSTRACT & COMMENTARY

Cortical Lesions Correlate with Disability in Patients with Multiple Sclerosis

By Jai S. Perumal, MD

Assistant Professor of Neurology, Weill Cornell Medical College; Assistant Attending Neurologist, New York-Presbyterian Hospital

SYNOPSIS: In a long-term, 30-year follow-up study of a cohort of patients with multiple sclerosis who presented with clinically isolated syndrome, the investigators found that, among the variables assessed, the presence of cortical lesions had the highest association with long-term physical and cognitive disability.

SOURCE: Haider L, Prados F, Chung K, et al. Cortical involvement determines impairment 30 years after a clinically isolated syndrome. *Brain* 2021;144:1384-1395.

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system that is diagnosed predominantly in young adults. The clinical course of MS is variable, with a spectrum of relatively mild disease with no significant disability, even years after the diagnosis, on one end, and other patients with significant impairment at the other end. Studies that have attempted to predict long-term disability at the time of diagnosis encountered several hurdles, including inadequate length of time for follow-up, patient drop-out, treatment effects, and patient enrollment at various time points after their diagnosis. Investigators also have examined the factors that best correlate with disability, such as magnetic resonance imaging (MRI) lesion volume and lesion location. Cortical pathology has been an area of immense interest with regard to studies looking at long-term disability.

The current study has one of the longest follow-up periods ever reported — 30 years. These patients were enrolled at onset when they presented with an initial clinically isolated syndrome (CIS), which provides a homogenous population observed from early disease onset. Patient demographics, including age, sex, disease duration, MRI metrics, and neurological examination, were collected. Subsequent regular assessments also included Expanded Disability Status Scale (EDSS), timed 25-foot walk, Paced Auditory Serial Addition Test (PASAT), and the Brief International Cognitive Assessment for MS (BICAMS) for measurement of cognitive function. The goal of the study was to evaluate MRI correlates of disability in this cohort at 30 years from disease onset. MRI was obtained using a 3T Phillips scanner. Linear regression models were used to correlate MRI metrics to clinical measures.

Sixty-three patients, from among 132 patients with CIS who were recruited for prospective longitudinal follow-up at the study site between 1984 and 1987, were included in the analysis. By year 30, out of the 63 patients, 27 patients developed relapsing-remitting multiple sclerosis (RRMS), 15 developed secondary progressive multiple sclerosis (SPMS), and 21 patients remained in the CIS category. The RRMS patients in this cohort had EDSS scores between 0 and 2, which indicates a less disabled population with no limitations in their ability to walk.

From all the MRI metrics analyzed, the variable that revealed the greatest difference between the RRMS and SPMS groups was the number of cortical

lesions. Cortical lesions were present in three of the 27 patients with RRMS and all of the SPMS patients. None of the patients in the CIS category had cortical lesions. Cortical lesions correlated with both physical disability and cognitive impairment.

The limitations of this study include the relatively smaller number of patients who were followed for the full 30 years, and the few patients who were recruited initially but not followed to completion because of death. Some of the deaths were related to the MS diagnosis, and this could have biased the study toward those with less disability. Also, the cognitive impairments observed in this study were not predictive of future disability and were a contemporaneous correlate of current impairment.

■ COMMENTARY

In this 30-year, long-term follow-up study of patients who presented initially with CIS, the authors showed that cortical pathology correlated the most with physical and cognitive disability. Traditionally, MS was believed to be predominantly be a white matter disease, but the role of gray matter lesions is being increasingly recognized as a vital component of disease pathogenesis and progression. More studies examining gray matter involvement, particularly early in the disease course, might help identify a subset of patients who may have a worse long-term prognosis. A focus on developing more sensitive MRI sequences would help identify gray matter injury that currently is not evident on our present clinical scans. ■

ABSTRACT & COMMENTARY

Treatment of Seizures After Spontaneous Intracerebral Hemorrhage

By Joseph W. Doria, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: The reported incidence of post-stroke seizures varies and appears to have a higher incidence following hemorrhagic stroke. Post-stroke seizures have been associated with a greater length of hospitalization, increased mortality, and complications. This study compared four seizure prophylaxis strategies to determine the greatest net benefit for patients with spontaneous intracerebral hemorrhage. There was a better outcome with short-term antiepileptic medication use compared to long-term use.

SOURCE: Jones FJS, Sanches PR, Smith JR, et al. Seizure prophylaxis after spontaneous intracerebral hemorrhage. *JAMA Neurol* 2021; Jul 26;e212249. doi:10.1001/jamaneurol.2021.2249. [Online ahead of print].

The leading cause of seizures beyond the age of 60 years is cerebrovascular disease. The incidence of post-stroke seizures varies greatly and appears to have a higher incidence following hemorrhagic stroke. Following hemorrhage various causes can lead to seizures. Acutely, these include transient irritation of the cortex because of products of blood metabolism, and, chronically, hemosiderin depositions and gliotic scarring.

Post-stroke seizures have been associated with a greater length of hospitalization, increased mortality, and complications. Moreover, seizures may affect quality of life substantially with unpredictable reoccurrence, social and employment challenges, and additional associated costs. Thus, timely detection of seizures and optimal management are essential. Currently, there are no guidelines widely agreed upon for prophylactic use of antiseizure drugs following a brain hemorrhage, and there can be great variation in medication type, dosage, and duration.

Subsequent seizure risk potentially can determine if a patient will benefit from prophylactic/treatment strategies. Seizures can be classified as acute symptomatic seizures (early seizures), which occur seven days or less after a stroke injury, or seizures, which occur more than seven days after a stroke or injury. There is a suggested higher risk of recurrent seizures/epilepsy in patients with late seizures. Tools for predicting early (2HELPS2B score) and late (CAVE score) seizure risks can aid in prophylactic treatment decisions.[1,2]

The 2HELPS2B score is an electroencephalogram (EEG)-based seizure risk stratification tool based on the frequency of any periodic or rhythmic patterns > 2 **Hz** (excluding rhythmic delta activity), independent sporadic **E**pileptiform discharges, **L**ateralized periodic discharges, "**P**lus" features (superimposed fast, rhythmic, or sharp activity), prior **S**eizure/**S**uspicious event for clinical seizure, and **B**rief potentially ictal rhythmic discharges (BIRDs). Based on the score, the tool will recommend duration of EEG monitoring to detect 95% of seizures and the risk of seizures within 72 hours. The 2HELPS2B is helpful if there is accessibility to EEG monitoring.[2] The CAVE score is a rapid method to calculate, with a high

correlation, between risk factors and late seizures/epilepsy. This score is calculated based on **C**ortex involvement, **A**ge < 65 years, hemorrhage **V**olume > 10 mL, and **E**arly seizure (seven days or less after the intracerebral hemorrhage) for a maximal score of 4. In this model, a higher score correlates to higher risk of late seizures.[1]

This study by Jones et al evaluated and compared four seizure prophylaxis strategies for patients with spontaneous intracerebral hemorrhage. This was a decision analysis study and simulation model of four cases representing common clinical scenarios with a presentation of intracerebral hemorrhage without a history of epilepsy and receiving seizure prophylaxis:
- Case 1: A patient with a low risk of late seizure and average antiseizure drug adverse reaction and efficacy;
- Case 2: A patient with a low risk of late seizure, high risk of antiseizure drug adverse reaction, and low efficacy;
- Case 3: A patient with a high risk of late seizure and average antiseizure drug adverse reaction and efficacy;
- Case 4: A patient with high risk of late seizure, high risk of antiseizure drug adverse reaction, and low efficacy.

Within these four scenarios, four treatment strategies, based on primary vs. secondary prophylaxis, timing of seizures (early vs. late), and duration of therapy short (one week) vs. long (indefinite), were compared for a primary outcome of maximal quality-adjusted life years (QALYs):
1. Conservative: Patients with early seizures received short-term secondary early seizure prophylaxis.
2. Moderate: Patients monitored who developed early or late seizures received long-term secondary prophylaxis/therapy.
3. Aggressive: Patients received long-term primary prophylaxis on hospitalization.
4. Risk-guided: Patients underwent a screening EEG for early seizure risk stratification on admission using the 2HELPS2B score classified as low risk (0 points), medium risk (1 point), or high risk (> 2 points). Patients with low risk received conservative treatment, patients with medium and high risk received short-term primary prophylaxis, which was discontinued after one week if they remained seizure-free. If patients developed recurrent/late seizures, they received long-term secondary therapy.

The study suggested a better outcome with short-term antiseizure use over long-term medication use. In case 1, the risk-guided strategy (8.13 QALYs) outperformed conservative (8.08 QALYs), moderate (8.07 QALYs), and aggressive (7.88 QALYs) strategies. In case 2, the conservative strategy (2.18 QALYs) performed better than risk-guided (2.17 QALYs), moderate (2.09 QALYs), and aggressive (1.15 QALYs) strategies. In case 3, the aggressive (9.21 QALYs) strategy outperformed risk-guided (8.98 QALYs), moderate (8.93 QALYs), and conservative (8.77 QALYs) strategies. In case 4, the risk-guided strategy (11.53 QALYs) again per-formed better than conservative (11.23 QALYs), moderate (10.93 QALYs), and aggressive (8.08 QALYs) strategies.

These findings suggested that, overall, the risk-guided strategy and the conservative treatment strategy performed best for most scenarios in this simulation, with the exception of high-risk seizure patients (case 3, with a CAVE score ≥ 3) and patients with lower risk of long-term antiseizure medication adverse reactions (younger age with few comorbidities or comedications), for whom an aggressive strategy may be beneficial.

■ COMMENTARY

These findings are in keeping with clinical practice and published literature suggesting that the risk for post-stroke seizures is greater following hemorrhagic strokes. There is a greater risk of seizures with cortical involvement than with hemorrhages within deeper structures. Additionally, studies have found a higher risk of recurrent seizures/epilepsy in patients with late seizures than in patients with early seizures. There should be a low threshold for EEG monitoring in post-stroke patients with altered mental status that is out of proportion for the clinical picture. This study supports a risk-guided treatment strategy using seizure risk stratification tools, such as the 2HELPS2B and CAVE scores, to help guide treatment strategies and avoid prolonged and potentially unnecessary antiseizure medications. When treating with antiseizure medications, it is important to consider concurrent medication use and comorbidities to decrease potential adverse reactions.

The limitations of this study are related to using a simulated model with published data and assuming the lifetime late-seizure risk was equivalent to the CAVE derived risk. Further prospective studies would be beneficial to determine the optimal choice and duration of antiseizure drug use in the prevention and treatment of seizures in post-stroke patients. ■

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2. Moffet EW, Subramaniam T, Hirsch LJ, et al. Validation of the 2HELPS2B seizure risk score in acute brain injury patients. *Neurocrit Care* 2020;33:701-707.

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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.

CME QUESTIONS

1. **In patients who survive herpes simplex encephalitis, which of the following clinical features predict(s) a poor functional outcome?**
   a. Age > 60 years
   b. Age < 60 years
   c. Presence of brain hemorrhages
   d. Blood-brain barrier disruption

2. **Which of the following forms of focal chronic inflammatory demyelinating polyneuropathy is *least* likely to progress to multi-limb involvement?**
   a. Focal demyelinating sensory and motor neuropathy (F-SMN)
   b. Focal demyelinating motor neuropathy (F-MN)
   c. Focal brachial or lumbosacral inflammatory demyelinating plexus neuropathy (F-PN)
   d. Focal demyelinating autonomic neuropathy (F-DAN)

3. **A quantitative trait locus is a statistical method that:**
   a. determines the linkage disequilibrium between a location in the genome with a disease under study.
   b. correlates a DNA sequence variation (e.g., a single nucleotide polymorphism) at a particular location with a trait that is quantifiable (levels of RNA, protein, small metabolite, etc.).
   c. is a definitive indicator of a monogenic cause of disease.
   d. can be determined using small numbers of subject data points.

4. **Which of the following imaging abnormalities on magnetic resonance imaging correlates with disease severity in patients with multiple sclerosis?**
   a. White matter lesions in the optic nerves
   b. White matter lesions in the cerebellum
   c. Lesions in the cortical gray matter
   d. Generalized brain atrophy

5. **Which location of intracranial hemorrhage has the greatest potential risk of subsequent seizures?**
   a. Thalamic
   b. Internal capsule
   c. Cortical
   d. Basal ganglia

6. **Which model can help estimate the risk of late seizures following intracranial hemorrhage?**
   a. 2HELPS2B score
   b. $ABCD^2$ score
   c. CHA_2DS_2-VASc score
   d. CAVE score