EYERS pioneered the surgical treatment of Parkinson’s disease (PD) in the 1930s, initially with resection of the caudate nucleus and subsequently with lesioning in the ansa lenticularis. Chemopallidotomy was reported for the treatment of PD by Narabayashi and Okumä in 1953, whereas Guiot and Brion reported successful pallidotomy in which thermocoagulation was used in the same year. The initial surgical target was in the anterodorsal portion of the medial globus pallidus (GP), but Svennilson and colleagues noted better surgical outcomes with a more posterodorsal location.

With the introduction of levodopa in the late 1960s there was a dramatic decline in surgery for PD. However, pallidotomy regained popularity in 1992 when Laitinen, et al., reported their experience using Leksell’s posterodorsal target in patients in whom conventional drug therapy had failed. They found that levodopa-induced dyskinesias were greatly improved or completely abolished in almost all patients. In addition, most patients demonstrated improvement in all three cardinal symptoms of PD: tremor, rigidity, and bradykinesia.

Since then, practitioners at numerous centers have reported similarly good results in selected patients with PD whose symptoms were refractory to conventional pharmacological management. With the advent of improved stereotactic techniques, along with microelectrode and macrostimulation techniques for intraoperative localization of lesions, pallidotomy has become a safe and reproducible procedure. However, at present few data have been published regarding the effects of lesion size and placement in individual patients.

We present two patients who had unsatisfactory results after their first unilateral pallidotomy but attained dramatic and long-lasting improvement with repeated surgery. The results obtained in these cases indicate that patients who have a good clinical outcome initially but relapse rapidly after surgery should be considered for repeated pallidotomy if the initial lesion was not placed in the optimal location.

Key Words • pallidotomy • Parkinson’s disease • basal ganglion • stereotaxis

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Case Reports

Case 1

History. This 47-year-old right-handed man had a 17-year history of PD that began with tremor in his right hand. Although initially he had an excellent response to dopamine replacement therapy, 5 years into his clinical course he began to experience severe “on” and “off” motor fluctuations. During “on” periods he experienced severe dyskinesias in the arms and legs, more prominent on the right side, which caused a peculiar and debilitating goose-stepping gait. During “off” periods he experienced severe rigidity, bradykinesia, and resting tremor. He was confined to a wheelchair during these periods and was
unable to perform activities of daily living independently. He was classified as Hoehn and Yahr Stage III while “on” and Stage V when “off” and was functioning at 80% on the Schwab and England scale for activities of daily living while “on” and 60% while “off.”

Examination and First Operation. The patient was evaluated at another institution and underwent a computerized tomography (CT)–guided posteroventral left pallidotomy. The calculated target coordinates were defined as 2 mm anterior to the midcommissural point, 5 mm below the intercommissural plane, and 22 mm lateral to the midline. Macrostimulation was used to confirm lesion placement. Radiofrequency thermolesions were made at 6, 4, 2, and 0 mm above the target by heating the electrode to 84˚C for 60 seconds at each site.

First Postoperative Course. In the immediate postoperative period, the patient noted a decrease in contralateral dyskinesias and improvement in his gait. However, within a few days his symptoms recurred. Reevaluation 6 months later at Massachusetts General Hospital demonstrated severe rigidity, bradykinesia, and tremor when “off,” and marked dyskinesias when “on.” All of these signs were more severe on the right side. In addition, the abnormal gait had returned. A lesion was demonstrated in the left GP 23 mm lateral to the midline and 6 mm anterior to the midcommissural point (Fig. 1A and B) on magnetic resonance (MR) imaging.

Second Operation. The patient underwent a second left-sided pallidotomy at our institution with the aid of MR imaging and CT stereotactic guidance 8 months after the initial surgery. A stereotactic head frame (CRW; Radionics, Burlington, MA) with the appropriate localizers was used for imaging and intraoperative target localization. A target was selected 3 mm posterior and 2 mm medial to the initial lesion. Macrostimulation, using a macrolesioning electrode (Radionics) with a 1.8 × 2-mm uninsulated tip, was begun 4 mm above the target and repeated at 2-mm intervals as the electrode advanced. Low-frequency stimulation (2 Hz) resulted in contractions of the right side of the patient’s face, with a threshold of 4 V at 4 mm above the target. The threshold decreased to 2.9 V at the target. High-frequency stimulation (50 Hz) at the target resulted in mildly increased tremor and a reduction in rigidity of the contralateral limbs at a threshold of 2 V, but no visual symptoms were observed. Radiofrequency lesions were made at 3 mm above, 1 mm above, and at the target by heating the electrode to 85˚C for 60 seconds at each site.

Second Postoperative Course. In the immediate postoperative period, the patient’s gait was markedly improved. Over the next several weeks he gained considerable functional independence, performing all of his activities of daily living without assistance, and was able to walk several miles daily. Evaluation at 3 months revealed complete abolition of the right-sided dyskinesias with bilateral improvement in rigidity and bradykinesia. When “on,” he was classified as Hoehn and Yahr Stage II and was functioning at 90% on the Schwab and England scale. During “off” periods he was Hoehn and Yahr Stage III and was functioning at 70% on the Schwab and England scale. A postoperative MR image obtained at 3 months revealed that the new lesion had been placed posterior and medial to the initial lesion (21 mm lateral to the midline and 2 mm anterior to the anterior–posterior commissure line; Fig. 1C and D), in the posteroventral medial GP. This remarkable improvement has now been sustained for 4 years after his second surgery. Fifteen months after his successful left-sided pallidotomy he underwent a rightsided pallidotomy with similarly good results.

Case 2

History. This 69-year-old woman had a 10-year history of PD that began with tremor in the right hand and she responded to Sinemet. By the time she presented as a candidate for pallidotomy her clinical course was characterized by severe motor fluctuations despite numerous manipulations of her medical regimen. During “on” periods, she suffered from disabling bilateral dyskinesias that were more severe on the right side and severe diaphoresis. She experienced progressive weight loss due to the dyskinesias. During “off” periods, she suffered from incapacitating rigidity and bradykinesia, also greater on the right.
She was estimated to be Hoehn and Yahr Stage III while “on” and Stage IV while “off.” Her Schwab and England scores were 90% while “on” and 60% while “off.”

Examination and First Operation. After thorough evaluation, MR imaging– and CT-guided left-sided stereotactic pallidotomy was performed. The lesion target was calculated for a position 2 mm anterior to the midcommissural point, 19 to 20 mm lateral to the midline, and 5 mm below the intercommissural plane. Macrostimulation was used to confirm the electrode position. At 5 mm above the target, low-frequency stimulation (2 Hz) revealed contractions in the fingers of her right hand at a threshold of 5 V, but there were no contractions of the tongue, which was atypical. The motor threshold dropped to 3.5 V at the target. High-frequency stimulation (50 Hz) at the target failed to produce the usual visual symptoms of flashing lights in the contralateral hemifield. The electrode was advanced 2 mm beyond the target but again no visual symptoms were elicited. A lesion was made at this level by heating the electrode to 70˚C for 60 seconds. The electrode was then withdrawn in 2-mm increments, with lesions being made at 2 and 4 mm above the initial lesion by heating the electrode to 85˚C for 60 seconds.

First Postoperative Course. In the immediate postoperative period the patient appeared to have diminished dyskinesias and a decrease in right-sided rigidity and bradykinesia. However, during the ensuing weeks her symptoms gradually returned to their preoperative level. An MR image obtained 3 months postsurgery revealed a lesion in the left GP (Fig. 2A and B). The lesion was 21 mm lateral to the midline, 2 mm anterior to the midcommissural point, and 8 mm inferior to the intercommissural plane.

Second Operation. Five months after the initial operation a second left-sided pallidotomy was performed. The coordinates were calculated for a target posterior and superior to the initial lesion. Macrostimulation was again used to guide lesion placement. In contrast to the stimulation parameters obtained during the first surgery, motor thresholds were obtained for both tongue and hand. In addition, an appropriate visual threshold was obtained. At the target, the motor thresholds were approximately 2.7 V, whereas the visual threshold was approximately 3.3 V. A lesion was made with the electrode heated to 85˚C for 60 seconds. The electrode was then withdrawn in 2-mm increments, and four lesions were made, one atop the other, by using the same lesion parameters. A postoperative MR image revealed the lesion to be located in a more optimal location 20 mm lateral to the midline, 2 mm anterior to the midcommissural point, and 6 mm below the intercommissural plane, in the posteroventral medial GP (Fig. 2C and D).

Second Postoperative Course. One day postoperatively, the patient was found to have a decrease in contralateral dyskinesias and rigidity. At 3 months, she reported considerable improvement of her right-sided dyskinesias, her sweating episodes had stopped, and she had gained 12 lbs. On examination she was found to have complete abolition of the dyskinesias on the right. Additionally, she demonstrated a significant reduction in rigidity, bradykinesia, and tremor on the right side. Overall, she had improved to Hoehn and Yahr Stage II in both the “on” and “off” conditions, whereas her Schwab and England score improved to 90% while “on” and 80% while “off.” These improvements have been sustained for 2 years following the repeated pallidotomy and appear to be long lasting. The patient subsequently underwent a right-sided pallidotomy with similarly good results.

Discussion

Svennilson, et al., 23 established that the symptoms of PD could be successfully alleviated by creating lesions in the posteroventral pallidum. However, the mechanism by which pallidotomy alleviates the symptoms of PD and the optimal lesion size and location remain topics of debate. Laitinen and coworkers 13,14 have suggested that the dorsomedial pallidum is involved in the initiation of movement and that this area is abnormally inhibited in PD. Presumably, stereotactically guided lesions in the posteroventral pallidum interrupt some striopallidal or strio-subthalamopallidal pathways and thereby block this inhibition, reestablishing normal function in the medial...
Repeated pallidotomy

pallidum. A more widely accepted view is that the loss of dopamine in PD ultimately results in increased inhibitory output from the GP internus (GPI) to the ventrolateral thalamus.1 Pallidotomy abolishes the excessive output from the GPI, thereby releasing the thalamus from the abnormal inhibition.2 There is considerable evidence for this latter view, including the finding that microelectrode recordings obtained in monkeys rendered parkinsonian by the administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine have revealed overactivity of neurons in the GPI when compared with control animals.7

The ideal target for pallidotomy is not known with certainty and lesion locations have been reported to be 17 to 25 mm lateral to the midline, 3 to 8 mm below the intercommissural line, and 2 to 3 mm anterior to the midcommissural point.3,5,10–14,16,17,22 Microelectrode recordings of human pallidal neurons in patients with PD are beginning to yield information that may be helpful in rationally choosing pallidial targets. For example, several studies have shown that neurons in the medial and lateral GP differ in their frequency and pattern of activity.16,21 Furthermore, the description of a sensorimotor area of the GPI, with at least partial somatotopic organization located in the posteroventral GPI, is in agreement with the empirical finding that the optimal lesion target lies in the medial posteroventral GP.3,15,17

Important information regarding optimal lesion location can also be gained by empirically reviewing cases in which lesioning failed. Laitinen, et al.,15 noted excellent results in patients who had suffered visual field defects as a result of pallidotomy. They concluded that the most effective lesion was one that was placed ventrally as close as possible to the optic tract without causing injury. This may reflect the importance of creating a lesion in the inferiorty located ansa lenticularis. These authors also reported that patients who had partial or total recurrence of symptoms after pallidotomy had smaller or more dorsally placed lesions when compared with other patients.14 In their series, Lang, et al.,15 reported that one patient had a poor outcome after placement of an initial lesion anterior and dorsal to the optimal location. That patient achieved a good outcome after repeated surgery. In another series one patient had a poor outcome after a lesion was placed primarily in the GP externus.12 Poor outcomes have been reported in other studies after poorly placed lesions and subsequent reoperation, although few details were provided.4

Although it seems prudent to create the smallest effective lesions, there are no definitive studies relating lesion size to outcome. The range of reported lesion volumes varies from 50 to 181 mm³. In some studies poor responses secondary to small lesion size and an improvement after repeated pallidotomy have been reported, although the size of the initial small lesions was not specified.11,22 Hariz9 examined postoperative CT scans in 19 patients who had undergone thalamotomy or pallidotomy for PD. The small number of patients did not allow for statistically significant conclusions to be drawn, although larger lesions appeared to be associated with more complications. Krauss, et al.,12 found no consistent relationship between outcome and lesion size as determined from postoperative MR imaging, indicating that lesion location may be the more important variable. The technique used at our institution creates lesions with a diameter of 4 to 5 mm and a height of 6 to 8 mm on MR images obtained immediately postoperatively, with a corresponding mean volume of approximately 75 mm³ (range 40–150 mm³). A significant reduction in the lesion volume is evident at 3 months. This lesion size appears to be associated with good clinical outcome and few complications.

The outcomes in the cases described in this report support the contention that the posteroventral medial GP is the optimal site for lesioning in the treatment of PD. Although the initial lesions were only a few millimeters away from the optimal target location, they were clearly ineffective. In both cases, the repeated lesions measured on the MR images obtained immediately postoperatively were relatively small (90 and 105 mm³, respectively), compared with some of the values reported in the literature3,5,6,16 but successfully produced impressive, long-lasting benefit, particularly with regard to alleviation of the levodopa-induced dyskinesias. From analysis of these limited data we infer that lesion location is the more critical factor, because both the initial and the repeated lesions were small and did not appear to overlap significantly. Based on these cases, and our subsequent experience, the optimal lesion location appears to be in the posteroventral medial GP, which corresponds to a position 19 to 21 mm lateral to the midline, 2 to 3 mm anterior to the midcommissural point, and 5 to 6 mm inferior to the anterior–posterior commissure plane. These coordinates represent an appropriate initial target but must be confirmed with the use of intraoperative stimulation and/or microelectrode recordings.

The cases described in this report reinforce the need for accurate lesion placement for permanent relief of symptoms. In the usual situation, the most inferior aspect of the lesion is determined by the proximity of the electrode to the optic tract, which is ascertained by obtaining visual stimulation thresholds of the appropriate magnitude. Indeed, as mentioned previously, it may be desirable to place the lesion as close as possible to the optic tract without causing a visual deficit. However, if the electrode is positioned slightly too anterior or lateral, it is possible to slide past the optic tract completely as it adopts a more medial location, reflecting its origin in the optic chiasm. Consequently, adequate visual thresholds may not be obtained and the electrode is advanced deeper. That appears to be the sequence of events in both of our cases, which led to the placement of lesions that were ultimately ineffective.

Whether microelectrode recordings might have prevented the errant positioning of the initial lesions in these two cases remains an open question. Microelectrode recording has been reported to be helpful in identifying the sensorimotor portion of the GPI and delineating the boundaries of the GP and the optic tract.3,5,6,15,17 However, even in medical centers that rely on microelectrode recording inappropriately placed lesions have been reported.3,6,12,13 It seems that with either technique, microelectrode- or macroelectrode-guided surgery, considerable experience is needed to place lesions reliably in the optimal location. The second patient reported on here was treated relatively early in our experience. Since then we have performed nearly 100 pallidotomies by using macrostimulation, with
very reliable and reproducible results. Our experience with nonmicroelectrode-guided pallidotomy will be the subject of a future report.

Conclusions

Early clinical improvement postpallidotomy followed by deterioration in patients with bona fide PD may result from a lesion that is not optimally placed. The effects of edema or other reversible changes may be responsible for the short-term clinical improvements. If early clinical deterioration is accompanied by evidence on MR imaging of suboptimal lesion placement, then reoperation should be considered. An initially poor outcome does not preclude suboptimal lesion placement, then reoperation should be considered. Further delineation of the optimal target site will require careful clinical correlation with detailed radiographic studies and intraoperative macrostimulation and microelectrode recordings.

References


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