Scientific Position Paper of the Movement Disorder Society
Evaluation of Surgery for Parkinson’s Disease

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There are numerous options now available for the surgical treatment of patients with Parkinson’s disease (PD). The field is advancing rapidly, and there are many variations in the techniques, even for a single procedure. This has led to some confusion as to what is inappropriate, what is experimental, and what is now acceptable for standard care. The Therapeutics and Technology Assessment Committee of the American Academy of Neurology assembled a task force to write a position paper on this topic which has now been approved by the Academy and published in Neurology.1 This document has also been approved by the Scientific Issues Committee (Chair, David Brooks, MD) and the International Executive Committee of the Movement Disorder Society. A brief summary of the results is noted here; the original should be consulted for details. The document was prepared by formal procedures and is based entirely on the published literature through December 1998. Almost all papers included were “class III,” peer-reviewed, used, validated methods of assessment and provided consistent clinical data. Although most studies considered were prospective, only two included a concurrent control group, a requirement necessary to meet “class II” evidence.2,3 Publications in 1999 are noted here as updates but recommendations have not been altered.

Comments Applicable to All Procedures
The procedures require neurosurgeons with a high level of expertise in stereotactic techniques. The majority of reporting centers have multidisciplinary teams of neurosurgeons, neurologists, neuropathologists, psychiatrists, psychologists, and neuroradiologists with expertise in the diagnosis, assessment, and treatment of movement disorders. Inexperienced centers will likely have less good results and more adverse side effects. In general, cognitive impairment is a predictor of poor outcome and patients of advanced age derive decreased benefit. Significant coexisting medical conditions, psychiatric disease, or focal abnormalities on brain imaging are relative contraindications. The final recommendations for each procedure are shown in Table 1.

Thalamotomy
Thalamotomy directed to the Vim nucleus is indicated for asymmetric, severe, medically intractable tremor, particularly when the tremor is not associated with other important symptoms of PD. Thalamotomy on the second side has a good chance at decreasing tremor but a high incidence of speech and swallowing problems. Therefore, if surgery is considered for the second side, deep brain stimulation (DBS) of the Vim is the treatment of choice. The operation is generally not appropriate for atypical parkinsonism, including multiple system atrophy, but in the rare patient with severe disabling tremor, thalamotomy might be beneficial.

Pallidotomy
Unilateral pallidotomy is indicated for advanced PD with motor fluctuations and drug-induced involuntary movements (dyskinesias) along with significant bradykinesia and rigidity, with or without tremor. The indications are detailed in another expert statement.4 The improvements in these cardinal features of PD last at least 2 years, and the efficacy was demonstrated in a prospective, randomized, single-blind trial.5 The magnitude of the improvement appears to be greatest for drug-induced dyskinesias. Benefits are predominantly contralateral, suggesting that asymmetric patients stand to improve the most with pallidotomy. There are insufficient reliable data on the indications, safety, or benefits of bilateral
pallidotomy, and investigators are wary of bilateral procedures because of side effects. An unfavorable risk–benefit ratio for bilateral pallidotomy was reported in a publication in 1999. If symptoms on the other side become significant, DBS for the second side might eventually be demonstrated to be acceptable.

**DBS of the Vim Nucleus of the Thalamus**

DBS of the Vim nucleus of the thalamus, as an alternative to thalamotomy, was approved by the Food and Drug Administration (FDA) in 1997 for the treatment of contralateral tremor in PD and essential tremor. DBS of the thalamus was introduced in Europe in 1987 and approved there in 1993. The indication for high-frequency stimulation of the Vim thalamic nucleus is severe and disabling tremor that is unresponsive to medical therapy but without significant other motor symptoms such as bradykinesia. Because of its low morbidity, it appears that DBS of the Vim can be performed bilaterally in patients with severe bilateral tremor, often during one surgical session, but there is not much published data on bilateral procedures.

**DBS of the Globus Pallidus**

DBS of the globus pallidus received European approval in 1998. Virtually all patients reported in the literature have had advanced idiopathic PD with associated motor fluctuations and drug-induced dyskinesias. In the off state, there are benefits to all aspects of parkinsonism, including bradykinesia, rigidity, and tremor, with less consistent effects on speech and walking. In the on state, which is more sustained, there is a marked reduction in dyskinesias but only marginal improvement in other features. Since completing this report, there have been additional series of patients reported adding to the evidence that this procedure is safe and effective.

**DBS of the Subthalamic Nucleus**

DBS of the subthalamic nucleus also received European approval in 1998. Indications have been limited to patients with severe PD with fluctuations, and virtually all cases have been operated bilaterally. The procedure may be useful for the major motor aspects of parkinsonism, including dyskinesias. Some motor features, such as speech, appear to be less responsive and may even deteriorate after surgery. With this procedure, unlike pallidal stimulation, the dose of oral medications is typically reduced. The beneficial effects for PD are impressive, but there are a number of complications that have occurred. Because there is limited published experience to date with DBS of the subthalamic nucleus, it still must be considered investigational. There is considerable enthusiasm for this procedure, particularly in Europe where it has already been approved for the treatment of PD. Since completing this report, there have been additional series of patients reported, adding to the evidence that this procedure is safe and effective. In relation to approaches to the subthalamic nucleus, subthalamotomy is also being investigated in a few centers, but only preliminary results have been reported.

**Adrenal Medullary Transplants**

The literature is clear that with the published procedures, risks exceed benefits.

**Human Fetal Mesencephalic Cell Transplants**

Indications are patients with idiopathic PD who are poorly controlled with medication and who have motor fluctuations are candidates for transplants. The reports generally have only a few patients and are not controlled, but improvement may start after 3 to 6 months and last up to 5 years. A few additional patients studied in open trials have been reported since completing this re-
port. The first prospective, double-blind, controlled trial in Parkinson surgery (class I evidence) was reported in abstract form. Because of the small number of subjects and risk–benefit considerations, this procedure clearly remains experimental.

CONCLUSION

In carefully selected cases, thalamotomy and DBS of the thalamus (Vim nucleus) can safely and effectively control tremor. In a recent randomized comparison of the two, they were similarly effective for tremor, but DBS had fewer adverse effects and produced greater improvement in function. It is clear, however, that they cannot help bradykinesia which typically is, or will become over time, the most important symptom. Hence, other procedures should always be considered even if tremor is the main symptom. When the problem is severe dyskinesias and on–off fluctuations, unilateral pallidotomy has been demonstrated to be effective and reasonably safe. For bilateral pallidotomy, the risks can be substantial, limiting its potential use. Pallidal DBS, currently investigational, may well be demonstrated to be a good alternative, and it can be done bilaterally more safely. For bradykinesia, DBS of the subthalamic nucleus, typically done bilaterally, is a consideration, although also investigational. Comparisons are needed between pallidal and subthalamic nucleus DBS; the one small series so far reported showed similar results. Other considerations are that procedures such as thalamotomy and pallidotomy are immediate in effect and essentially complete at the time of operation but irreversible. DBS makes no major lesion but requires intensive postoperative adjustments and lifelong maintenance. For improvement of bradykinesia, fetal implantation surgery is also promising but remains investigational. Implantation with other types of cells, including engineered cells, will be used in the future, and preliminary studies of fetal porcine mesencephalic cells are already underway. Adrenal implantation surgery has been abandoned. Implants are not immediate in their effect and may require immune suppression. In making a decision about any type of surgery, the risks should be weighted against any possible benefit. It is important to recognize that, aside from drug-resistant tremor, none of the current surgical procedures are very effective against symptoms that persist in the best on-state, such as freezing. Because these procedures are under intense investigation, new knowledge is expected to accrue rapidly and the recommendations concluded here will evolve.

REFERENCES