Stereotactic Neurosurgery: What's Turning People On?

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In 2006, the world of stereotactic and functional neurosurgery continued to touch many aspects of neurosurgery. The field included the neurosurgery of movement disorders, epilepsy, pain, brain tumors and vascular malformations, behavioral disorders, the study and incorporation of innovative image-guided technology into practice, robotics, radiosurgery, and restorative approaches. For this report, I was asked to select three topics of current interest in this field. This year, clinical and basic research in the field of stereotactic and functional neurosurgery has embraced a wide variety of topics. Some of these have included new radiosurgery technologies, guidelines for deep brain stimulation, the return of psychosurgery, neuromodulation for pain, radiosurgery for functional disorders, brain-machine interface research, and cortical stimulation. I have selected three separated topics to address.

BEHAVIORAL NEUROSURGERY

In years past, neurosurgery for behavioral disorders has been referred to in different ways. Such titles have included "psychosurgery," "limbic system surgery," "behavioral neurosurgery," "neuromodulation," "behavioral neuromodulation," and "surgery for neuropsychiatric illness." Perhaps the latter of these terms best describe the field. Procedures that provide therapy for patients with neuropsychiatric illnesses have a long history.

An electrical stimulation device was invented by Dr. John Butler of New York with a description in the magazine, *Harpers* (1881). It was said to be "especially salubrious in cases of rheumatism, nervous exhaustion, neuralgia, and paralysis." In an era before medical therapy, before imaging, and before stereotactic frame-based technology, there were poor options for those with severe psychiatric disease. These included insulin coma, simple restraints, and seizure induction. In the 1930s and 1940s, the first era of surgery for neuropsychiatric illness began. Following the pioneering work of Lima and Moniz, and the later wider introduction of surgery by Walter Freeman and James Watts in the United States, *Time* magazine in the 1940s referred to this time as "the era of mass lobotomies." The first prefrontal lobotomy was performed in the United States September 14, 1936. Egas Moniz later received the Nobel Prize for his "conception and execution of a valid operation for a mental disorder." In the November 30, 1942, issue of *Time* magazine, a photograph of James Watts and Walter Freeman in the operating room was shown. At that time, a simplistic description of the effects of lobotomy noted that "there was nothing worse than an evil frontal lobe." The effects of the frontal lobe on more posterior brain targets was such that the brain itself was not liberated to function normally and appropriately unless the evil frontal lobe was severed by disconnection. The first and second volume of *Psychosurgery*, written by Freeman and Watts, described, mainly in anecdotal fashion, the indications and outcomes of the use of surgical procedures for different neuropsychiatric illnesses. For example, the "precision method of prefontal lobotomy," a freehand technique, began at the coronal suture with an understanding of the angles and directions down toward the sphenoid ridge to allow a proper disconnection of the frontal lobe. Often, globules of lipiodol were placed along the tract and were sometimes seen in the frontal horn of the lateral ventricle. If one surgery was not successful, it was often repeated. Surgeries for schizophrenia, major affective disorder, other anxiety neuroses, and behavioral disorders were common. By the mid-1950s and into the 1960s, an era of medical therapy, behavioral therapy, new regulations, and ethics committees led to an end for the practice of surgery for neuropsychiatric illness in its first iteration.[2,3]

MODERN BEHAVIORAL NEUROSURGERY

Now, in an era of stereotactic frames, functional imaging, medication failures, study of more focal rather than broad effects via stimulation or lesioning, validated outcome scales, new ethics regulations, institutional review board reviews, informed consent, and patient requests for procedures has allowed exciting translational research in a number of areas of neuropsychiatric illness. To date, these have focused on obsessive-compulsive disorder, major depression, and Tourette's syndrome. Other anxiety neuroses have also been studied. Through deep brain stimulation of the anterior internal capsule, cingulate gyrus, cingulotomy or capsulotomy, cortical stimulation or vagal nerve stimulation, research studies into these various illnesses have been conducted.[14]

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The problem of major depression is one that affects people all over the world. The World Health Organization notes that more than 120 million people worldwide suffer from depression, that there are 800,000 suicides per year, and that depression affects one in four families. It is important that neurosurgeons learn the diagnostic criteria for major depression, including the need for five or more symptoms for longer than a 2-week interval. Today, novel approaches include different medical therapies, drug delivery, nerve stimulation, transcutaneous magnet stimulation, vagal nerve stimulation, deep brain stimulation, and cortical stimulation. Whether such device-based approaches will act as a "switch" to turn depression on or off remains to be seen, although results from early studies show interesting results in individual patients. The September 10, 2006, issue of *New York Times* (business section) contained a lead article entitled *Battle Lines in Treating Depression: A Controversial Implant Has a Company on Edge*. This article describes the research and eventual approval by the United States Food and Drug Administration of vagal nerve stimulation. It seems that the enthusiasm over vagal nerve stimulation in the treatment of depression has not been overwhelming. Part of the issue may be the lack of a known mechanism of action. What is indeed the target for depression? Does stimulation work on cells or nerve fiber tracts? Does stimulation work through low- or high-frequency approaches? What volume of tissue requires the effect? What impacts better on that volume: electric current, radiation, or some other approach? Pioneering neuroimaging studies performed by Mayberg et al.,[6] in their study of the positron image tomography response of the cingulate gyrus region 25 in patients with major depression were provocative. Such research led to the clinical study of deep brain stimulation for that brain target, and four of the six first patients had improvement of depression. Most of these noted a sudden intense calm in the operating room and noted increased motor speed, improved color perception, and visual clarity. Five of these six patients have failed previous electroconvulsive therapy and the patients were of a mean age of 46 years. Subgenual cingulate cortex (Brodmann area 25) was overactive on positron emission tomographic scans in these patients. It is interesting that a patient with major depression who improves with drug therapy, electroconvulsive therapy, or cingulotomy may have decreased activity of Brodmann area 25. Dr. Andres Lozano (personal communication) reported that 18 patients to date had had surgery, with a clinical response in approximately two-thirds, with stimulation parameters similar to those used in Parkinson's disease.

ACOUSTIC NEUROMA MANAGEMENT: A MICROSURGICAL OR STEREOTACTIC PROBLEM?

Patients with acoustic neuromas (vestibular schwannomas) can be managed using a number of different strategies. These could include observation with serial imaging studies to identify the growth rate of the tumor before choosing a treatment course, microsurgical resection of the tumor performed via one of many approaches, stereotactic radiosurgery, or fractionated radiation therapy. During the past 20 years, there has been a dramatic increase in the numbers of patients who choose radiosurgery for care of their tumor. This is particularly the case for patients with small- or medium-sized tumors. Patients with large tumors continue to require surgical resection, but may be appropriate for radiosurgery if there is a residual tumor or a later recurrence.

During this time period, there have been questions regarding the short- and long-term outcome after radiosurgery in comparison with surgical resection. However, at present, we have four matched cohort (nonrandomized) studies that compare outcomes with information on imaging results, clinical outcomes, and quality of life[7, 11–13].

The first study from the University of Pittsburgh in 1995 compared outcomes in tumors smaller than 2.5 cm in extracanalicular diameter and within 3 years of initial treatment.[12] All outcomes were either better in the radiosurgical group or equal. The tumor control rates were the same. This paper was controversial in that it was the first real comparison of these two different approaches.

The next report, published in 2002, from Marseille, France, was a noncontemporaneous comparison of functional outcomes after gamma knife radiosurgery or microsurgical resection. The time frame for management was different in the two groups (the microsurgical group was first, the radiosurgical group was second).[13] Similar to the Pittsburgh study, clinical outcomes were either better after radiosurgery or the same. For example, the outcomes for the symptoms of tinnitus and imbalance were no different between both groups. The morbidity after radiosurgery was less. The quality of life measures were better after radiosurgery.[13]

A third study from Bergen, Norway, published in 2005,[7] compared clinical results and quality of life after gamma knife radiosurgery or surgical resection in 86 resected versus 103 radiosurgery patients at a mean follow-up of 6 years. Again, posttreatment facial nerve function, hearing, complication rates, and quality of life were better after radiosurgery.

This year, the most recent report was published from the Mayo Clinic.[11] Pollock et al.[11] compared prospectively collected outcomes in a cohort of patients after gamma knife radiosurgery or resection. Thirty-six patients had resections and 46 patients underwent radiosurgery. The groups were well matched, and the mean follow-up was 42 months. Normal facial function and preservation of useful hearing was better in the radiosurgery patients, and those undergoing a resection had a significant decline in different elements of the health-status question at 3 months after management. Patients in the surgical resection group continued to have a significant decline in physical functioning and bodily pain at 1 year. There was no difference in tumor control between the two groups.

These four studies show that early outcomes were better for vestibular schwannoma patients after radiosurgery compared with surgical resection (Level II evidence). Thus, for patients with small or medium-sized tumors, the present evidence from four similar studies, all with their limitations, argues for the use of radiosurgery in this setting. All four reports studied only the use of gamma knife technique.

FUNCTIONAL RADIOSURGERY

As the number of patients undergoing functional procedures, particularly deep brain stimulation, increases, those who are elderly, medically infirm, or who choose not to have implanted hardware have sought alternate approaches. At present, the high resolution provided by magnetic resonance imaging has allowed radiosurgery to become again a viable alternative to some patients. Thus, could there be a return to lesioning in selected patients?

At present, patients with medically refractory, essential tremor can undergo placement of a thalamic stimulator to reduce the activity of kinesthetic tremor cells in an attempt to reduce their disability.[4] However, gamma knife radiosurgery using a single 4-mm collimator and a maximum dose of 140 to 150 Gy ablates a volume that roughly matches the stimulation volume, and tremor relief can be achieved less invasively. Although radiosurgery does not use physiological localization and relies on anatomic localization via imaging, the necrotic focus of the radiosurgical volume is surrounded by a peripheral zone of tissue change.[9] That also can impact tremor control. Thus, radiosurgery may be more "forgiving" than radiofrequency lesioning, and this peripheral effect caused by the radiation fall-off may mimic the peripheral effects of stimulation. Depending on dose and patient sensitivity, a larger than expected lesion can be created, leading to new neurological deficits.[1,10] Typically, such effects lessen with time.

Similarly, patients with tremor from other causes, such as multiple sclerosis, may benefit from radiosurgery.[5,8] Most patients undergoing surgery for Parkinson's disease receive subthalamic nucleus or globus pallidus stimulation, in which radiosurgery has not been well evaluated. Those elderly patients with disabling tremor related to Parkinson's disease may be suitable candidates for a gamma knife thalamotomy.

Although functional radiosurgery has been performed for more than four decades and was the reason for the initial creation of the radiosurgical technique, there has been a renewed interest in the merger of stereotactic radiosurgery and functional neurosurgery. There is a current interest in radiosurgical lesioning of the anterior internal capsule (anterior capsulotomy) in the patients with medically refractory obsessive-compulsive disorder. A series of patients from Brown University and the University of Pittsburgh have been presented at national meetings. The surgical capsulotomy is performed only after comprehensive psychiatric evaluation and management leading to a diagnosis of severe obsessive-compulsive disorder, and after failure of nonsurgical approaches.

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