1. INTRODUCTION

An appreciation of the important modulatory role played by the subthalamic nucleus (STN) in regulating basal ganglia projections to the motor thalamus and brainstem, has led to interest in the STN as a target for the treatment of Parkinson's disease (PD). In 1990, DeLong and colleagues first demonstrated the reversal of motor symptoms by lesioning the STN in monkeys with MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-induced parkinsonism (1). Concern about the possibility of irreversible side effects from the generation of bilateral STN lesions, and experience with the safety (2) but limited efficacy of thalamic stimulation, prompted Benabid and colleagues to attempt STN deep brain stimulation (DBS) (3). Recent reports from several centers demonstrating the safety and efficacy of chronic high-frequency STN DBS have generated interest in the STN as a target of choice in the surgical treatment of PD.

Despite its clinical success, the mechanism of action of DBS for the treatment of movement disorders remains unknown. The prevailing theory proposes that DBS causes a blockade of neuronal firing, thereby mimicking the effects of a lesion. The virtue of DBS as opposed to the generation of a lesion is that DBS is reversible and adjustable, allowing for maximal efficacy while minimizing adverse effects.

2. ANATOMY AND PHYSIOLOGY OF THE HUMAN STN

The human STN is composed of approx 300,000 neurons (4) and is situated beneath the thalamus, above the substantia nigra, posterior and medial to the pallidum and internal capsule, and anterior to the medial lemniscus. The human STN measures approx 7 mm in medial-lateral, 9 mm in anterior-posterior, and 5 mm in dorsal-ventral dimension (5,6). The STN is ellipsoid in shape, with the rostral end lying superior to the caudal end of the nucleus in the sagittal plain (5,6).

The STN sends projections to both the globus pallidus internus (GPi) and the substantia nigra pars reticulata (SNr) (7), the two output nuclei of the human basal ganglia, as well as to the globus pallidus externa (GPe). Projections from the STN are excitatory and glutamate-secreting (8), whereas the output of GPi and SNr to motor thalamus, the pedunculopontine nucleus (PPN) and the mesencephalic area (MEA) of the brainstem is inhibitory and GABA-secreting. The PPN and MEA are believed to play a role in the control of posture and locomotion. The GPe receives inhibitory projections from the striatum via the direct pathway. The GPe sends inhibitory projections to the STN by means of the indirect pathway.
The substantia nigra pars compacta (SNc) sends dopaminergic projections to the striatum. Striatal output neurons send inhibitory projections to both the GPi and SNr (direct pathway), and to the GPe (indirect pathway). Dopamine released by the nigrostriatal pathway is believed to have opposite effects on the neurons contained within the two different striato-pallidal projections; dopamine inhibits striatal neurons that project to the GPe (largely containing D2 receptors), and excites neurons projecting to the GPi (D1 predominant). In PD, the progressive loss of dopaminergic neurons in the SNc leads to increased activity of the GPi and SNr, secondary to a loss of inhibition from the direct pathway and increased excitation from the indirect pathway (9). The latter derives from hyperactivity of the STN (10,11). This hyperactivity of the GPi/SNr causes an increase in inhibition of thalamocortical activity, and the cardinal symptoms of Parkinson’s disease—bradykinesia/akinesia, rigidity, and tremor—become manifest (9). The rationale for surgical targeting of the STN is to block the increased basal ganglia output that leads to inhibition of thalamocortical activity and thereby alleviate the motor signs of Parkinson’s disease.

3. PATIENT SELECTION

First, patients being considered for surgery for PD must meet the clinical criteria for this diagnosis. The cardinal signs of PD include tremor, rigidity, and bradykinesia/akinesia. Generally, patients with a diagnosis of a parkinson-plus syndrome or atypical parkinsonism (e.g., multiple system atrophy, progressive supranuclear palsy) are excluded from consideration for STN DBS, based on their usual lack of response to L-dopa treatment and general experience that they respond poorly to surgery. Patients should demonstrate significant disability despite optimization of medications. Advanced age is not necessarily a contraindication for surgery but patients must be able to tolerate a lengthy awake procedure, during which their cooperation and participation is required. Additionally, patients must not have bleeding disorders and must be able to tolerate the general anesthesia required for the internalization of electrode leads and pulse generator placement. Patients who come from remote areas must have ready access to centers with expertise in DBS programming and the resources to deal with possible hardware complications.

All potential surgical candidates are evaluated in the “practical off” (12 h without medication) and “on” state (1 h after the morning dose of medication). The evaluation requires assessment based on objective, standardized PD rating scales, such as the Unified Parkinson’s Disease Rating Scale (UPDRS), and the Hoehn and Yahr Scale. Formal neuropsychological testing is useful in assessing cognitive function and motivation and in checking for the presence of significant depression. Major mood disturbances require appropriate therapy before a patient can be considered for surgery. Evidence of dementia is a contraindication to surgery in most centers as this will compromise the likelihood of successful therapy and may even worsen in the postoperative period.

The presence of a complete or near-complete response of parkinsonian symptoms to L-dopa treatment is considered to be predictive of a good response to STN DBS surgery. With the exception of tremor, symptoms that do not respond significantly to L-dopa, are believed unlikely to improve significantly with stimulation (12,13). Tremor, which is sometimes resistant to L-dopa in conventional doses, responds particularly well to STN DBS and is therefore not a contraindication to STN DBS.

4. OPERATIVE TECHNIQUE

4.1. MRI-Based Anatomical Target Localization

Patients are admitted to hospital on the morning of surgery, having been off medication the preceding night. Although this may prove difficult for some patients, it allows for the accentuation of both clinical symptoms and microelectrode findings that contribute to intraoperative localization of optimal electrode placement.

The patient is brought to the radiology suite on the morning of surgery, where a stereotactic frame is assembled and affixed to the patient’s head. Magnetic resonance (MR) images are then obtained.