

Stereotactic posteroventral pallidotomy for Parkinson's disease

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Abstract

There has been renewed interest in posteroventral pallidotomy (PVP) as a treatment for Parkinson's disease (PD) because the effects of medications waned after several years and the patient is beset with motor fluctuations. Laitinen and co-workers were largely responsible for this resurgence of pallidotomy when they reported long-lasting improvement of the cardinal symptoms of PD in 81 to 92% of patients. The rationale for PVP lies in the hypothesis that dopamine deficiency leads to overactivity of the globus pallidus interna (GPi) due to disinhibition of excitatory glutaminergic neurons originating in the subthalamic nucleus (STN). This leads to thalamocortical inhibition with the development of parkinsonian features. Making a lesion in the Gpi or STN results in a reduction of this inhibition. From a few published studies, PVP is most effective in ameliorating dopa-dyskinesias, and it improves tremor, rigidity and bradykinesia in a decreasing order of effectiveness. Axial symptoms, such as freezing and postural instability, may not be improved significantly. Bilateral STN stimulation may be more effective for bradykinesia, rigidity and axial features.

Key words: pallidotomy, Parkinson's disease, dyskinesia, stereotaxis, deep brain stimulation

Medications for Parkinson's disease (PD) are effective for several years, but is followed by motor fluctuations, dyskinesias and progression of bradykinesia and rigidity. This is the reason why surgical therapies for PD have enjoyed a resurgence of interest. Surgical treatment began in the 1930s when Putnam^{1,2} sectioned the pyramidal tracts of the spinal cord and Bucy^{2,3} removed portions of the motor cortex. This improved tremor and rigidity, but produced limb weakness.

Meyers, in the late 1930s, began experimenting with resection of portions of the basal ganglia.⁴ He showed that tremor and rigidity could be improved, without affecting the corticospinal tract. In 1947, Spiegel first introduced stereotactic surgical techniques in humans. Cooper accidentally ligated the anterior choroidal artery in a patient with PD causing a globus pallidus (GP) infarct, and he noted improvement of contralateral parkinsonian signs.⁵

Narabayashi gave procaine oil injections into the GP using stereotactic apparatus in 1952⁶ and in 1953, Guiot and Brion⁷ reported on electro-coagulation of the pallidum. Lars Leksell began performing anterodorsal pallidotomies in 1952, but found that he could obtain better results in shifting the target to the posteroventral part of the pallidum. The pallidal target was abandoned

when Hassler and Riechert in 1954⁸ demonstrated dramatic improvement in tremor with a lesion in the ventrolateral thalamus. Thalamotomy has no effect on bradykinesia which is often the most disabling symptom. The demise of surgical therapies started in 1966 when levodopa was introduced.

A student of Leksell, Laitinen in 1992, published the results of posteroventral pallidotomy (PVP) in 38 PD patients. He reported complete or almost complete relief of rigidity and bradykinesia in 92% of his patients. Dopa-induced dyskinesias were also markedly improved.⁹ Several papers followed¹⁰⁻¹² demonstrating the efficacy of this technique, and that by utilizing micro-electrode recordings, complications can be minimized. PVP appears to be more effective for dopa-induced dyskinesias. It also improves tremor, rigidity and bradykinesia in a descending order of effectiveness. Axial symptoms such as freezing and postural instability are less likely to improve. The symptoms improve largely on the side contralateral to the surgical lesion, but milder ipsilateral improvement is also observed.

Two studies^{10,11} have demonstrated that the benefits of pallidotomy are sustained at one year after surgery, and younger patients seemed to derive greater improvement than the elderly. Those with moderate to severe dementia

benefited less from surgery.¹² Baron et al applied extensive neuropsychological tests to their patients undergoing pallidotomy and these did not show any significant change six months following surgery, except for the Backward Digit Span score which showed an improvement in attention. Swallowing was improved throughout the follow-up period at one year, but postural stability and freezing worsened after an initial improvement at three months.¹² A recent study found that unilateral pallidotomy resulted in a persistent contralateral improvement and unexpected ipsilateral improvement after four years.¹⁴ PD symptoms did not appear to progress, even ipsilaterally, and the effectiveness of levodopa was maintained at almost the same dosage.

The risk of major complications from surgery is small, ranging from 2 to 3%. These include contralateral limb paresis, subdural hematoma, homonymous visual field defects, dysphagia and dysarthria. Micro-electrode recordings allow precise identification of the basal ganglia structures by single cell neuronal recordings, and stimulation through the electrode allows the optic tract and internal capsule to be identified and avoided. Although not proven, there are strong reasons to believe that using microelectrode recordings will enable more precise targeting and a lower incidence of complications.

From studies of primates treated with 1 - m e t h y l - 4 - p h e n y l - 1 , 2 , 3 , 6 tetrahydropyridine (MPTP) to induce parkinsonism,¹⁴ it was observed that dopamine depletion resulted in excessive neuronal activity in the subthalamic nucleus (STN) and GPi. Improvement of bradykinesia in these parkinsonian primates occurred after lesioning the STN. In humans, the GPi, is more assessable, with low mortality and morbidity, and does not cause hemiballismus as a lesion in the STN would. The overactivity of the GPi due to the disinhibition of excitatory glutaminergic neurons originating in the STN leads to thalamocortical inhibition with the development of parkinsonian features. The reason for beneficial ipsilateral effects after unilateral pallidotomy is not clear. Some explanations include bilaterality of cortical projections onto the striato-pallidal-thalamocortical loop and bilateral pallido-thalamic projections.¹⁶

In Tan Tock Seng Hospital, we perform micro-electrode guided stereotactic posteroventral pallidotomy under local anesthesia. A Radionics MRI-compatible CRW

stereotactic frame is applied to the patient's head and T1-weighted spin echo and Fast Gradient Recalled Echo MRI brain scans are obtained. The coordinates for the advancement of electrode are plotted based on MRI and Electronic Brain Atlas.¹⁵ A platinum-iridium micro-electrode with a tip of one micron is gradually inserted and neuronal recordings begun. A globus pallidus interna (GPi) lesion is made when the ventral and posterior borders of the GPi are identified, and where microstimulation does not evoke a visual, motor or somatosensory response. Lesion making is done for 60 seconds at 90°. We have performed PVP on four advanced Parkinson's disease patients with severe motor fluctuations. Our results corroborate what was reported in the published studies. Although there was decreased 'off' time, medication doses could not be reduced.

There is recent work, largely pioneered by Benabid and co-workers in Lyon, France, to suggest an alternative stereotactic target.¹⁷ High frequency deep brain stimulation of the subthalamic nuclei (STN) may be superior to pallidotomy because STN not only projects to GPi, but to other brain regions such as substantia nigra pars reticulata which are not influenced by pallidotomy. Gait and axial features, which are not improved much by pallidotomy, showed marked improvement after bilateral STN stimulation. Bradykinesia and rigidity may be improved to a greater extent by this procedure compared with pallidotomy.

In summary, posteroventral pallidotomy improves all the cardinal features of Parkinson's disease, namely tremor, rigidity and bradykinesia. It is especially effective in ameliorating dopa-induced dyskinesias. Axial features such as postural instability and freezing may not be improved greatly by this procedure. The stereotactic procedure of choice in the future may be bilateral subthalamic nucleus stimulation which appears to improve both bradykinesia, rigidity and axial symptoms tremendously.

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