Circuits and Circuit Disorders of the Basal Ganglia

DeLong and Wichmann (page 20) point out that the anatomy and function of the basal ganglia and their role in motor and nonmotor disorders have undergone major revisions over the past decades. They review the evidence that the basal ganglia are now appreciated as components of parallel, re-entrant cortico-subcortical circuits, which take origin from individual cortical areas, traverse the basal ganglia and thalamus, and terminate in their respective areas of origin in the frontal lobe. This view underlies current thinking about the physiology of normal basal ganglia function and in abnormal circuit functions underlying Parkinson disease and other common movement disorders. They emphasize that circuit disorders is an appropriate designation to describe diseases of the basal ganglia resulting from pathologic disturbances in neuronal activity throughout specific cortico-subcortical loops. It is a clear and compelling explanation and review of the functions of the basal ganglia in health and disease written by the principal investigators.

Trigeminal Autonomic Cephalgia

Favier and colleagues (page 25) analyzed 27 published and 4 new cases with trigeminal autonomic cephalgia in whom treatment of a structural lesion had resulted in substantial relief of symptoms. Trigeminal autonomic cephalgia includes cluster headache, paroxysmal hemicrania, and short-lasting unilateral neuralgiform headache with conjunctival injection and tearing. Thus, trigeminal autonomic cephalgias can be caused by an underlying structural lesion, and all patients with trigeminal autonomic cephalgia should get neuroimaging.

Younger Stroke Survivors and Inadequate Care

Levine and colleagues (page 37) assessed age-related differences in access to physician care and medications among stroke survivors (aged 45-64 years vs 65-85+ years) in the National Health Interview Survey (years 1998-2002) (Figure). In a comprehensive analysis, they report that stroke survivors younger than 65 years old reported worse access to physician care and medication affordability than older stroke survivors. Their findings provide population-based estimates of uninsured status, physician visits, and medication affordability. Editorial perspective is provided by Steven R. Levine, MD.

Progranulin Mutations in Primary Progressive Aphasia

Primary progressive aphasia (PPA) is a language-based dementia characterized by a fluent or nonfluent language disorder as its principal feature. Two families, PPA1 and PPA3, were studied by Mesulam and colleagues (page 43). Genomic DNA was isolated from 3 of the 4 siblings in PPA1, all 3 siblings in PPA3, and more than 200 controls. All 12 coding exons of progranulin (PGRN) and the 5’ and 3’ untranslated regions were amplified by polymerase chain reaction and sequenced in both directions using relevant primers. They report that both affected members of PPA1 for whom DNA was available and both affected sisters of PPA3 had a PGRN mutation not found in the unaffected siblings or in controls. The mutations are likely to cause a null allele and a reduction in the level of functional PGRN protein. Both affected members of PPA1 with autopsies had frontotemporal lobar degeneration with tau-negative ubiquinated inclusions.

Figure. Access to physician care and medications among stroke survivors by age according to the National Health Interview Survey from years 1998 to 2002. The P values are associated with χ² test for trend.
Recurrent Ischemic Lesions on Diffusion-Weighted Imaging in Symptomatic Intracranial Atherosclerosis

Kang et al (page 50) investigated differential patterns of early recurrent ischemic lesions on diffusion-weighted imaging among stroke subtypes, particularly in intracranial large-artery atherosclerosis. They found that early recurrent ischemic lesions in intracranial large-artery atherosclerosis are relatively frequent and have different patterns than in extracranial large-artery atherosclerosis or cardiomegaly.

Frontotemporal Dementia and Dysphagia

Lingamore and colleagues (page 58) encountered swallowing abnormalities in 4 of 21 patients with frontotemporal dementia. They conclude that dysphagia indicates the dysfunction of brainstem motor systems. Frontotemporal dementia with dysphagia may provide support for the presence of motor neuron disease as part of a clinical spectrum of disease.

H63D Mutations in HFE and Amyotrophic Lateral Sclerosis

Mutations in HFE, a gene defect that can disrupt iron metabolism, have been implicated in increasing the risk of developing amyotrophic lateral sclerosis (ALS). Sutedja et al (page 63) genotyped for 2 common HFE mutations on 289 patients with ALS and 5886 population-based controls in the Netherlands. In a detailed study, they report that H63D mutations in HFE play a role in the pathogenesis of ALS and this association may involve a later-onset subset of ALS.

Multiple Sclerosis After Infectious Mononucleosis

Infectious mononucleosis caused by the Epstein-Barr virus has been associated with increased risk of multiple sclerosis. Nielsen and colleagues (page 72) examined a cohort of 25,234 Danish patients with mononucleosis for the occurrence of multiple sclerosis. They found that the risk of multiple sclerosis was persistently increased for more than 30 years after infectious mononucleosis. Thus, they conclude that the risk of multiple sclerosis is increased in persons with prior infectious mononucleosis, regardless of sex, age, and time since infectious mononucleosis or severity of infection. The risk of multiple sclerosis arises early and persists for at least 30 years after the infection.

Cortical Demyelination in Multiple Sclerosis

Bo et al (page 76) studied whether subpial cortical demyelination in multiple sclerosis is associated with focal and diffuse white matter pathologic features by magnetic resonance imaging. In an elegant study, they conclude that extensive subpial demyelination was not associated with a significant increase in the area of focal or diffuse white matter pathologic features. Thus, the lack of association of multiple sclerosis gray matter demyelination with diffuse or focal white matter changes indicates that gray matter demyelination in multiple sclerosis occurs largely independent of white matter pathologic features. Further, they conclude that the extent or distribution of white matter abnormalities cannot be used to identify extensive cortical pathologic features in the clinical setting.

Higher Folate Intake and Lower Risk of Alzheimer Disease

Luchsinger and colleagues (page 86) studied whether higher intake of folate, pyridoxine, and cobalamin may decrease the risk of Alzheimer disease through lowering of homocysteine levels. In a comprehensive longitudinal study, they report that higher folate intake may indeed decrease the risk of Alzheimer disease independent of other risk factors and levels of pyridoxine and cobalamin.

Metabolic Syndrome and Alzheimer Disease

Razay et al (page 93) point out that the metabolic syndrome is a risk factor for cardiovascular diseases, which have been linked to Alzheimer disease (AD). They found that patients with AD compared with controls had significantly larger waist circumference and higher plasma concentrations of triglycerides and glucose. Patients with AD had lower plasma concentration of high-density lipoprotein cholesterol and lower systolic blood pressure. This study suggests that AD is associated with the metabolic syndrome, which could have implications for the prevention and treatment of AD.

Neurocognitive Status and Markers of Immune Activation as Predictors of Time to Death in Advanced Human Immunodeficiency Virus Infection

Sevigny and colleagues (page 97) evaluated whether neurocognitive status and baseline levels of plasma and cerebrospinal fluid immune biomarkers are associated with time to death in a cohort...
with advanced human immunodeficiency virus infection. They found that human immunodeficiency virus–associated dementia is an independent predictor of time to death. These findings underscore the importance of assessment for cognitive impairment in those with advanced human immunodeficiency virus infection.

Total Cholesterol Changes in 26 Years and Incident Dementia: The Honolulu-Asia Aging Study

The relationship between total cholesterol levels and dementia was studied by Stewart and colleagues (page 103) in Japanese-American men who were screened for dementia on 2 occasions between 1991 and 1996. They found that cholesterol levels in men with dementia, and in particular those with Alzheimer disease, had declined at least 15 years before the diagnosis and remained lower than those in men without dementia throughout that period. Thus from these data, a decline in serum total cholesterol levels may be associated with early stages in the development of dementia.

Medial Temporal Atrophy Predicts Progression of Mild Cognitive Impairment to Dementia

DeCarli and colleagues (page 108) studied the added value of qualitative measures of medial temporal atrophy to estimate the relative risk of progressing from mild cognitive impairment to dementia. In a thorough and well-designed study, they conclude that medial temporal atrophy scores greater than 2.0 were associated with a greater than 2-fold increased likelihood of progression to dementia.

Psychiatric Manifestations Among Preclinical Huntington Disease Mutation Carriers

Marshall et al (page 116) investigated for the presence of psychiatric features among preclinical mutation carriers for Huntington disease with absent or minimal motor signs of the disease. This study identified specific psychiatric symptom features that differentiated nonmutation carriers from individuals in the early preclinical stages of Huntington disease.

Call for Papers

The ARCHIVES launched a new ARCHIVES Express section in the September 2000 issue. This section will enable the editors to publish highly selected papers within approximately 2 months of acceptance. We will consider only the most significant research, the top 1% of accepted papers, on new important insights into the pathogenesis of disease, brain function, and therapy. We encourage authors to send their most exceptional clinical or basic research, designating in the cover letter a request for expedited ARCHIVES Express review. We look forward to publishing your important new research in this accelerated manner.

Roger N. Rosenberg, MD