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Evidence-based summaries of the latest clinical neurology research

SPECIAL ISSUE: STROKE

Special Report from the 2020 International Stroke Conference, Los Angeles

By Matthew E. Fink, MD, Editor

Feil Professor and Chairman, Department of Neurology, and Assistant Dean of Clinical Affairs, Weill Cornell Medical College; Neurologist-in-Chief, New York Presbyterian Hospital

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

Message from the editor: The following reviews of studies presented at the 2020 International Stroke Conference were written after my personal attendance at the presentations, followed by review of the simultaneous publications in Stroke. *All comments and opinions are solely those of this editor.*

Safety and Efficacy of Endovascular Treatment for Basilar Artery Occlusion

SOURCE: Writing Group for the BASILAR Group, Zi W, Qiu Z, et al. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. *JAMA Neurol* 2020; Feb. 20. doi:10.1001/jamaneurol.2020.0156. [Online ahead of print].

The efficacy of endovascular treatment for acute ischemic stroke in the anterior circulation has been well established but is uncertain in patients with acute basilar artery occlusion. This study was a nationwide prospective registry of patients presenting with an acute basilar artery occlusion at 47 comprehensive stroke centers across 15 provinces in China. Patients who presented within 24 hours of estimated stroke onset were divided into two groups: standard medical treatment alone or standard medical treatment plus endovascular therapy. The primary outcome measure was improvement in the modified Rankin scale (mRS) score at 90 days and adjusted for pre-specified prognostic factors. Safety outcomes included symptomatic intracerebral hemorrhage and 90-day mortality.

Over a five-year period, 829 patients were recruited into the study, with 647 treated with

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Neurology
[ALERT]

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endovascular therapy in addition to standard medical therapy, and 182 treated with standard medical therapy alone. Ninety-day functional outcomes were better with endovascular therapy (odds ratio [OR] = 3.07, $P < 0.001$). In addition, endovascular therapy was associated with a higher rate of improvement with an mRS ≤ 3 at 90 days (OR = 4.70, $P < 0.001$). Patients treated with endovascular therapy also had a lower rate of 90-day mortality, although they did have an increased rate of symptomatic intracerebral hemorrhage (7.1% vs. 0.5%, $P < 0.001$).

In this prospective observational registry, endovascular therapy demonstrated improved functional outcome and reduced mortality. ■

BP Management After Mechanical Thrombectomy for Ischemic Stroke

SOURCE: Petersen NH, Silverman A, Strander SM, et al. Fixed compared with autoregulation-oriented blood pressure thresholds after mechanical thrombectomy for ischemic stroke. *Stroke* 2020;51:914-921.

Endovascular thrombectomy is now a standard treatment for patients who present with acute ischemic stroke from large vessel occlusions. The optimal management of blood pressure following thrombectomy is controversial, with current guidelines recommending maintenance of blood pressure < 180/105 mmHg for at least 24 hours after the procedure. However, there have been no randomized trials to determine the optimal blood pressure. The feared post-procedure complications are hemorrhage and malignant cerebral edema, because of disruption of cerebral autoregulation. This novel study used near-infrared spectroscopy correlated with continuous blood pressure measurement to develop an autoregulation algorithm that could be determined for each individual patient. By using this algorithm, investigators could identify the optimal blood pressure range where autoregulation was intact. The details of the technique should be reviewed by interested readers in the full paper.

The investigators enrolled 90 patients who were undergoing endovascular thrombectomy. Autoregulatory function was determined using near-infrared spectroscopy-derived tissue oxygenation in response to changes in arterial blood pressure. For each patient, an ideal blood pressure range was determined. The mean age of patients was 71.6 years, with 47% female, and mean National Institutes of Health stroke scale = 13.9. Patients who had a percentage of time with the mean arterial pressure above the upper limit of autoregulation as determined by this method had a worse 90-day outcome, (odds ratio per 10% time = 1.84, $P = 0.002$), and this also was correlated with a higher rate of hemorrhagic transformation. This was an observational study without randomization or comparative groups, but the technique of determining autoregulation appears to be sound, and further study is warranted to evaluate this technique to improve the post-procedure treatment of patients undergoing endovascular thrombectomy. ■

Diabetes Education for Patients Hospitalized with Stroke

SOURCE: Stone S, Drobycki N, Johnson M. Abstract NS5: Use of a multidisciplinary approach to successfully improve inpatient diabetes self-management education and diabetes medication reconciliation at discharge for persons with diabetes and stroke at a major academic medical center. *Stroke* 2020;51:ANS5.

A team of nurses at UT Southwestern Medical Center in Dallas undertook a project to improve diabetes education for stroke patients. At their center, they noted that 40% of stroke patients have diabetes, yet only 11% received diabetes education and only 59% had diabetes medication prescribed at the time of discharge from the hospital. The team initiated an educational program to improve these parameters. The endocrinology team was consulted for all stroke patients with a history of diabetes or those who had an A1c level of 7% or more. They worked with the neurology team and provided diabetes education for the patient and advised the neurology team on the appropriate discharge medication regimen and follow-up. Stroke coordinators provided

reminders to the teams and to the patients to order consultations for patients who had hemoglobin A1c 7% or greater. Comparing 2017 to 2019, inpatient diabetes education improved from 11% to 96%, and discharge medications improved from 59% in 2017 to 93% in 2019. These metrics reflect improvement in care as the result of an inpatient educational program. ■

Disability After Minor Stroke and TIA — Secondary Analysis of the POINT Trial

SOURCE: Cucchiara B, Elm J, Easton JD, et al. Disability after minor stroke and transient ischemic attack in the POINT trial. *Stroke* 2020;51:792-799.

Early treatment of minor stroke and transient ischemic attacks (TIAs) with antiplatelet medication reduces the risk and severity of recurrent stroke. The POINT trial demonstrated that dual antiplatelet treatment with aspirin and clopidogrel resulted in a lower rate of recurrent stroke than with aspirin alone. The investigators then did a secondary analysis to determine if disability at 90 days was different between the two groups as well.

At 90 days, 9.6% of patients enrolled with TIA and 18.2% of patients enrolled with minor stroke were disabled. Overall disability was similar between the groups whether assigned to dual antiplatelet therapy or aspirin alone (14.7% vs. 14.3%). However, there were fewer patients with disability in conjunction with the primary outcome event in the dual antiplatelet treatment arm, but this did not reach statistical significance. The investigators also analyzed the combination of the index event with recurrent stroke and thought that there was a decrease in disability in the dual antiplatelet treatment arm. A multivariate analysis was performed and indicated that risk factors for disability following TIA included age, subsequent stroke, serious adverse events, and major bleeding. Although the data from this analysis suggest that disability might be less with dual antiplatelet therapy, differences between the groups were small, did not show robust findings, and did not reach statistical significance in most of the analyses. ■

Survival After Ischemic Stroke Has Improved During the Past 25 Years

SOURCE: Waziry R, Heshmatollah A, Bos D, et al. Time trends in survival following first hemorrhagic or ischemic stroke between 1991 and 2015 in the Rotterdam study. *Stroke* 2020;51:STROKEAHA119027198.

The Rotterdam study is a prospective community-based cohort study that started in 1990 and followed residents aged 55 years and older. They participated in baseline examinations and follow-up regarding cerebrovascular events. The investigators analyzed their follow-up data to determine if there was a temporal trend in survival, changes in age-standardized death rates, or changes in survival probabilities from the 1990s until 2015.

In evaluating the hemorrhagic stroke group, investigators found that 144 deaths occurred during 386 person-years. The investigators observed a similar mortality rate over the years, with 30 per 100 person-years in 2015 compared to 25 per 100 person-years in 1991. Similarly, mortality rates remained unchanged for hemorrhagic stroke between the years 1991 and 2015. However, in the ischemic stroke group, they observed a decline in mortality rates in 2015 of 11 per 100 person-years compared with the 1991 rates of 29 per 100 person-years. This translates to a favorable trend in the latest time period, with a hazard ratio of 0.71, $P < 0.01$. The investigators concluded that survival following ischemic stroke has improved over the past several decades, while no change has been observed in survival following hemorrhagic stroke. ■

Trends in Stroke Incidence Over Time

SOURCE: Madsen TE, Khoury JC, Leppert M, et al. Temporal trends in stroke incidence over time by sex and age in the GCNKSS. *Stroke* 2020;51:1070-1076.

The greater Cincinnati/Northern Kentucky Stroke Study is a prospective survey of all strokes among residents ≥ 20 years of age in all local hospitals for a population of 1.3 million people. The data were collected during five periods — July 1993 to June 1994, and calendar years 1999, 2005, 2010, and 2015. Sex-specific incidence rates were calculated and adjusted for age and race. Sex-specific case fatality rates also were reported. Over the five study periods, there were 9,733 strokes, and 56.3% were in women. In the period 1993/1994, women had 229 incident strokes per 100,000 population, and in 2015, they had 174 strokes per 100,000 population. For men, there were 282 strokes in 1993/1994, and 211 in 2015. Rates decreased between the first and last study periods for both sexes for ischemic stroke, but the rates for intracerebral hemorrhage and subarachnoid hemorrhage did not decline over the years. The investigators also noted that stroke incidence increased for men in the 22- to 44-year-old age group. Future studies should investigate the reasons for increasing stroke rates in the younger age groups, and why there has been no improvement in the incidence and survival in patients with hemorrhagic stroke. ■

Mobile Stroke Unit in Australia Speeds up Time to Thrombectomy

SOURCE: Zhao H, Coote S, Easton D, et al. Melbourne mobile stroke unit and reperfusion therapy: Greater clinical impact of thrombectomy than thrombolysis. *Stroke* 2020;51:922-930.

Mobile stroke units (MSUs) are specially designed ambulances that have an integral computed tomography scanner, connect to a stroke neurologist via telemedicine, and carry thrombolytic drugs that can be administered in the field. Many reports have demonstrated that these units can treat patients with intravenous thrombolysis significantly faster than traditional ambulance transportation to a hospital emergency room. A recently deployed unit in Melbourne, Australia, reported its experience in the first year with intravenous thrombolysis, as well as the effect of the unit on time to endovascular thrombectomy.

In the first year of operation, prehospital thrombolysis was administered to 100 patients (mean age 73.8 years, 62% were male). The median time savings per MSU patient compared to controls, measuring time from dispatch to hospital arrival, was 26 minutes, and 15 minutes faster from hospital arrival to thrombolysis. The calculated overall time savings from time of dispatch to thrombolysis was 42.5 minutes. During the same period of time, 41 MSU patients were treated with endovascular thrombectomy, with a median dispatch-to-treatment time savings of 51 minutes ($P < 0.001$). This included a median time savings of 17 minutes from arrival at the hospital to arterial puncture. Using a calculation for disability-adjusted life-years, MSU evaluation and treatment resulted in reduced disability life-years of 20.9 for intravenous trauma lysis and 24.6 for endovascular thrombectomy. The investigators emphasized that the benefits of prehospital evaluation and triage for endovascular centers is facilitated workflow and reduced time to endovascular thrombectomy. ■

Mobile Stroke Units Result in Improved Functional Outcome After Ischemic Stroke

SOURCE: Ebinger M, Siegerink B, Kunz A, et al. LB5 - Effects of pre-hospital acute stroke treatment as measured with the modified Rankin scale; the Berlin - Pre-Hospital Or Usual Care Delivery trial (B_PROUD). Presented at the International Stroke Conference, Feb. 20, 2020.

Mobile stroke units (MSUs) have been deployed in multiple cities in Europe, North America, Australia, and Asia, and all have demonstrated reduction in time to the administration of intravenous thrombolysis compared to conventional ambulance transport. The MSU team in Berlin, Germany, has been operating for several years, and presented their data regarding functional outcomes. This was a prospective observational trial with blinded outcome assessment, comparing functional outcomes of patients with acute ischemic stroke, 18 years of age or older, who requested medical dispatch during the hours of MSU operation. For inclusion, stroke codes were called within four hours of the onset of symptoms, and patients were excluded if symptoms resolved before the ambulance arrived. If there were absolute contraindications for either thrombolysis or thrombectomy, patients were excluded. The primary outcome was functional disability as measured by the three-month modified Rankin Scale scores, with disability ranging from 0 (no neurological deficits) to 6 (death) at three months. The coprimary outcomes were other functional categories: 1) able to ambulate, 2) able to live at home, 3) living with severe disability, or 4) living in an institutional setting.

Between Feb. 1, 2017, and May 8, 2019, there were 1,543 patients evaluated, and the primary outcomes were assessed in 1,506. Availability of the MSU for treatment reduced the odds ratio significantly for disability and death at three months (0.74, $P = 0.003$) but not in the coprimary outcome of functional categories (0.75, $P < 0.057$). Patients treated on the MSU had a higher rate of thrombolysis (60% vs. 48%), and alarm-to-treatment times were faster (50 minutes, $P = 0.001$). In concluding, the investigators stated that MSU availability improved functional outcome in patients with acute ischemic stroke, if they were eligible for thrombolysis and/or thrombectomy. ■

Sex Hormone-Binding Globulin and Stroke Risk in Women

SOURCE: Madsen TE, Luo X, Huang M, et al. Circulating SHBG (sex hormone-binding globulin) and risk of ischemic stroke. Findings from the WHI. *Stroke* 2020;51:1257-1264.

The role of endogenous sex steroids such as estradiol in postmenopausal women is controversial, and studies have conflicting results regarding their impact on cardiovascular diseases. Nevertheless, premenopausal women have a lower risk of ischemic stroke compared to men, and this finding disappears in postmenopausal women. Sex hormone-binding globulin (SHBG) is thought to play a role and has been shown to be inversely related to

obesity, diabetes mellitus, and other cardiovascular disorders. SHBG is a protein that binds to and regulates testosterone and estradiol. It is thought to play a role in vascular risk factors, including insulin resistance, inflammation, diabetes mellitus, metabolic syndrome, and coronary heart disease. The Women's Health Initiative (WHI) looked at the relationship of this globulin to ischemic stroke in an observational cohort of 161,808 postmenopausal women enrolled in the WHI from 1993 to 1998.

Investigators identified 13,192 participants free of stroke at baseline. These participants were included in the follow-up studies and had levels of serum SHBG measured. They were stratified into quintiles, and had risk adjustments for body mass index, hypertension, alcohol use, smoking, physical activity, reproductive risk factors, and diabetes. After an average follow-up of 11.6 years, 768 ischemic stroke events were identified. Compared to the highest quintile of measured SHBG, women in the lowest quintile had an increased risk of ischemic stroke with a hazard ratio of 1.88 ($P < 0.05$). Risk adjustment did not eliminate the inverse associations between SHBG and ischemic stroke. Measurements of estradiol and testosterone and adjustment of SHBG levels for hormone levels did not eliminate the inverse relationship between SHBG and ischemic stroke, suggesting that this globulin may play an independent role as a stroke risk factor. ■

Benefits of Targeting LDL Cholesterol Below 70 mg/dL

SOURCE: Amarenco P, Kim JS, Labreuche J, et al. Benefit of targeting LDL (low-density lipoprotein) cholesterol <70 mg/dL during 5 years after ischemic stroke. *Stroke* 2020;51:1231-1239.

In the SPARCL trial (*N Engl J Med* 2006;355:549-559), treatment of patients with atorvastatin 80 mg per day resulted in a 16% relative risk reduction in stroke during 4.9 years of follow-up, compared to placebo. In a subgroup with carotid artery stenosis, the relative risk reduction was 33%. Patients who had a low-density lipoprotein (LDL) cholesterol less than 70 mg/dL had a 28% relative risk reduction compared to patients who only achieved an LDL cholesterol of 100 mg/dL or above. Amarenco et al specifically focused on targeting an LDL cholesterol below 70 mg/dL in patients who had ischemic stroke or transient ischemic attack (TIA) with evidence of atherosclerosis. The patients were stratified into two groups, where statins were titrated to reach an LDL cholesterol of less than 70 mg/dL or with an LDL of 100 mg/dL. Investigators were free to use any statin of their choice, and this could be combined with ezetimibe or other medications as needed. This was an open-label trial, and patients and investigators were not blinded to treatments. The primary endpoint was the composite of nonfatal stroke, nonfatal myocardial infarction, unstable angina, TIA, and vascular death. Patients were enrolled from 2010 until 2018. The study was ended early, after 277 primary endpoints were accrued, because of lack of funds. Median follow-up was 3.5 years.

The groups achieved mean LDL cholesterol of 66 mg/dL and 96 mg/dL, respectively. The primary endpoint occurred in 9.6% and 12.9% of patients, respectively, with a hazard ratio in favor of lower cholesterol of 0.74, $P = 0.019$. Ischemic stroke or urgent carotid revascularization following TIA was reduced by 27%. The primary outcome was reduced by 25%. There was no significant difference in the numbers of intracranial hemorrhages that occurred between the two groups. The investigators concluded that after an ischemic stroke of atherosclerotic origin, targeting LDL cholesterol to less than 70 mg/dL resulted in a significant reduction in subsequent major vascular events and no increase in intracranial hemorrhage. ■

ABSTRACT & COMMENTARY

Zilucoplan for Myasthenia Gravis

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: Zilucoplan, a macrocyclic peptide that binds complement component C5, showed promise as an effective agent for treatment of generalized myasthenia gravis in a Phase II trial.

SOURCE: Howard JF, Nowak RJ, Wolfe GI, et al. Clinical effects of the self-administered subcutaneous complement inhibitor zilucoplan in patients with moderate to severe generalized myasthenia gravis: Results of a phase 2 randomized, double-blind, placebo-controlled, multicenter clinical trial. *JAMA Neurol* 2020; Feb. 17. doi:10.1001/jamaneurol.2019.5125. [Online ahead of print].

Upward of 85% of patients with generalized myasthenia gravis (gMG) have detectable anti-acetylcholine receptor antibodies (AchR-Ab). Evidence indicates that these antibodies, as opposed to anti-muscle-specific kinase (MuSK) antibodies, activate the classic complement cascade. Post-synaptic membrane simplification, with associated reduced AchR density, is the ultrastructural correlate of impaired neuromuscular transmission in gMG, and it appears that the terminal complement cascade plays a role. Eculizumab, a monoclonal antibody to complement component 5 (C5) inhibitor, was shown to be effective in treating gMG patients previously refractory to other therapies, supporting complement inhibition as a new therapeutic approach in gMG. Zilucoplan, a macrocyclic peptide that binds C5 with high affinity and specificity, is thus the subject of this study to determine its efficacy in gMG.

Between December 2017 and August 2018, MG patients, ages 18 to 85 years, were recruited from 25 North American study sites to participate in this randomized, double-blind, placebo-controlled, Phase II clinical trial. Inclusion criteria required a clinically confirmed diagnosis of MG (Myasthenia Gravis Foundation of America [MGFA] Class II-IVa), AchR-Ab positivity, Quantitative MG (QMG) score of 12 or greater, with no intravenous immunoglobulin (IVIg), plasma exchange (PLEX), or change in therapy for four weeks prior to randomization, and no thymectomy or rituximab in the prior six months. Patients were assigned randomly, in a 1:1:1 ratio, to daily subcutaneous self-injection of zilucoplan 0.1 mg/kg, zilucoplan 0.3 mg/kg, or placebo, for 12 weeks.

No change in ongoing therapy was permitted during the 12-week trial, and patients were evaluated at baseline and weeks 1, 2, 4, 8, and 12. IVIg or PLEX was allowed in the event of worsening, based on investigator discretion. A change in QMG score, a 13-item scale evaluating muscle strength, ranging from 0 (normal) to 39 (severe weakness), was the primary endpoint, with improvement of two to three points considered clinically meaningful, depending on baseline disease. Pyridostigmine was not allowed in the 10 hours prior to QMG measurements. Secondary endpoints included the MG Composite (MGC) and the 15-item Myasthenia Gravis Quality-of-Life Revised Scale (MG-QoL15r). The key secondary endpoint was the change in MG Activities of Daily Living (MG-ADL) score, an eight-item scale assessing daily functions, ranging from 0 (normal) to 24 (severely affected), by study completion. Statistical analysis used an analysis of covariance model and least squares means, with Fisher exact test used to analyze categorical endpoints.

Among 57 patients assessed for eligibility, 12 did not meet inclusion criteria, leaving 45 patients for randomization (15 per arm of the trial). All but one received the study drug, with the exception lost to follow-up when he did not return for the dosing visit. Rapid, clinically meaningful, and statistically significant improvement in the QMG score was seen in the 0.3 mg/kg zilucoplan arm compared to placebo, with a score change of -6.0 points in the former, compared to -3.2 in the latter, and improvement beginning after one week. Beginning after four weeks, a less pronounced and slower but clinically meaningful and statistically significant improvement also was appreciated with 0.1 mg/kg zilucoplan. MG-ADL showed similar results, favoring zilucoplan over placebo, and 0.3 mg/kg over 0.1 mg/kg, at week 12. MG-QoL15r and MGC followed a similar pattern, although the former favored the 0.1 mg/kg zilucoplan arm, perhaps because of its higher baseline scores. No significance was found in the analysis of the covariance model for age, sex, duration of disease, treatment history, prior thymectomy, or history of thymoma.

Three patients in the placebo arm required rescue therapy with IVIg or PLEX, one patient in the 0.1 mg/kg zilucoplan arm, and none in the 0.3 mg/kg zilucoplan arm. The study drug was well-tolerated, with a moderate injection-site reaction (ISR) in only one placebo patient, all other ISRs being mild. Other adverse events were mostly mild, were considered unrelated to study drug, and resolved spontaneously. No meningococcal infections, life-threatening adverse events, or deaths occurred during the trial, and no anti-zilucoplan antibodies were detected. Zilucoplan appears safe and effective for the treatment of AchR-Ab positive gMG.

■ COMMENTARY

Like eculizumab, zilucoplan is a terminal complement inhibitor, but, unlike the former, it is administered subcutaneously. A synthetic macrocyclic peptide, zilucoplan binds C5, preventing its cleavage into C5a and C5b, and preventing the production of the membrane attack complex. Complement inhibition increases the risk for meningococcal infection since the complement system ordinarily protects against encapsulated bacterial infections, and prior vaccination may be required.

The results of this study are promising, and preparations for a Phase III trial are underway. ■

ABSTRACT & COMMENTARY

Cognitive Symptoms in Genetic Forms of Parkinson's Disease May Help in Distinguishing the Various Types

By Harini Sarva, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

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

SYNOPSIS: This paper illustrates that, of the confirmed genetic forms of Parkinson's disease, there are common cognitive and psychiatric features, thus adding to our knowledge of the clinical phenotype of these genetic forms.

SOURCE: Piredda R, Desmarais P, Masellis M, Gasca-Salas C. Cognitive and psychiatric symptoms in genetically determined Parkinson's disease: A systematic review. *Eur J Neurol* 2020;27:229-234.

This systematic review assessed the cognitive and psychiatric manifestations of well-established Mendelian genetic forms of Parkinson's disease (PD) as a result of the following mutations: SNCA, LRRK2, VPS35, PINK1, parkin, and DJ1. The first three are autosomal dominant and the last three are recessive.

A literature search from January 1997 to April 2018 yielded 95 papers, which were reviewed further by the authors. Among the 151 SNCA carriers, the cognitive and psychiatric impairments were dependent on the mutation types, with triplication mutations having the greatest rates of dementia in comparison to missense and duplication mutations.

Depression and visual hallucinations were the most common psychiatric manifestations among SNCA carriers. Among the 1,625 LRRK2 mutation carriers, frontal lobe deficits and depression were the most common cognitive and psychiatric features, respectively. When comparing LRRK2 carriers to idiopathic PD patients, LRRK2 carriers had less depression but similar levels of anxiety. Seven out of 24 VPS35 carriers had cognitive impairment, and depression was quite common among those studied. Twenty-five of 81 parkin carriers, who had complete neurocognitive testing, demonstrated only three with mild cognitive impairment or dementia. Sixty-five of 89 had psychiatric assessments, and half had at least one of the following: depression, impulse control disorders, or anxiety. Among eight DJ1 carriers two had dementia and four had anxiety. Of 24 patients with PINK1 mutations, 17 had cognitive assessments and of these, five had dementia. Thirteen of the 24 had depression.

■ COMMENTARY

In addition to the motor and demographic features of genetic forms of PD, cognitive and psychiatric features can aid in the treatment and prognostication of these patients. Approximately 2,000 patients with well-established genetic forms of PD demonstrated various levels of cognitive and psychiatric features. However, these features alone may not aid in diagnosis, since mild cognitive impairment, frontal lobe deficits, depression, and anxiety are common among nongenetic forms of PD.

In addition, the studies had variable sizes, did not always use the same scales for cognitive and psychiatric measures, and did not always have populations with the same mutations. Among the SNCA mutation carriers, those with a triplication mutation were more likely to have dementia, but how different mutations among the other groups of genetic forms of PD contribute to cognitive or psychiatric manifestations is unclear.

Another important consideration is the diverse pathophysiological processes that result from these mutations, which may play a role in the timing and degree of cognitive and psychiatric manifestations. Although these manifestations can give a clue to clinicians about the different forms of PD, the motor features and demographics all should be combined to formulate a diagnostic plan and guide genetic testing. Future studies with larger sample sizes using longitudinal formal neuropsychiatric batteries are needed to assess the cognitive and psychiatric changes that occur in genetic forms of PD. ■

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. **Endovascular thrombectomy for acute basilar occlusion results in better clinical outcomes than medical therapy alone, in appropriately selected patients.**
   a. True
   b. False
2. **The optimal range for regulating blood pressure after mechanical thrombectomy for ischemic stroke has been determined from clinical trials.**
   a. True
   b. False
3. **Diabetes mellitus is a significant risk factor for stroke and its effective treatment can reduce stroke risk.**
   a. True
   b. False
4. **After minor stroke or transient ischemic attack, treatment with aspirin alone or dual antiplatelet therapy does not seem to make a significant difference in 90-day disability.**
   a. True
   b. False
5. **Over the past several decades, survival has improved significantly for both ischemic stroke and hemorrhagic stroke.**
   a. True
   b. False
6. **The Greater Cincinnati/Northern Kentucky Stroke Study demonstrated a decline in incidence and mortality from ischemic stroke from 1993 until 2015.**
   a. True
   b. False
7. **Mobile stroke units enable stroke neurologists to administer intravenous thrombolysis and triage to thrombectomy centers significantly faster than traditional ambulances.**
   a. True
   b. False
8. **Mobile stroke unit availability results in faster time to definitive treatment and better functional outcomes at three months after acute ischemic stroke.**
   a. True
   b. False
9. **Sex Hormone-Binding Globulin has a direct relationship between plasma levels and ischemic stroke risk in women.**
   a. True
   b. False
10. **Lowering LDL cholesterol below 70 mg/dL in patients with ischemic stroke due to atherosclerosis results in a significant reduction in recurrent vascular events, compared to the usual target of 100 mg/dL.**
    a. True
    b. False
11. **Zilucoplan:**
    a. is administered intravenously.
    b. is a humanized monoclonal antibody.
    c. is a terminal complement inhibitor.
    d. is Food and Drug Administration-approved for the treatment of refractory myasthenia gravis.
12. **Which of the following statements is *not true* about genetic forms of Parkinson's disease (PD)?**
    a. DJI, parkin, and PINK1 are recessive forms of PD.
    b. Triplication mutations in the SNCA gene have a higher likelihood for dementia than missense and duplication mutations.
    c. Depression and anxiety are common psychiatric manifestations among all genetic forms of PD.
    d. LRRK2 mutation carriers have higher rates of depression than idiopathic PD.

[IN FUTURE ISSUES]

Neurological Consequences of COVID-19 Infection