Section Editor
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Emerging Subspecialties in Neurology: Deep brain stimulation and electrical neuro-network modulation

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Deep brain stimulation (DBS) is a surgical therapy that involves the delivery of an electrical current to one or more brain targets. This technology has been rapidly expanding to address movement, neuropsychiatric, and other disorders. The evolution of DBS has created a niche for neurologists, both in the operating room and in the clinic. Since DBS is not always deep, not always brain, and not always simply stimulation, a more accurate term for this field may be electrical neuro-network modulation (ENM). Fellowships will likely in future years evolve their scope to include other technologies, and other nervous system regions beyond typical DBS therapy.

HISTORY Electrical stimulation of the nervous system has been employed therapeutically over the past 2,000 years.[1] However, modern neurostimulation had its genesis in a parallel expansion of functional neurosurgery, which focused on the placement of ablative brain lesions (e.g., pallidotomy, thalamotomy, subthalamotomy, cingulotomy) to address disabling symptoms of movement and neuropsychiatric disorders.[2] The invention and improvement of the stereotactic head frame in 1947 by Spiegel et al.[1–3] allowed surgeons to target within a few millimeters of an intended region, and fueled an explosive increase in these types of neurosurgical procedures, which were commonly performed in the 1950s and 1960s. Later, advances in imaging and neurophysiology (microelectrode recording) further refined targeting and accuracy, and the field rapidly evolved to employ the use of DBS and other novel technologies. Indications for surgery were also influenced by advances in medication therapy, as well as limitations of pharmacotherapy, and changes in the philosophy of drug application.[4]

Chronic stimulation for movement disorders was not widely utilized until 1987, when Benabid et al.[5] published thalamic DBS effects on tremor. The therapy later gained Food and Drug Administration approval in 1997 for essential tremor, in 2002 for Parkinson disease, in 2003 for dystonia, and in 2009 for obsessive-compulsive disorder. DBS has also been applied therapeutically and experimentally for a variety of neurologic and neuropsychiatric disorders (Tourette syndrome, major depression, epilepsy, cluster headache, traumatic brain injury, amnestic cognitive impairment of Alzheimer disease, chronic pain, gait/freezing, hypertension, obesity, eating disorders, and others).[1,6] DBS is not always deep, since similar electrical currents can be applied superficially in motor cortex stimulation and also in other locations in the central, peripheral, autonomic, as well as nervous system coverings. The mechanism of action remains unknown, but involves inhibition and excitation, changes in firing rates and patterns, changes in neurochemistry, changes in blood flow, effects on both astrocytes and neurons, and possibly neuroplasticity.[4,7] Consideration of a neuroprotective mechanism is currently being explored.[8] The sum total of effects induced by DBS makes it likely that its mechanism includes the influence on a wide neural network that involves multiple basal ganglia/limbic motor and nonmotor pathways.

Thus, this therapeutic device has helped shape a new role for DBS neurologists in movement and neuropsychiatric disorders. Current and future generations of neurologists must be expert in diagnosis, medical management, intraoperative placement, DBS programming, and management of DBS hardware-related issues.

TECHNICAL ASPECTS The classical DBS device consists of a quadripolar electrode inserted into a brain target utilizing stereotactic and physiologic guidance. An internal pulse generator (IPG), also referred to as a neurostimulator, is placed under the clavicle (sometimes in the abdomen), and a connector wire is attached and run subcutaneously between the electrode and IPG.

The DBS neurologist and neurosurgeon together will choose a safe trajectory toward a target region. Indirect targeting is performed using standard atlas coordinates, and can be further refined by neurophysiology obtained from microelectrode recording. The microelectrode mapping procedure consists of passing a small, usually platinum iridium, glass-tipped (or a Tungsten) probe into the brain. By advancing the microelectrode

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1 millimeter at a time, the neurologist or physiologist can confirm the location of specific brain cells and regions by noting auditory and visual patterns heard through speakers and observed on an oscilloscope. The striatum, thalamus, globus pallidus externa, globus pallidus interna (GPi), subthalamic nucleus (STN), nucleus accumbens, PPN, and substantia nigra pars reticularis have signature firing patterns, recognized by a specialty-trained eye and ear. Upon reaching the intended target, the neurologist can proceed to map out a sensorimotor region. Passive (kinesigenic) or active movement of a contralateral (and sometimes ipsilateral) limb joint can inform hand, arm, and leg representations within a target structure, when a corresponding change in the firing pattern of a cell or group of cells is observed. These changes can be utilized for identifying specific brain targets such as the STN and GPi. In the thalamus, active and passive movement, deep tactile, and light tactile maneuvers can aid in mapping the divisions between thalamic subnuclei. Several microelectrode passes through an individual target site can create a map to select the best location for a DBS lead. This technique can, in expert hands, improve target accuracy, and overcome potential errors in DBS lead location. Microelectrode recording can also aid if there has been a brain shift. Stimulation can be applied through the microelectrode to identify the proximity to the internal capsule (observing contralateral limb contraction), sensory pathways (paresthesias), or other regions. Similarly, light stimulation can be applied to determine proximity to the optic pathway. Identification of these regions is important to avoid chronic adverse side effects of DBS when a final lead location is selected. Once the recording is complete, the DBS lead is placed and macrostimulation can be applied. Some recent DBS targets (e.g., nucleus accumbens region) have not required microelectrode mapping, though in some cases firing rates and patterns can be decoded. In most cases, patients are awake for the surgery and off their medications, in order to preserve firing rates and patterns, and also to preserve clinical signs which may be masked by anesthesia or symptom-suppressing medications.

One major role for the DBS-trained neurologist is the preoperative evaluation. Potential DBS candidates are carefully selected following multidisciplinary and specialized evaluations to determine risk-benefit ratios. DBS candidates must be deemed resistant to conventional medication trials and, in some cases, behavioral-based therapy. Patient expectations are carefully weighed in each case, and a determination is rendered as to whether DBS will have the potential to impact one or more disabling symptoms for an individual disease sufferer. This evaluation includes optimization of medications and behavioral treatments, as well as recording standard validated symptom rating scales. Current best practice for a DBS evaluation is evaluation by a multidisciplinary team, headed by a DBS-trained neurologist and neurosurgeon with expertise in stereotactic and functional neurosurgery, and including a neuropsychologist, psychiatrist, physical therapist, occupational therapist, speech therapist, and in some cases a social worker or a financial counselor. Each specialty will individually evaluate potential DBS candidates, and meet to discuss important questions (patient expectations, symptoms targets, risk/benefit ratio, unilateral vs bilateral, staged vs single operation, rescue leads for DBS failures, or hardware issues). Once a board decision has been rendered, the patient is usually contacted to discuss the details and, if appropriate, scheduled for a surgery. A clear understanding of the time commitment required from the patient, family, and medical team prior to surgery is paramount, as there will usually be multiple visits over the next 6–12 months. Additionally, for many patients there will be a lifetime commitment to device management.

DBS neurologists play an active role postoperatively by confirming the correct lead location, usually through the interpretation of imaging. They also record thresholds for symptomatic benefit and side effects at each contact point on each DBS lead in order to confirm imaging findings. The DBS neurologist must be skilled at the identification of the best setting parameters (voltage, current, pulse width, frequency, scheduled stimulation, chronic stimulation). The patient is typically followed monthly for the first 6 to 12 months, and then periodically thereafter, to check the device. Important aspects for postoperative DBS care include medication management, preemptive plans for end of battery life, troubleshooting device complications, and counseling/treatment for disease progression.

TRAINING OPPORTUNITIES Neurology fellowships offering formal DBS (and ENM) training began to emerge approximately a decade ago, typically as an extension of a movement disorders fellowship. Prior to formal fellowships, neurologists learned DBS as apprentices, particularly from the early pioneers of basal ganglia physiology (e.g., Delong, Vitek), and through clinical experience (e.g., Benabid et al.[5]).[2,9] More formal fellowship experiences have been evolving, mainly as part of movement disorders training programs. The most common training scenario is for established movement disorders fellowships to offer exposure to DBS programming and management, and in some cases intraoperative experience. Both movement disorders fellowships and DBS fellowships are non–Accreditation Council for Graduate Medical Education accredited. A handful of programs offer either a dedicated year or two of DBS fellowship (sometimes following a general year of movement disorders fellowship) or alternatively an integrated experience. Components of a comprehensive DBS (and ENM) fellowship experience would typically include the following:

- Experience in evaluation of potential DBS candidates for typical indications (Parkinson disease, essential tremor, dystonia), as well as other more novel indications
- Participation in the multidisciplinary/interdisciplinary selection committee meeting/DBS Board (direct interactions with neurosurgery, neuropsychology, psychiatry, physical/occupational/speech therapy)
- Intraoperative training for direct and indirect targeting and for DBS and microelectrode recording/macrostimulation (at least weekly)
- Evaluation of postoperative imaging (and measurement of lead locations)
- Management of initial and subsequent DBS programming for multiple targets, and also medication adjustments for DBS patients
- Experience in evaluation of patients with failed or suboptimal DBS outcomes

One-year DBS-dedicated fellowships are available at only a few expert institutions. Occasionally these programs incorporate ENM procedures (motor cortex stimulation, spinal stimulation, central, peripheral, and autonomic stimulation), or include implantation and management of pump technology (Duodopa, baclofen, apomorphine, pain pumps). DBS subspecialty training is not limited to movement disorder neurologists, and has been utilized by neurosurgeons, psychiatrists, physiatrists, and other neurology subspecialists (e.g., neuromuscular specialists, epileptologists, behavioral neurologists).

The American Academy of Neurology (AAN) Web site has a comprehensive list of movement disorders fellowships, and this Web site includes an option to search for DBS-specific fellowships. Continuing Medical Education–accredited courses are offered at the AAN, the Movement Disorders Society, and the American Society for Stereotactic and Functional Neurosurgery, among others. There are several potential sponsors for fellowships (e.g., institutions, foundations, and industry), though there has been an overall concern that these critical experiences are underfunded.

The increasing complexity of screening and management, along with the expanding number of DBS target sites and indications, have led to a demand for fellowship-trained DBS specialists. DBS management is both an art and science, requiring experience and patience. The evolutions in technology and hardware, and improvements in safety, have solidified an important role for DBS neurologists. There are more than 80,000 neurostimulators implanted worldwide to date, and this number will continue to increase.[10] Thus, we expect the demand for expertise to remain high for the foreseeable future.

RESEARCH DBS, and more broadly ENM, will offer neurologists exciting and novel research opportunities. The mechanisms of DBS and ENM are becoming clearer, but remain to be completely defined. Understanding the effects of electrical stimulation on motor, limbic, and cognitive circuitries will be important for developing improved technologies. As the field evolves, there will likely be a shift from disease-specific therapy to symptom-specific therapy (i.e., a more personalized medicine approach). For example, a future patient presenting for DBS will seek treatment for a specific disabling symptom or set of symptoms (e.g., tremor), rather than simply because of a specific disease (e.g., Parkinson disease). DBS devices will continue to get smaller and more sophisticated, and will likely add remote "telecapabilities," making programming more available to those living in remote regions. In the future, scheduled and responsive technologies will replace basic chronic stimulation, especially as signature brain patterns emerge for particular symptoms or behaviors. Many disorders and symptoms lack prospective trials, and future DBS trials will be required to have sham stimulation arms. DBS and ENM will feed research in epidemiology, public health, and health outcomes. Additionally, the ability to turn the devices on and off will facilitate important research into disease mechanisms.

DISCUSSION DBS/ENM has become an important subspecialty within movement and neuropsychiatric disorders. The specialty has evolved to include more than just basal ganglia and movement disorders. Most current DBS fellowships are embedded into movement disorders programs, but a few expert institutions offer more dedicated experiences, especially in the second year of fellowship training. The worldwide expansion of device implants, and the explosion in new technologies, will likely solidify DBS and ENM fellowships as important training opportunities that will support critical public health and research needs.

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