CIRCUITS AND CIRCUIT DISORDERS

Circuits and Circuit Disorders
Approaches to Neuromodulation

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This theme issue on “Circuits and Circuit Disorders: Approaches to Neuromodulation” is the result of a symposium held at the annual meeting of the American Neurological Association in Chicago, Illinois, on September 26, 2015, and cosponsored by JAMA Neurology and the Annals of Neurology. The speakers were Mahlon DeLong, MD, Emory University (Keynote Speaker), Philip Starr, MD, University of California, San Francisco, Jonathan Mink, MD, PhD, University of Rochester, Helen Mayberg, MD, Emory University, and Bryan Roth, MD, PhD, University of North Carolina. The symposium also honored DeLong, who received the 2014 Lasker DeBakey Clinical Medical Research Award with Alim-Louis Benabid, MD, Université Joseph Fourier, for developing deep brain stimulation (DBS) of the subthalamic nucleus as effective therapy for patients with Parkinson disease. It is estimated that more than 100 000 Parkinson disease patients have been treated with DBS with reduction in bradykinesia and tremors and with overall improvement in motor function. Deep brain stimulation is credited as being the most important therapeutic advance for Parkinson disease since the introduction of L-dopa in the 1960s.

In this issue of JAMA Neurology, DeLong and Wichmann examine in their review1 the scientific foundations and rationale for the use of ablative and DBS for the treatment of neurologic and psychiatric diseases, using Parkinson disease as the primary example. They provide evidence in support of the view that signs and symptoms of movement disorders result from signature abnormalities in one of several parallel and largely segregated basal ganglia thalamocortical circuits forming the “motor circuit.” Recently, they are exploring the pedunculopontine nucleus to study gait disorders responding poorly to levodopa and conventional DBS targets.

Miocinovic and coauthors2 emphasize that isolated dystonia and Parkinson disease are disorders of the basal ganglia-thalamocortical network. They view isolated dystonia as associated with elevated cortical neuronal synchronization similar to Parkinson disease. Deep brain stimulation, they show, is effective to reduce cortical synchronization, thus providing a basis for their similar therapeutic responses to basal ganglia stimulation.

Choi and coauthors3 provide evidence that DBS of the subcallosal cingulate in an acute intraoperative setting alters behaviors. Structural connectivity showed that “best” responses had a pattern of connections to bilateral ventromedial frontal cortex and cingulate cortex. These are remarkable findings that support their concept of defining the “Depression Switch.”

English and Roth4 review the exciting, new, and rapidly expanding field of Designer Receptors Exclusively Activated by Designer Drugs (DREADS) and present evidence of its potential as a powerful tool to augment neuronal and glial signaling and activity with both basic and translational applications.

Jonathan Mink, a speaker in the symposium, anticipates making a contribution to another JAMA Neurology theme issue on this subject.

Circuits and circuit disorders are now shown to be the fundamental basis for several neurological and psychiatric diseases including Alzheimer disease, Parkinson disease, isolated dystonia, amyotrophic lateral sclerosis, frontotemporal lobar degenerations, depression, Tourette disease, and obsessive-compulsive disorder. Modulation of the circuit abnormalities in these disorders with DBS leading to effective therapies was emphasized in the symposium and in this collection of articles. They create scientific insights and optimism supporting the view that rapid advances are expected, providing clinical benefit to many patients.