Deep Brain Stimulation for Parkinson’s Disease

Atsushi Umemura

Department of Neurosurgery, Nagoya City University Graduate School of Medicine
1 Kawasumi, Mizuho-ku, Nagoya 467-8601, Japan
aume@med.nagoya-cu.ac.jp

Abstract: Parkinson’s disease (PD) is a progressive nervous disorder caused by degeneration of dopamine-producing cells in the substantia nigra. The main symptoms are movement-related, including tremor, rigidity, bradykinesia, postural instability, gait disturbance, and so on. Other symptoms include autonomic, sensory, psychiatric and cognitive problem. In general, motor symptoms of PD are initially treated with dopaminergic medications. Recently, deep brain stimulation (DBS) has been performed as another treatment option for medically refractory PD. DBS is an adjustable and reversible treatment using implanted medical devices to deliver electrical stimulation to precisely targeted areas of the brain. DBS modulates neurological function of the target region. The most common target for PD is the subthalamic nucleus (STN). DBS is particularly indicated for patients suffering from motor complications of dopaminergic medication such as fluctuations and dyskinesia. Although there is currently no cure for PD, a combination of medical treatment and DBS provide long-term relief of motor symptoms.

Keywords: Selected keywords relevant to the subject.

1. Parkinson’s Disease

Parkinson’s disease (PD) is a progressive nervous disorder caused by degeneration of dopamine-producing cells in the substantia nigra. The main symptoms are movement-related, including tremor, rigidity, bradykinesia, postural instability, gait disturbance, and so on. Other symptoms include autonomic, sensory, psychiatric and cognitive problem. Although there is currently no cure for PD, motor symptoms of PD are initially treated with dopaminergic medications such as levodopa and dopamine agonists. However, they may lose effectiveness over time or cause troubling side effects.

Recently, deep brain stimulation (DBS) has been widely performed as another treatment option for medically refractory PD.

2. Deep brain stimulation

DBS is a surgical treatment involving the implantation of medical devices to deliver electrical stimulation to precisely targeted areas of the brain. Expectation of DBS is based on functional alteration in the target area. The DBS system consist of three components: the implantable pulse generator (IPG), the lead with four contacts, and the extension (Fig. 1).

DBS is an adjustable and reversible treatment. The IPG can deliver pulses with three variable parameters. Frequency (2-185 Hz), width (60-450 µsec), amplitude (0-10.5 V), and the selection of the stimulating contact can be set by electromagnetic programmer.

3. Mechanism of DBS in PD

There is a long history of surgical treatment for PD. Formerly, ablative stereotactic neurosurgical procedures such as thalamotomy or pallidotomy were performed for
medically refractory movement disorders. Surgical treatment is based on the following functional alteration within the basal ganglia-thalamo-cortical circuit (Fig. 2). In PD, increased excitatory activity of the subthalamic nucleus (STN) caused by depletion of dopamine in substantia nigra pars compacta (SNc) abnormally activates the internal portion of the globus pallidus (Gpi) which inhibit activity of the thalamus and thalamocortical neurons. The reduced thalamic and cortical activity account for the hypokinetic symptoms of PD such as rigidity and akinesia. Therefore, reducing the overactivity of STN or Gpi through ablative procedure or DBS might have a considerable clinical effect in PD.

DBS seems to produce a functional lesion in the brain and reduces activity in the focal area as well as ablative procedure. However, the true mechanism of the action in DBS is not well understood. Recently, the most common target of DBS for PD is the STN.

5. Surgical Procedure of STN DBS

The clinical efficacy of STN DBS depends largely on the lead localization. Therefore, precise implantation of the DBS lead into the STN is a goal of this surgery. In general, MRI is used for initial targeting and physiological refinement with microelectrode recording (MER) is a gold standard to identify the STN.

Quadripolar DBS electrodes (lead 3389, Medtronic) are implanted into the STN stereotactically with MRI guidance under local anesthesia. The target localization is based on the Schaltenbrand-Wahren atlas and on direct visualization on the MRI using surgical planning software (Frame Link, Medtronic) (Fig. 3).

A burr hole is placed in the skull and the electrode is inserted. The target is refined physiologically by single tract MER (Fig. 4). When sufficient length of STN activity (length more than 4.0 mm) is obtained, DBS lead is implanted at the trajectory.
A test stimulation is performed to assess symptom relief and to evaluate the threshold for adverse effects. Then, general anesthesia is induced and the IPG (Soletra, Medtronic) is placed in an infraclavicular subcutaneous pocket. The extension wire is tunneled subcutaneously and connected to the IPG.

As for surgical complications, intracranial hemorrhage and infection are the most commonly reported complication of DBS.

The stimulator is turned on about a few days after the surgery. Initially, we test monopolar stimulation with the contact negative and the stimulator case positive. The frequency and pulse width of the stimulation are set at 130 Hz and 90 µsec. The contact that induces the best clinical effect with the minimum voltage and without side effects is searched for continuous stimulation. Most patients require additional visits to outpatient clinic to determine the most suitable setting of stimulation. Usually, dopaminergic medication may be reduced by 50-60% with stimulation.

6. Effect of STN DBS in PD

The main scale used to analyse the intensity of symptoms in PD is the Unified Parkinson’s Disease Rating Scale (UPDRS). STN DBS results in a significant reduction in the patients’ UPDRS motor score while in the medication-off state but does not alter the score while they are in the medication-on state. STN DBS effectively improves levodopa-responsive symptoms of PD and significantly reduces dyskinesias, motor fluctuations, and the need for dopaminergic medication. Recent long-term studies revealed that the effects of STN DBS are sustained over time. However, STN DBS may be complicated by increased depression, apathy, impulsivity, worsened verbal fluency, and executive dysfunction in a subset of patients.

7. Role of DBS in long-term treatment

Though both dopaminergic medication and DBS improve cardinal motor symptoms of PD, they are not cures to control the progression of the disease. Typically, STN-DBS can maintain improvement in motor symptoms such as tremor, rigidity, and bradykinesia over a long period. Nevertheless, some patients develop deterioration in axial symptoms such as freezing of gait and postural instability after a few years. Progressive worsening of axial symptoms seems to be consistent with the natural history of PD.

Fig. 5 shows roles of medication and DBS in long-term treatment of PD. DBS does not replace medication, but a combination of both treatment provides long-term relief of motor symptoms in advanced PD.

8. Other indication of DBS

Recently DBS has been established in the management of other movement disorders such as essential tremor and dystonia. In addition, DBS is currently under investigation in many other neurological and psychiatric disorders including obsessive compulsive disorder, depression, Tourette syndrome, epilepsy, cluster headache, and so on. Of course, the target site of DBS depends on the disorder.

References