The Neurosurgical Treatment of Movement Disorders

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ABSTRACT

The management of movement disorders has been historically treated with both surgical and medical modalities. While L-Dopa has been the medical mainstay for Parkinson’s Disease, surgical techniques have evolved over the past century to the current state of stereotactic procedures in focal parts of the central nervous system. Presented here is a review of the history of this evolution.

Over the past century, the approach of the medical institution to the treatment of movement disorders has evolved from neurosurgery to medical therapy and back to a combination of both, with significant improvement in each domain. Specifically, the current use of neurosurgery for the treatment of movement disorders has been greatly enhanced by the precision of stereotactic procedures. However, before the advent of stereotactic technology, neurosurgery for movement disorders progressed through various stages of experimentation with different methods and sites. An overview of that evolution is presented here.

The earliest attempts to operate on the central nervous system (CNS) were aimed at the pyramidal system on the belief that the neural mechanisms responsible for normal movement must be responsible for the abnormal movements characterized by chorea, athetosis, hemiballismus, and parkinsonian tremor. Since then, the neurosurgical treatment of movement disorders within the central CNS has developed in both rationale and location, ranging from targeting the entire motor system to the current use of precise stereotactic procedures aimed at focal CNS components, particularly the basal ganglia, thalamus, and subthalamic nucleus (STN).

The primary motor cortex, located in the precentral gyrus, was the first target of a neurosurgical approach to movement disorders. In 1890, Horsley reported that he had excised the corresponding portion of motor cortex in an attempt to treat athetosis, resulting in cessation of abnormal movement for two weeks (Horsley, 1890). In 1910, he also reported excising Brodmann’s Area 6 of the right premotor cortex with relief of symptoms for 14 months. However, the patient suffered a significant loss of sensory and motor function, only regaining partial voluntary movement after three weeks (Horsley, 1909). Similar results were achieved over the next few years with varying side effects (Gabriel and Nashold, 1998).

Over the next 20 years, several other CNS and extra-CNS sites were targeted to relieve movement disorders, frequently with irreproducible results and limited publication. These included posterior rhizotomies (ablation of the spinal or cranial nerve root), sympathetic ramisection and/or sympathetic ganglionectomy, dorsal cordotomy, thyroidectomy, and cerebellar dentatectomy (Gabriel and Nashold, 1998). Some of these sites would be revisited by neurosurgeons years later, but for the most part the results were not outstanding. Despite the possible side effects of transient or permanent hemiparesis and/or hemianesthesia, the excision of the corresponding contralateral motor or premotor cortex was the standard approach for the next 20 years, with variations on the method of cortical ablation, including the induction of necrosis with ethanol injection (Nafzigger, 1937). However, the unacceptable side effects of cortical procedures, including paresis, aphasia, and seizures, prompted surgeons to explore distal sites in the pyramidal system such as the spinal cord, basal ganglia, and brainstem.

In 1931, Putnam attempted to intervene at the spinal cord level. He first performed an anterolateral cordotomy for the treatment of athetosis, excising the anterior section of the cervical spinal cord medial to the dentate ligament. All five patients experienced diminished athetosis with the only adverse events being a mild motor deficit and hemianalgiesia (Putnam, 1933). In a larger sample, 17 of 23 patients experienced improvement of athetosis for up to 5 years, but adverse effects included transient flaccid paralysis, transient incontinence, hemianesthesia, decreased male sexual function, and respiratory complications that led to death in three patients (Putnam, 1938, 1940).

Parkinsonian tremor, however, was not relieved by anterolateral cordotomy. To focus on this problem, Putnam shifted his method to a lateral pyramidotomy; 20 of 22 patients reported initial relief and one-third reported long-term relief (Putnam, 1940, 1950). This approach was extended by Ebin in 1949 to a combined lateral and ventral pyramidotomy; all nine patients operated on experienced a reduction of tremor at rest for up to 20 months, with consequential motor strength reduction, loss of contralateral pain and temperature sensation, and transient urinary dysfunction.
(Ebin, 1949). Ventrolateral cordotomy was also used in the 1950’s to treat ipsilateral hemiballismus with good results. (Brown and Walsh, 1954; Strain and Perlmutter, 1957).

In 1940, Meyers reported first attempting to operate on the basal ganglia for the treatment of postencephalitic tremor (Meyers, 1940). This may have been based on the fortuitous observation made by Browder, who, while performing a frontal lobectomy, excised part of the anterior caudate nucleus and relieved parkinsonian tremor, albeit accidentally (King, 1940). In 1951, Meyers reported on ten years of experience operating on the basal ganglia for various movement disorders (Meyers, 1951). His approaches included excision of the anterior two-thirds of the head of the caudate nucleus or the entire nucleus, various parts of the striatum, sections of the anterior limb of the internal capsule, and ansotomy (section of the ansa lenticularis), either at the globus pallidus or near the foramen of Monro (Meyers, 1942, 1951, 1955, 1958). Overall, he found that excision of the caudate along with part of the anterior limb of the internal capsule or ansotomy relieved tremor quite effectively and reduced rigidity, all without paresis or spasticity. However, his approach did not alleviate chorea or athetosis and retained a high mortality rate.

Similar approaches were attempted, including excision of the dorsal head of the caudate nucleus and various lengths of the anterior limb of the internal capsule. Importantly, attempts were made to decrease the mortality of basal ganglia procedures by introducing new methods of interrupting the basal ganglia circuitry other than with excision. One such method was the introduction of an electrode into the brain with coagulation of either the basal ganglia nuclei directly or the ansa lenticularis (Spiegel and Wycis, 1950) as well as with the injection of procaine into the globus pallidus (Cooper, 1954a).

In 1948, Walker began attempting to treat movement disorders with a cerebral pedunculotomy. According to the initial report, he performed a left cerebral pedunculotomy on a 49-year-old female experiencing four weeks of hemiballismus. After a brief period of flaccidity in the right arm, she reported no severe involuntary movements throughout her first post-operative year (Walker, 1949).

Next, Walker reported performing this procedure for the treatment of parkinsonian tremor as well, with two of four patients being completely relieved of tremor but hemiparetic, and the other two patients partially relieved of tremor but hemiparetic; within three years, all four patients had some form of dyskinesia (Walker, 1952, 1955). Subsequently, few other procedures were attempted or successful at the brainstem level. In 1952, a stroke of luck enabled the next step in the development of neurosurgical treatment of movement disorders. During a cerebral pedunculotomy for tremor and rigidity, Cooper accidentally cut the anterior choroidal artery. The vessel was clipped and the procedure stopped, but post-operatively little tremor or rigidity persisted, without paresis (Cooper, 1954b). Cooper also reported several more cases of the relief of tremor by ligation of the anterior choroidal artery without hemiplegia or hemianesthesia (Cooper, 1953). Over the next several years he continued to work on alleviating movement disorders by ligating the anterior choroidal artery, thus infarcting the globus pallidus, ansa lenticularis, and ventrolateral nucleus of the thalamus. In a population of 55 patients, Cooper reported relief of tremor in 65% and reduction of rigidity in 75%, with only 4 cases of hemiparesis (which resolved in two weeks) and three cases of permanent hemiplegia (Cooper, 1956). However, results were unpredictable and mortality remained high, most probably due to the variable vascular territory of the anterior choroidal artery.

The major obstacle was the high level of morbidity associated with open craniotomy procedures. In 1947, Spiegel and Wycis designed and used a stereoecephalotome to operate on humans, based on experiments with animals (Spiegel et al., 1947). The following year, they performed the first stereotactic pallidotomy (via ethanol injection) and thalamotomy (via electrolysis of bilateral dorsomedial thalami) on a 53-year-old patient with Huntington’s Disease, which resulted in the relief of chorea and no adverse effects. However, involuntary movement returned 18 months later (Spiegel and Wycis, 1950). Similar attempts substituting ethanol injections with electrolysis and attempts at other regions were also problematic.

The same approach was used to treat parkinsonian tremor by performing stereotactic mesencephalotomy (ablation of afferent fibers in the midbrain tegmen tum), thalamotomy, and ansotomy. The first two approaches were not effective, but ansotomy successfully relieved tremor for several months in six patients with no motor or sensory deficits (Wycis and Spiegel, 1952; Spiegel and Wycis, 1954). Spiegel and Wycis published the text Stereoecephalotomy based on their experiences with stereotactic procedures, including pallido-ansotomy to treat tremor, pallidotomy to treat chorea, athetosis, and hemiballismus, and lesioning the substantia nigra to treat hemiballismus, all with much success (Spiegel and Wycis, 1962). Based on the observation that successful cerebellar dentateotomy resulted in hypotonia, procedures were also attempted on the cerebellum, with only moderate success (Heimburger, 1967). Many variations of stereotactic technology and procedures followed, but none would be as important in the next stage in the history of movement disorders as the discovery of the role of dopamine in movement disorders.
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By 1960, the role of dopamine as a CNS neurotransmitter was known, and shortly thereafter its deficiency was implicated in Parkinson’s Disease (PD) (Roe, 1997). The subsequent use of L-Dopa, the physiologic precursor of dopamine, revolutionized the treatment of PD and nearly eradicated the use of neurosurgery. Its efficacy was far superior to surgical approaches, and the associated morbidity and mortality was significantly reduced. As experience with L-Dopa accumulated, however, it became apparent that there were serious limitations to its effectiveness in the treatment of PD. It was discovered that after five to ten years of L-Dopa therapy, efficacy declined and it became difficult to balance accumulating adverse effects of the medication with symptom control.

Meanwhile, advances in technology including computerized tomography (CT), magnetic resonance imaging (MRI), and intra-operative imaging allowed for more precise neurosurgical procedures with markedly less morbidity. This led to a renaissance of interest in the surgical treatment of movement disorders.

In addition to the precision brought about by stereotactic technology, new methods of inducing lesions have also improved modern neurosurgery for movement disorders. Two techniques currently predominate: neuroablation and deep brain stimulation (DBS). Ablation consists of creating a lesion by heating the tip of an electrode embedded in neural tissue, thus inducing necrosis (Tomlinson et al., 1991; Eskandar et al., 2000). DBS entails the implantation of an electrode which generates a high-frequency stimulation, accomplishing the same effect as an ablative lesion without actually inducing necrosis (Starr, et al., 1998). In addition, this method may result in the inhibition of surrounding neurons, perhaps due to GABA release or the creation of a depolarization blockade, although the mechanism is still unclear (Benazzouz et al., 1995; Dostrovsky et al., 2000; Beurrier et al., 2001).

The current understanding of the basal ganglia circuitry and its connections to the thalamus and cerebral cortex indicate that the globus pallidus interna and STN are overactive in PD (Albin et al., 1989). Accordingly, several procedures are currently performed for the relief of movement disorders: pallidotomy, pallidal stimulation, thalamotomy, thalamic stimulation (specifically the ventralis intermedius nucleus), and STN stimulation. Currently, DBS is approved by the Food and Drug Administration only for thalamic and STN stimulation.

Unilateral pallidotomy has been performed for the treatment of PD with moderate results: about 45% of patients reported improvement in resting tremor, rigidity, and bradykinesia; 80-90% reported reduction in contralateral dyskinesias, with most patients retaining at least some benefit at 2 years post-operatively. Additionally, few complications have been reported (Fazzini et al., 1997; Fine et al., 2000; Lai et al., 2000). The use of bilateral pallidotomy, on the other hand, is limited by side effects including dysphagia and dysarthria.

Thalamotomy, or thalamic DBS, has been performed predominantly for the treatment of tremor in PD, essential tremor, and multiple sclerosis. Both ablation and DBS abolished tremor in 80-95% of patients at the first year post-operatively (Limousin et al., 1999), although subsequent reports indicated that the relief of symptoms may actually diminish over time. Although the outcome of both thalamic ablation and DBS were similar, it seems that patients with implanted thalamic stimulators reported having a better functional outcome at one year post-operatively (Schurman et al., 2000).

Most institutions were reluctant to lesion the STN for fear of causing hemiballismus, although several centers have successfully studied this approach (Guridia and Obeso, 2001). However, since the development of DBS, in which the procedure is reversible, the amplitude of stimulation is adjustable, as opposed to an all-or-none necrosis, and the concern about the adverse side effect of hemiballismus is avoidable (Kumar et al., 1998; Limousin et al., 1998; Burchiel et al., 1999; Moro et al., 1999; Hueto et al., 2000; Rodriguez-Oroz et al., 2000; Guridi and Obeso, 2001; The Deep-Brain Stimulation for Parkinson’s Disease Study Group, 2001; Volkmann et al., 2001). Accordingly, the STN has recently become the target for the surgical treatment of movement disorders. This has become a common procedure and numerous patient series have demonstrated excellent results in patients refractory to medical and prior surgical therapies (Mogilner et al., 2002; Sterio et al., 2002).

Regardless of site, the surgery is planned using pre-operative MRI, CT, and angiography as well as intra-operative recording and stimulating electrodes to delineate precise margins (Lozano et al., 1996; Hutchison et al., 1998; Starr et al., 1999). Refinement of visualization displays (e.g. plasma high-definition monitors) and head-mounted displays have also evolved, with state-of-the-art operating microscope and helmet systems now standard in many centers (Liu and Apuzzo, 2003).

Current research investigates the possibility of tissue transplantation as the neuronal populations involved in movement disorders have been identified and their relationships with other structures have been described. Source tissue used in experiments has included adrenal medulla, porcine xenografts, and embryonic dopamine neurons (Madrazo et al., 1987; Jankovic et al., 1989; Schumacher et al., 2000; Villa et al., 2000; Freed et al., 2001). This area of investigation, however,
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has lost favor with most neurosurgeons because of poor preliminary experimental findings, the increasing clinical success of DBS, and the ethical and practical difficulties in procuring fetal tissues.

The current state of neurosurgical approaches to movement disorders is a far cry from where it began over a century ago. The improvements in technology, rationale, and experimental models have contributed a great deal to this development, and imply that there is nowhere to go but forward. It will certainly be stimulating to track this continuous evolution in a truly fascinating field. It will also be interesting to see how current research in plasticity, both physiologic and in response to pathological insults, will affect this field.

REFERENCES


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