372. ELECTROCONVULSIVE THERAPY: DOWAGER OR NEOPHYTE?

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Convulsive therapy is the treatment with longest history of continuous use in psychiatry, and its practitioners and researchers formed this society. Over this period, ECT can be credited with undoing the therapeutic nihilism that characterized biological psychiatry in the first half of the 20th century and setting the stage for the pharmacological revolution. However, until recent years, ECT administration centered only on the principle that the generalized seizure was necessary and sufficient for efficacy. This guiding belief has been proven wrong. Moreover, as a form of brain stimulation, the practice of ECT was out of keeping with knowledge about the neurophysiology of neuronal depolarization. It is now evident that generalized seizures can be reliably produced that lack therapeutic properties, that electrical dosage above threshold for seizure induction contributes to speed and likelihood of clinical response, and, perhaps most importantly, that seizure initiation in specific neural regions appears to be the key to efficacy. Consequently, there are opportunities to redefine ECT. New, physiologically-informed methods of electrical stimulation are being explored, as well as electrical and magnetic approaches to focal seizure induction. ECT remains our most effective antidepressant and antimanic treatment. These advances may extend its therapeutic potential.

373. DOUBLE-BLIND CONTROLLED TRIAL OF EMBRYONIC DOPAMINERGIC TISSUE TRANSPLANTS IN ADVANCED PARKINSON’S DISEASE

S. Fahn

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Forty patients with advanced Parkinson’s Disease (PD) were recruited into the study, half age <60 years (“younger”), and half >60 (“older”). Half in each group were randomly assigned to the placebo arm (“sham or imitation surgery”) and half to the implant arm (“real surgery”). To be eligible for enrollment, patients had to have PD for at least 7 years, continue to respond to levodopa therapy, have at least one of three intractable problems (intractable “offs” with an ADL >3; disabling dyskinesias; or “on” freezing). Exclusion criteria included active medical problems, dementia, depression, history of psychosis, and MRI evidence of cerebrovascular disease.

Clinical assessment of PD was carried out in Columbia’s NIH-supported General Clinical Research Center for two baseline (3 months apart) evaluation, and at 4-, 8-, and 12-months after surgery. After the 2nd baseline evaluation, the subject had a FDOPA PET scan at North Shore University Medical Center. Following this, the subjects were randomly assigned (50% in each group—younger and older) to imitation surgery (4 twist drill holes in forehead, no penetration of dura) or to actually receiving four cannula tracks of dopaminergic implants into the putamina (one human embryo each in each track). The implants were embryonic mesencephalic dopamine cells that obtained from elective abortions 7 to 8 weeks post conception. Maternal informed consent was obtained which complied with Federal and State laws governing fetal tissue use. The tissue remained in tissue culture prior to surgery to test dopaminergic viability (production of homovanillic acid), to test for the presence of viral and bacterial pathogens, and to determine blood type. The surgical approach used four needle passes through the forehead, with a superior and inferior pass into each putamen in each of the four tracks. No immunosuppression was given to any of the subjects.

In-patient assessments at each hospitalization evaluated 3-4 UPDRS “off” and 3-4 “on” states, timed motor responses to a predetermined dose of dopa, neuropsychometric assessment, motor control physiology during “off” and “on” states, speech and quality of life. Drug dosage was kept constant unless the clinical condition warranted a change. Adverse events and drug dosages were monitored throughout the study. All assessments were carried out by blinded raters. A repeat blinded FDOPA PET scan was carried out after the 12-month evaluation. Because the manuscript describing the results is under editorial review, I am not presenting the results in writing. These will be presented during the talk.

374. DEEP BRAIN STIMULATION: A NEW TREATMENT FOR PARKINSON’S DISEASE WITH MOOD ALTERING POTENTIAL

R. Kumar

Colorado Neurology Movement Disorders Center, Englewood, CO

The most anatomically discrete, and most invasive, method of stimulating deep brain structures is deep brain stimulation (DBS). In this technique, a thin electrode is inserted directly into the brain. Then different currents are applied at varying depths until the desired effects are found. Recently, high frequency (>80Hz) electrical stimulation of the subthalamic nucleus has been found effective in Parkinson’s Disease (PD) (Limousin et al. 1998). PD leads the neuropsychiatric field in terms of understanding the involved pathological circuitry. DBS has the advantage over brain surgery (pallidotomy) of being reversible, although there is morbidity and mortality associated with the implant procedure. Although this technique has not been used to treat major depression, mood effects of the stimulation have been reported. In one Parkinson patient who had never suffered from depression in her life, the testing of the stimulation caused the acute onset of tearfulness, sadness and despair. These symptoms remitted immediately when the surgeon moved the stimulator away from the substantia nigra, directly below the subthalamic nucleus. As the neuroanatomy of other neuropsychiatric disorders (mood, anxiety, psychosis) becomes better understood, it is conceivable that DBS may be helpful to otherwise treatment-resistant patients, although to date DBS has only been shown to cause depression symptoms, rather than to relieve them. This talk will review the latest knowledge of the mood altering potential of DBS.

PRESIDENTIAL INVITED LECTURE

Consciousness of Extrapersonal Space—A Model System for Understanding Neurocognitive Networks and Their Hemispheric Asymmetry

Saturday, May 13, 11:15 AM–12:00 PM
Location: Regency A & B
Speaker: Marcel Mesulam