Visual Evoked Potential Guidance for Posteroventral Pallidotomy in Parkinson’s Disease

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Abstract

Visual evoked potentials (VEPs) to photic stimulation of the eyes were used to identify the optic tract and thus determine the location of the globus pallidus internus (GPI) in eight patients with Parkinson’s disease who then underwent posteroventral pallidotomy. Distinct waves appeared at 1 or 2 mm below the target (4 to 5 mm below the intercommissural line) and the amplitude significantly increased at 5 or 6 mm below, strongly suggesting that the electrode was in contact with the optic tract. In the medio-lateral direction, potentials were successively recorded in an area of 4 to 8 mm length, indicating the width of the optic tract. The trajectory at the mid point showed the most significant potentials which suggested the center of the optic tract. The site of the first lesion was placed 0 to 2 mm lateral to this trajectory and 5 mm above the point at which the amplitudes of responses increased. The actual lesion site significantly differed from the tentative target in a medio-lateral direction by 1 to 5 mm (mean 3.0 ± 1.5 mm, n = 6). The Unified Parkinson’s Disease Rating Scale score significantly improved and magnetic resonance imaging taken 2 or 3 weeks after the operation showed a lesion within the GPI in each patient. Recording of VEPs greatly facilitates accurate determination of the GPI.

Key words: Parkinson’s disease, visual evoked potential, stereotactic surgery, pallidotomy

Introduction

Posteroventral pallidotomy (PVP) has significant therapeutic effects on rigidity, bradykinesia, and tremor in patients with Parkinson’s disease (PD) that is refractory to medical therapy. The most common anatomic target is located within the globus pallidus internus (GPI). Electrical stimulation and microelectrode recording have been used to identify the GPI before positioning of a lesion. The GPI is located just above the optic tract, so accurate determination of the optic tract will allow easy identification of the GPI. We describe the use of visual evoked potentials (VEPs) to photic stimulation of the eyes to identify the optic tract and to anatomically determine the GPI for PVP.

Materials and Methods

Eight of 17 consecutive patients with PD who underwent PVP first had VEPs recorded to identify the optic tract. The tentative target was between 18 to 20 mm lateral to the midline, 2 to 3 mm anterior to the midcommissural point, and 4 to 5 mm below the intercommissural line. The target point was determined by ventriculography, and placement of the electrode was coordinated by Todd-Well’s stereotactic system. Plate electrodes were placed at Fpz (international 10-20 electrode system) for reference and on the ear lobe for grounding. A radiofrequency lesioning probe (Radionics, Burlington, Mass., U.S.A.) of 1.1 mm diameter with an exposed 1 mm tip and an impedance of 500 kΩ at 1 kHz was used as the active electrode, and was introduced to the target through a frontal burr hole, 2.5 cm lateral to the sagittal suture at the level of the coronal suture. The eyes were stimulated with a flashing light at 1 Hz, and the signals from the electrodes were led into an amplifier (Synax; NEC Sanei, Tokyo) through shielded wires with a band pass of 100 Hz to 1 kHz. The responses were analyzed up to 100 msec after stimulation and were summed 20 times. The results were displayed on a cathode ray tube and recorded on a disk.
The location of the optic tract was determined from the VEP findings. Electrical stimulation and microelectrode recording were used for further identification of the GPi. One or two lesions were made in the GPi at 70°C for 60 seconds with the radiofrequency probe, which had 1.1 mm diameter and the first 5 mm was uninsulated.

**Results**

The recording of VEPs started from the target point to 6 or 8 mm below at 1 or 2 mm steps along the trajectory of the electrode. Potentials consisted of multiphasic waves with an onset latency of 30 to 40 msec after the stimulation. When potentials were not obtained from the initial trajectory, the target was moved medially or laterally until the potentials appeared. Recording was continued further medially or laterally until the potentials were not obtained any more.

Figure 1 shows the VEPs of Case 4 in whom the tentative target was 2 mm anterior to the midcommissural point, 20 mm lateral to the midline, and 5 mm below the intercommissural line. VEPs were obtained at 1 mm intervals in a medio-lateral direction and along the trajectory. Potentials appeared at 2 mm below the target and their amplitudes increased and maximized at 5 mm below the target along the trajectory between 20 and 24 mm lateral to the midline. The most significant potentials were obtained along the trajectory at 22 mm lateral to the midline, which was the mid point of the trajectories. The amplitude, measured by the peak to peak method, at 5 mm below the target along this trajectory was 131.8 μV. Amplitudes along the other trajectories ranged from 30.8 to 99.2 μV. These results suggested that the optic tract was located at 20 to 24 mm in a medio-lateral direction and 5 mm below the target.

![Fig. 1 Case 4. Visual evoked potentials which have an onset latency of 30 to 40 msec and a duration of 40 to 50 msec appeared at 2 mm below the target along the trajectories between 20 and 24 mm lateral to the midline. The most significant potentials were obtained along the trajectory at 22 mm located at the mid point in a medio-lateral direction. The amplitudes maximized when the electrode reached 5 mm below the target in each trajectory, suggesting that the optic tract is located at 20 to 24 mm in a medio-lateral direction and 5 mm below the target. Arrow: stimulation.](image)
The site of the lesion in the GPi was therefore determined to be on the trajectory of 23 mm lateral to the midline and 5 mm above the point where the amplitude maximized. Low (2 Hz)- and high (50 Hz)-frequency electrical stimulation in this region with an intensity of up to 3 V caused no motor or visual responses. Recording of neural activity along the trajectory at 23 mm lateral to the midline was performed through a microelectrode (USK-100-TB-24L; Unique Medical, Tokyo) with an impedance of 100 kQ at 300 Hz. Recorded neural activity was not discernable from the background noise. The first lesion was made at this point and a second was made 1 mm medial to the first with the 1.1 mm diameter probe. Figure 2 shows a reconstruction of the trajectories which shows the relationship between the optic tract and the lesion sites. Each trajectory made an angle of 9° to the vertical plane and 60° to the horizontal plane. The lesions were made along the trajectories of 22 and 23 mm lateral to the midline. The lesion sites were estimated to be in the medial part of the globus pallidus internus (GPi). GPe: globus pallidus externus.

The site of the lesion in the GPi was therefore determined to be on the trajectory of 23 mm lateral to the midline and 5 mm above the point where the amplitude maximized. Low (2 Hz)- and high (50 Hz)-frequency electrical stimulation in this region with an intensity of up to 3 V caused no motor or visual responses. Recording of neural activity along the trajectory at 23 mm lateral to the midline was performed through a microelectrode (USK-100-TB-24L; Unique Medical, Tokyo) with an impedance of 100 kQ at 300 Hz. Recorded neural activity was not discernable from the background noise. The first lesion was made at this point and a second was made 1 mm medial to the first with the 1.1 mm diameter probe. Figure 2 shows a reconstruction of the trajectories which shows the relationship between the optic tract and the lesion sites. Each trajectory made an angle of 9° to the vertical plane and 60° to the horizontal plane. The site of lesion was estimated to be in the medial part of the GPi. Magnetic resonance (MR) imaging taken 2 weeks after the operation showed a lesion with surrounding edema within the GPi (Fig. 3).

Figure 4 shows the VEPs in Case 6 in whom the tentative target was 2 mm anterior to the midcommissural point, 18 mm lateral to the midline, and 5 mm below the intercommissural line. The recordings were performed at 2 mm intervals in a medio-lateral direction and up to 6 mm below the target. The potentials were obtained at 2 mm intervals in a medio-lateral direction and up to 6 mm below the target. The potentials were obtained at 16 to 22 mm in a medio-lateral direction, and at 2 mm below the target with maximum amplitudes at 5 mm below. The most significant potentials were obtained along the trajectory of 18 mm lateral to the midline. The amplitude at 5 mm below the target of this trajectory was 225 μV. Amplitudes on the other trajectories ranged from 54 to 90 μV. The optic tract was estimated to be 16 to 22 mm in a medio-lateral direction and 5 mm below the target. Although the most significant potentials appeared along the trajectory of 18 mm, the mid point of the optic tract was considered to be at 19 mm. The lesion site in the GPi was determined to be on the trajectory of 21 mm lateral to the midline and 5 mm above the optic tract. Electrical stimulation along this trajectory induced scintillation from 0 to 3 mm and motor responses of increased muscle tonicity in the contralateral upper extremity at 3 mm above the optic tract. Microelectrode recording along the 21 and 22 mm trajectories
showed neural activities which were not separable from the background noise. The lesion was made at 5 mm above the optic tract along both trajectories of 21 and 22 mm. Figure 5 shows a reconstruction of the trajectories in this patient. Each trajectory crosses the vertical plane at an angle of $8^\circ$ and the horizontal plane at $60^\circ$. The lesion sites were estimated to be at the center of the GPi. MR imaging taken 2 weeks after the operation showed a lesion within the GPi (Fig. 6).

Table 1 summarizes VEPs, target coordinates, and perioperative scores of the Unified Parkinson’s Disease Rating Scale (UPDRS). VEPs were successively recorded at 4 to 8 mm length in a medio-lateral direction in the last six patients. The site of the first lesion was placed 0 to 2 mm lateral to the trajectory which represented the mid point of the optic tract, and the second lesion was placed 2 mm medial to the first in the first five patients and 1 to 3 mm lateral in the last three patients. The first actual lesion site differed from the tentative target by 1 to 5 mm (mean $3.0 \pm 1.5$ mm, $n = 6$) in a medio-lateral direction. The site of lesion was 6 mm above the point at which the amplitudes of potentials maximized in the first two patients and 5 mm above in the others. The lesion site 5 mm above this point coincided with the level of 5 mm below the intercommissural line except in Case 5. The UPDRS scores postoperatively improved significantly by a mean decrease of 40. There was no postoperative morbidity in any patient.

**Discussion**

Electrical stimulation in the target area has been the most common method used and its most frequent effect in the pallidal region is reported to be the increase of tremor or of muscle tonicity. However, these responses do not indicate that the stimulating electrode was precisely within the GPi, because stimulation of the putamen, the globus pallidus externus, and the ansa lenticularis also facilitates tremor and muscle tonicity. Visual sensations, such as scintillation or hallucination,
evoked by stimulation indicate that the electrode tip was on or near the optic tract. However, as reported by other centers, these responses were inconstant and observed in less than half of our patients. Therefore, the effects of electrical stimulation in the pallidal region are not so correlated well with anatomical structure as those in the thalamic region. An alternative method to check the localization of the electrode relative to the GPi is needed. The GPi is located just above the optic tract, and the identification of this tract will help to localize the GPi and prevent injury to the optic tract from lesioning. As our data showed, the optic tract was easily and constantly identified by recording of VEPs, which were obtained by replacing wire from the electrode by shielded wire. Recording of VEPs was followed by electrical stimulation and microelectrode recording of neural activity for evaluating the neurophysiological property of the target area. Lozano et al., recently reported that microelectrode stimulation is superior to the microelectrode recording of VEPs for identifying the optic tract. Our data are contrary to this, and this difference may be due to the electrode used. A macroelectrode with a low impedance of 500 kΩ has been used in our institute and a microelectrode with a high impedance of 1 to 2 MΩ in their institute. We think that a low impedance macroelectrode, such as a lesion electrode, is more suitable for recording VEPs than a high impedance electrode. Unfortunately, their results are only briefly summarized and the clinical efficacy of their method remains uncertain.

VEPs recorded from an electrode within the brain are near field potentials and their amplitudes presumably reflect the distance between the electrode and the neural structure originating the potentials. Distinct waves appeared at 1 or 2 mm be-
Table 1 Summary of visual evoked potentials (VEPs), target coordinates, and perioperative Unified Parkinson's Disease Rating Scale (UPDRS) in eight patients

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age</th>
<th>Sex</th>
<th>Tentative target</th>
<th>VEPs (Mid point)</th>
<th>Lesions</th>
<th>UPDRS</th>
</tr>
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<tr>
<td>1</td>
<td>71</td>
<td>M</td>
<td>X = 18, Y = 3, Z = -4</td>
<td>X = 18</td>
<td>1: X = 18, Y = 3, Z = -4; 2: X = 15, Y = 3, Z = -4</td>
<td>92 51</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>F</td>
<td>X = 18, Y = 3, Z = -5</td>
<td>X = 19</td>
<td>1: X = 19, Y = 3, Z = -4; 2: X = 16, Y = 3, Z = -5</td>
<td>96 43</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>F</td>
<td>X = 18, Y = 2, Z = -4</td>
<td>X = 16-20 (18)</td>
<td>1: X = 18, Y = 2, Z = -5; 2: X = 16, Y = 2, Z = -5</td>
<td>86 24</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>M</td>
<td>X = 18, Y = 2, Z = -5</td>
<td>X = 20-24 (22)</td>
<td>1: X = 23, Y = 2, Z = -5; 2: X = 22, Y = 2, Z = -5</td>
<td>99 53</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>F</td>
<td>X = 20, Y = 2, Z = -5</td>
<td>X = 22-26 (24)</td>
<td>1: X = 24, Y = 2, Z = -6; 2: X = 22, Y = 2, Z = -5</td>
<td>63 32</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>F</td>
<td>X = 18, Y = 2, Z = -5</td>
<td>X = 16-22 (19)</td>
<td>1: X = 21, Y = 2, Z = -5; 2: X = 22, Y = 2, Z = -5</td>
<td>55 16</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>F</td>
<td>X = 21, Y = 2, Z = -5</td>
<td>X = 14-18 (18)</td>
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<td>66 46</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>F</td>
<td>X = 20, Y = 2, Z = -5</td>
<td>X = 14-22 (18)</td>
<td>1: X = 19, Y = 2, Z = -5; 2: X = 21, Y = 2, Z = -5</td>
<td>51 21</td>
</tr>
</tbody>
</table>

X, Y, and Z are the distances from the midline, the intercommisural point, and the commissural line, respectively. The first actual lesion site differed from the tentative target by 1 to 5 mm (mean 3.0 ± 1.5 mm, n = 6) in a medio-lateral direction.

low the target and a significant increase of the amplitudes occurred at 5 or 6 mm below. This increase of amplitude strongly suggests that the electrode was in contact with the optic tract. In the medio-lateral direction, potentials were successively obtained in an area of 4 to 8 mm length, which seems to indicate the width of the optic tract. The trajectory on which the most significant potentials were obtained indicates the mid point of the optic tract.

The atlas of Shaltenbrand and Wahren shows that the medial border of the GPi is located above the mid point of the optic tract with the ventral border about 1 mm from the dorsal surface of the optic tract at the level of 2 mm anterior to the midcommissural point. Microelectrode recording of neural activity in the GPi and the optic tract revealed that the ventral border of the GPi is actually located 3 to 4 mm above the optic tract. Therefore, we placed the lesion site on the trajectory which represented the mid point of the optic tract or 1 to 2 mm lateral to it and 5 mm above the point where the amplitudes of potentials increased. Determination of the lesion site in a medio-lateral direction requires measurement of the angle of the trajectory which crosses the vertical plane, because this angle demonstrates how the trajectory passes through the GPi. This angle ranged from 4° to 10° in our patients. A small angle indicated that the trajectory is close to the internal capsule, and the lesion site should be placed on the more lateral trajectory.

Microelectrode recording of neural activity in the globus pallidus is the most reliable method to determine the GPi, because the deficiency of dopamine in PD ultimately results in hyperactivity of the GPi. The patterns of neural discharge differ between the two pallidal segments in the primate model of parkinsonism, as most cells in the internal segment show a characteristic, sustained but irregular, fluctuating high-discharge rate, and those in the external segment exhibit interrupted high- or low-frequency, long lasting bursts. Our experiences with microelectrode recording show it is very difficult to obtain neuronal discharges which are clearly separable from the background noise to confirm their neural discharge pattern. A computer analyzing system which enables "on-line" analysis of the discharge patterns will overcome these problems in the near future. Recording of VEPs can easily and accurately determine the GPi, and in conjunction with micro-electrode recording of neural activity, facilitates identification of the GPi. More data will be needed to define the optimal lesion site in the globus pallidus which yields the maximal clinical efficacy.

References

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Neurol Med Chir (Tokyo) 37, March, 1997


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Commentary

In this interesting and suggestive study the authors described a reliable method to confirm the localization of the electrode for posteroventral pallidotomy (PVP) by means of VEP recordings. Nowadays, PVP for Parkinson's disease is generally accepted as one of the effective surgical modalities to alleviate not only hyperkinetic symptoms but also akinesia and parkinsonian gait. In spite of splendid clinical benefits in some cases, PVP may have rather unreliable operative results comparing with thalamotomy. In this instance, PVP still has problems to be solved concerning the indication, optimal target in the globus pallidus internus (GPI) and its physiological confirmation during the procedure.

At the moment, extracellular recording of the neural activity is thought to be the most reliable method for identification of the target. Pathological parts of the GPI are identified by the spontaneous high-frequency discharges and abnormal kinesthetic cells. The topographical localization of pallidal kinesthetic cells has been studied but unfortunately the relationships with the clinical symptoms of Parkinson's disease are not clear.

Practically, better clinical results can be expected by setting the target in the ventral border of the GPI. With this VEP method, the authors positioned the target 5 mm above the dorsal surface of the optic tract to prevent visual field defect. We are curious to know how far the optimal target is from the optic pathway and whether the lesion should be made within the GPI or together with the ansa lenticularis located ventrally to the GPI. Technical ease and stability of recording conditions are advantageous points of this method in practical use. By accumulating such information, the therapeutic topography in and around the GPI can be established to improve the surgical results and to understand the pathophysiological mechanism in the GPI.

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Nearly all neurosurgeons performing pallidotomy accept that anatomical identification of the target by neuroradiological imaging is insufficient and therefore that some form of neurophysiological confirmation is necessary, both to lessen complications due to damage to the optic tract or internal capsule and to in-
crease the likelihood of a good functional result. There is controversy between experts concerning how far these physiological studies need to be taken. The simplest course is to direct the lesioning macroelectrode to the anatomical target and establish by stimulation to given thresholds that the optic tract and internal capsule are out of range. The most detailed methods map the globus pallidus and optic tract with multiple microelectrode recordings. The latter are more expensive both in time and in equipment and theoretically the increased number of brain penetrations may be related to more risk of cerebral hemorrhage.

This paper summarizes visual evoked potentials data from 8 Parkinson's patients, indicating that good optic tract recordings of VEPs may be obtained using a macroelectrode with averaging. While this certainly indicates the effectiveness of the technique in locating the optic tract, to make several penetrations of the basal ganglia and optic tract at 1 mm intervals in the medio-lateral direction using a probe electrode of 1.1 mm diameter will create a considerable amount of trauma. If any of the authors' attempts to record using microelectrodes were made subsequently down the same tracks, it is not surprising that recorded neural activity was indistinguishable from the background noise. Another factor not taken into account by the authors in their consideration of the apparent discrepancy of the depth of target is the displacement of the brain by insertion of a blunt probe even as small as 1 mm diameter. This displacement produces an overestimation of the depth of insertion. It should not happen using a tapered electrode such as a microelectrode. In the experience of other groups (Lozano et al. cited here as ref. 16), as well as this group, neural activity with excellent signal-to-noise ration can be recorded reliably with a microelectrode to indicate the position of the various cell and fiber groups in the globus pallidus region, including optic tract, without the need for averaging, while if the electrode has a fine taper down to its tip there is relatively little trauma in comparison with that produced by a lesioning probe. In particular, since penetration of the optic tract need only be done for up to 4-5 mm in order to verify the optic tract location, only the narrowest part of the electrode penetrates the optic tract, thus minimizing trauma.

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