Stroke-Related Translational Research

Caplan and colleagues (page 1110) point out that the many facets of cerebrovascular disease have proven to be very fertile ground for translational research. This research involves many aspects of cerebrovascular disease: risk factors and prevention, diagnosis, prognosis, acute treatment, potential neuroprotection, and recovery. Various disciplines and avenues are being explored, including genetics, molecular biology, animal models, brain and vascular imaging, stem cells, and magnetic and direct current stimulation.

Rapidly Progressive Alzheimer Disease

Schmidt and colleagues (page 1124) emphasize that different rates of progression have been observed among patients with Alzheimer disease. Risk factors accelerating deterioration have been identified, and some are under discussion. For example, risk factors include genetics, comorbidity, and early appearance of Alzheimer disease motor signs. Progressive forms of Alzheimer disease have been reported with rapid cognitive decline and disease duration of only a few years. Their short review aims to provide an overview of the current knowledge of rapidly progressive Alzheimer disease.

Effect of APOE ε4 Status on Intrinsic Network Connectivity in Cognitively Normal Elderly Persons

Machulda et al (page 1131) examine default mode and salience network functional connectivity as a function of APOE ε4 status in a group of cognitively normal age-, sex-, and education-matched older adults. They found reductions in posterior default mode network connectivity but a concomitant increase in salience network connectivity in elderly cognitively normal APOE ε4 carriers relative to APOE ε4 noncarriers at rest. The observation of functional alterations in default mode and salience network connectivity in the absence of structural changes between APOE ε4 carriers and noncarriers suggests that alterations in connectivity may have the potential to serve as an early biomarker. Editorial perspective is provided by William W. Seeley, MD (page 1107).

Comparison of Analytical Platforms for Cerebrospinal Fluid Measures of β-Amyloid 1-42, Total tau, and P-tau181 for Identifying Alzheimer Disease Amyloid Plaque Pathology

Fagan and colleagues (page 1137) compared the performances of the 2 most commonly used platforms, INNOTEST enzyme-linked immunosorbent assay and INNO-BIA AlzBio3 for measurement of CSF β-amyloid (Aβ) and tau proteins to identify the presence of amyloid plaques in a research cohort (n=103). They report that the INNOTEST and INNO-BIA CSF platforms perform equally well in identifying individuals with underlying amyloid plaque pathology. Differences in absolute values, however, point to the need for assay-specific diagnostic cutoff values.

Cerebrospinal Fluid Biomarkers, Education, Brain Volume, and Future Cognition

Roe et al (page 1145) evaluate the combination of cerebrospinal fluid biomarkers of Aβ42, tau, and phosphorylated tau with education and normalized whole-brain volume to predict incident cognitive impairment and test the cognitive/brain reserve hypothesis. They find that in individuals with higher levels of cerebrospinal fluid tau and phosphorylated tau but normal cognition at baseline, time to incident cognitive impairment is moderated by education and brain volume as predicted by the cognitive/brain reserve hypothesis.

Glucose Transporter 1 Deficiency as a Treatable Cause of Myoclonic Astatic Epilepsy

Mullen and colleagues (page 1152) note that patients with myoclonic-astatic epilepsy (MAE) share both a high rate of response to the ketogenic diet and electroclinical seizure types with glucose transporter 1 (GLUT1) deficiency syndrome due to mutations in SLC2A1. They thus hypothesize that a significant proportion of patients with MAE have GLUT1 deficiency. They report that 5% of their patients with MAE had SLC2A1 mutations, suggesting that patients with MAE should be tested for GLUT1 deficiency. Diagnosis of GLUT1 deficiency is a strong indication for early use of the ketogenic diet, which may substantially improve outcome of this severe disorder.
Rituximab-Associated Progressive Multifocal Leukoencephalopathy in Rheumatoid Arthritis

Clifford et al (page 1156) describe the development of progressive multifocal leukoencephalopathy (PML) in patients with rheumatoid arthritis (RA) treated with rituximab. Their study suggests an increased risk, about 1 case per 25,000 individuals, of PML in patients with RA being treated with rituximab. Inflammatory PML may occur in this setting even while CD20 counts remain low.

Clinical Characterization of a Kindred With a Novel 12-Octapeptide Repeat Insertion in the Prion Protein Gene

Kumar and colleagues (page 1165) report the clinical, electroencephalographic, and neuroradiologic findings in a kindred with a novel insertion in the prion protein gene, PRNP. This kindred has a unique combination of clinical and neuropathologic features associated with the largest base pair insertion identified to date in PRNP and underscores the need to consider familial prion disease in the differential diagnosis of a familial frontotemporal dementia–like syndrome.

Muscle Magnetic Resonance Imaging in Congenital Myopathies Due to Ryanodine Receptor Type 1 Gene Mutations

Klein et al (page 1171) provide a blinded analysis of muscle magnetic resonance imaging patterns of patients with congenital myopathies with dominant or recessive ryanodine receptor type 1 (RYR1) mutations and control patients without RYR1 mutations. Their results suggest that muscle magnetic resonance imaging is a powerful predictor of RYR1 involvement in patients with a congenital myopathy, especially if they carry a dominant mutation or recessive mutations without ophthalmoparesis.

Laboratory Abnormalities in Patients With Myotonic Dystrophy Type 2

Heatwole and colleagues (page 1180) analyze and compile the laboratory abnormalities of patients with myotonic dystrophy type 2 (DM2). They show that there is a high frequency of laboratory abnormalities in DM2. These abnormalities provide insight into the widespread pathological manifestations of DM2 and may form a basis for clinical monitoring and disease screening.