Characteristics and distribution of somatosensory evoked potentials in the subthalamic region

MAYUMI KITAGAWA, M.D., PH.D., JUN-ICHI MURATA, M.D., PH.D., HARUO UESEKI, M.D., PH.D., RITSUKO HANAJIMA, M.D., PH.D., YOSHIKAZU UGAWA, M.D., PH.D., AND HISATOSHI SAITO, M.D.

Departments of 1Neurology and 2Neurosurgery, Sapporo Azabu Neurosurgical Hospital, Sapporo; 3Department of Neurology, Tokyo University of Medicine, Tokyo; and 4Department of Neurology, School of Medicine, Fukushima Medical University, Fukushima, Japan

Object. The aim of the present study is to evaluate the topographical distribution of somatosensory evoked potentials (SSEPs) in the subthalamic area, including the zona incerta (ZI). Determination of this distribution may help in the correct placement of deep brain stimulation (DBS) leads.

Methods. Intraoperative SSEPs were recorded from contacts of DBS electrodes at 221 sites in 41 patients: three patients with essential tremor and 38 with Parkinson disease who underwent implantation of DBS electrodes for the relief of severe tremor or parkinsonism.

Results. Two distinct SSEPs were recorded in the subthalamic area. One was a monophasic positive wave with a mean latency of 15.8 ± 0.9 msec, which the authors designated subthalamic P16. Using both cephalic and noncephalic references, subthalamic P16 was only recorded in the ventral part of the ZI (mean 6.6 ± 1.3 mm posterior to the midcommissure point, 4.8 ± 1.2 mm inferior to the anterior commissure–posterior commissure line, and 9.7 ± 0.6 mm lateral to the midline). When bipolar recordings were made, the traces showed a phase reversal at the caudal part of the ZI. The second potential is a positive–negative SSEP recorded throughout the entire subthalamic area. The mean latencies of the initial positive peak and the major negative peak were 13.6 ± 1.1 msec and 16.4 ± 1.1 msec, respectively. Several small notches were superimposed on the peaks, and their amplitudes were largest at the contact close to the medial lemniscus.

Conclusions. The results indicate that intraoperative SSEPs from DBS electrodes are helpful in refining stereotactic targets in the thalamus and subthalamic areas.

Keywords • deep brain stimulation • somatosensory evoked potential • stereotactic target • subthalamus • zona incerta

Over the past decade, DBS has been used in the treatment of various movement disorders. Stimulation of the Vim has generally been used to treat severe tremor, and stimulation of the dorsolateral STN and adjacent subthalamic area can improve all levodopa-responsive symptoms in patients with PD. Recently some groups, including our own, have reported that stimulation of the posterior subthalamic region, which includes the ZI and the prelemniscal radiation, can improve not only severe tremor but also rigidity and akinesia in patients with PD.

Both radiological and electrophysiological studies are important in the determination of optimal target positions for stereotactic surgery. Microelectrode recording of spontaneous neuronal activities is used to ensure optimal placement for treatment. However, when the target is located in white matter areas such as the posterior subthalamic region, it is difficult to determine the target position by relying on recordings of spontaneous neuronal activities. In addition to spontaneous neuronal activities, SSEPs are also used for localizing the electrodes in the thalamus, ML, prelemniscal radiation, and STN. Using a quadripolar implanted DBS electrode, SSEPs can be recorded simultaneously from these four different sites 3 mm apart. We recently reported that SSEPs recorded in the presumed site of the ZI demonstrated a prominent positive component with fine notches. The aim of the present study is to evaluate the topographical distribution of SSEPs in the posterior subthalamic area (including the ZI), which may aid in the correct placement of the DBS lead.

Clinical Material and Methods

Patient Population

We analyzed 221 SSEPs recorded in 41 patients (three patients with essential tremor and 38 with PD) in whom
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DBS electrodes were implanted (Table 1). Electrodes were implanted in the region of the ZI and prelemniscal radiation in three patients with essential tremor and in 16 patients who had PD and a severe resting tremor rated at least 3/4 according to Item 20 of the Unified PD Rating Scale. Electrodes were implanted at the STN in 22 patients with advanced PD and severe motor function fluctuations. Informed consent was obtained from all patients.

Surgical Procedures

The surgical methods used were essentially the same as those previously reported by our group. Axial T2-weighted MR images (Signa Excite 1.5-tesla, General Electric; TR 4000 msec, TE 92.3 msec) were obtained in 2-mm slice thickness without interslice spacing on the day before surgery. The STN, red nucleus, AC, and PC were clearly identified on the high-resolution images. On the day of surgery, after a Cosman-Roberts-Wells frame (Radionics Inc.) had been attached to the patient’s skull, CT scans of 1-mm slice thickness were obtained. The MR and CT images were fused with the aid of ImageFusion (Radionics) so that a high quality of anatomical resolution could be maintained without spatial distortion. Tentative targets in either the subthalamic white matter or the STN were initially determined on the axial MR–CT fused images. The anatomical location of each target was confirmed using AtlasPlan software (Radionics), in which images from the Schaltenbrand–Wahren atlas are superimposed onto MR–CT fused images. The surgical methods used were essentially the same as those previously reported by our group. Axial T2-weighted MR images (Signa Excite 1.5-tesla, General Electric; TR 4000 msec, TE 92.3 msec) were obtained in 2-mm slice thickness without interslice spacing on the day before surgery. The STN, red nucleus, AC, and PC were clearly identified on the high-resolution images. On the day of surgery, after a Cosman-Roberts-Wells frame (Radionics Inc.) had been attached to the patient’s skull, CT scans of 1-mm slice thickness were obtained. The MR and CT images were fused with the aid of ImageFusion (Radionics) so that a high quality of anatomical resolution could be maintained without spatial distortion. Tentative targets in either the subthalamic white matter or the STN were initially determined on the axial MR–CT fused images. The anatomical location of each target was confirmed using AtlasPlan software (Radionics), in which images from the Schaltenbrand–Wahren atlas are superimposed onto MR–CT fused images with registration of the AC and PC as references. The tentative target for the ZI–prelemniscal radiation region was located at a point just lateral to the most lateral border of the red nucleus (~10 mm lateral to the midline), and 3 to 4 mm posterior to the posterior border of the STN on the axial slice in which the STN appeared largest. A trajectory was planned to pass through the Vim–ventrooralis posterior nuclei at an angle of approximately 60° from the AC–PC line. The procedure used to determine the STN target was similar to that reported in recent articles citing the MR imaging–based direct targeting method, and the trajectory was planned to pass through the center of the STN at an angle approximately 50° from the AC–PC line.

Electrophysiological Recording

Intraoperative macrostimulation was used to confirm therapeutic effects and check adverse responses at each target location. The probe was then replaced with a quadripolar DBS electrode (model 3387; Medtronic, Inc.) that had four contacts numbered 0, 1, 2, and 3 from the tip of the electrode. The contacts were 1.5 mm long and spaced 1.5 mm apart. Four extension cords from each contact were connected to different input ports on the evoked potential recorder (Synax, model ER2100; NEC). The Ag/AgCl surface cup electrodes were placed at several points, including the NC (noncephalic reference on the contralateral shoulder), Fz (midline frontal), and CPc (centroparietal). The contralateral median nerve was stimulated at the wrist by applying 5-Hz electric square wave pulses, 0.2 msec in duration, 1.1 to 1.2 times the motor threshold in intensity. Two hundred fifty single responses were averaged using a bandpass filter setting between 2 and 2500 Hz. Recordings were made from the four contacts of the DBS electrode with monopolar noncephalic (0-NC, 1-NC, 2-NC, 3-NC), monopolar cephalic (0-Fz, 1-Fz, 2-Fz, 3-Fz), and bipolar (0-1, 1-2, 2-3) configurations. After the electrode had been firmly affixed to the skull, the SSEPs were recorded again. The averaged responses were stored on data disks of the evoked potential recorder for later offline analysis. The peak latency and amplitude of major components of the SSEPs were measured on the recording provided by the fixed leads.

Electrode Localization

Immediately postoperatively, axial MR images were obtained with the same MR parameters. Using ImageFusion, postoperative MR images were fused with preoperative stereotactic CT scans to make the preoperative coordinate system available for the postoperative images. The deepest contact (Contact 0) was identified on the axial and
sagittal reconstruction images, with careful avoidance of the metallic artifacts that appeared just a few millimeters below the deepest contact. The coordinates of Contact 0 were calculated using the targeting software (StereoPlan, Radionics). The coordinates of the upper contacts (Contacts 1–3) were calculated by retracting the target along the trajectory by 3, 6, and 9 mm, respectively.

Results

Figure 1 shows an example of simultaneous SSEPs from the scalp and four contacts (0, 1, 2, and 3) of the DBS electrode along the trajectory to the ZI and the prelemniscal radiation. The scalp P9, P13/14, and N18 were well identified in the Cpc-NC and Fz-NC lead. The mean latencies of P13/14 and the initial negative peak of N18 were 13.6 ± 1.1 msec and 16.3 ± 1.1 msec, respectively. The scalp N20 was well identified in the Cpc-Fz lead, and the mean latency of N20 was 19.5 ± 1.1 msec.

Subthalamic Region SSEPs with Cephalic and Nonephalic References

Figure 2 shows examples of SSEPs from the DBS electrode along the trajectory to the ZI and prelemniscal radiation (Fig. 2A) and those to the STN (Fig. 2B). Using cephalic (Fz) and noncephalic references, two distinct SSEPs were recorded in the subthalamic area. One was a positive–negative wave recorded in various subthalamic areas including the prelemniscal radiation, ML, and STN. The other was a monophasic positive wave recorded only in the posteromedial subthalamic region. Figure 3 shows the distribution of SSEPs with identical configurations in the Schaltenbrand–Wahren atlas.

Positive–Negative Wave

Positive–negative waves were recorded in the various subthalamic areas including the prelemniscal radiation (2-Fz and 3-Fz, Fig. 1; 3-Fz and 3-NC, Fig. 2A), ML (0-Fz and 0-NC, Fig. 2A) and STN (0-Fz and 1-Fz, Fig. 2B). The peak latencies of the positive–negative SSEPs were almost the same as those of the scalp Cpc-NC and Fz-NC SSEPs (Fig. 1). The mean latency of the positive peak of the biphasic wave was 13.6 ± 1.1 msec (209 SSEPs), which was the same as that of scalp P13/14. The mean latency of the negative peak was 16.4 ± 1.1 msec, which was almost the same as that of N18. The mean amplitudes of the positive and negative peaks in relation to the sites of recording are summarized in Fig. 4. The amplitude of the initial positive peak was maximal in the ventral part of the ZI (6.0 ± 4.3 μV, 27 SSEPs), while the amplitude of the negative peak was maximal in the STN (6.9 ± 2.0 μV, 58 SSEPs).

Several small notches were distributed between initial positive and major negative peaks. The small notches became large when the contact was located close to the ML (Figs. 1 and 2A).
Monophasic Positive Wave

In the posteromedial subthalamic region, a monophasic positive wave was recorded using cephalic and noncephalic references (0-Fz and 1-Fz, Fig. 1; 1-Fz, 2-Fz, 1-NC and 2-NC, Fig. 2A). The latency of the monophasic positive wave was between P13/14 and N18 (15.8 ± 0.9 msec). The mean amplitude was 10.2 ± 4.5 μV. We designated this positive wave subthalamic P16. Subthalamic P16 was recorded only in the posteromedial subthalamic region (mean 6.6 ± 1.3 mm posterior to the MCP, 4.8 ± 1.2 mm inferior to the AC–PC line, and 9.7 ± 0.6 mm lateral to the midline, 12 SSEPs), which coincided with the ventral region of the ZI in the Schaltenbrand–Wahren atlas (filled circles in Fig. 3A). There was a transition of the positive–negative SSEP configurations over the boundary of the ventral region of the ZI and the immediately surrounding area (the ML and the prelemniscal radiation). Several small notches were superimposed on the monophasic positive SSEPs. Using the contact from which the monophasic positive SSEP was recorded, we applied stimulation at a low intensity, which led to improved tremor and rigidity and transient paresthesia in the contralateral hand. Using the deeper contact electrode located near the ML, we applied stimulation at 1.5 V and 130 Hz, which evoked moderate paresthesia in the entire contralateral side of the body.

Somatosensory Evoked Potentials in the Subthalamic Region With Bipolar Recordings

With bipolar recordings, we can minimize the contribution of far-field potentials. Positive potentials with a mean peak latency of 16.5 ± 1.2 msec were recorded in the ventral ZI (1-2 in Fig. 1, 2-3 in Fig. 2A, filled circles in Fig. 3B). The potential with reversed phase at the same latency was located immediately caudoventral to the ZI (between 0-1 and 1-2 in Fig. 2A). Negative potentials with mean a latency of 16.2 ± 0.7 msec, were recorded in the subthalamic region located immediately caudoventral to the ZI (open triangle in Fig. 3B).

From the pairs of contacts located in the dorsal border of the STN and the most rostral subthalamic area, small negative potentials were recorded (0-1, 1-2, and 2-3 in Fig. 2B; filled triangles in Fig. 3B). The mean latency was 16.0 ± 1.2 msec in 38 SSEPs. These negative potentials did not show phase reversal, and the amplitudes of the SSEPs from the lower pair of contacts were smaller than those from the upper pair of contacts (Fig. 2B). In the other subthalamic areas, no significant potentials were recorded with bipolar recordings (53% of SSEP recordings).

Discussion

We recorded SSEPs in response to contralateral median nerve stimulation from DBS electrodes implanted in subthalamic areas. Somatosensory evoked potential configurations depended on locations of the DBS electrode. Using cephalic and noncephalic references, positive–negative SSEPs at peak latencies similar to those of the scalp at P13/14 and N18 were recorded in the entire subthalamic area. In the ventral part of the ZI, a monophasic positive
SSEP at a latency of 16 msec (subthalamic P16) was recorded using both cephalic references and bipolar recordings. Because the ventral part of the ZI is a particularly effective target of DBS for severe proximal tremors, subthalamic P16 can be a landmark for the assessment of the best position for DBS in the posterior subthalamic area.

Monophasic Positive Wave

Monophasic positive SSEPs at similar peak latencies to those measured at subthalamic P16 have been recorded in the Vc. Although the amplitudes of the reported potentials were much larger than at subthalamic P16, there were many similarities between monophasic positive SSEP in the Vc and subthalamic P16. The positive SSEPs in the Vc did not extend to the immediately surrounding areas rostrally (Vim), ventrally (ML), or dorsally (the dorsal part of the Vc and the phase reversal occurred on the boundaries of the Vc–Vim and Vc–ML).

Subthalamic P16 also did not extend to the immediately surrounding areas dorsally (lemniscal radiation), rostrally (STN), or ventrally (ML or fasciculus Q), and showed a phase reversal at the boundary of the ZI and ML. Based on these findings, we consider it...
unlikely that subthalamic P16 was produced by a volume conduction of the positive potential generated at the Vc. In animal studies, the ventral subregions of the ZI have been found to receive dense direct afferent projections from the trigeminal complex and dorsal column nuclei, and to project to the sensory cortex from the rostral pole. Therefore subthalamic P16 may reflect excitatory postsynaptic potentials of neurons in ZI. Because the electrophysiological features of the ZI have not been well defined in humans, more studies of neuronal activities of the human ZI are needed to prove this hypothesis. Another possibility is that subthalamic P16 represents junctional potentials from the ML. Junctional potentials are generated at the bend of the sensory tract. According to the Schaltenbrand–Wahren atlas, the ML has lateral bending at approximately 9 to 10 mm lateral to the midline. This position is compatible with the site of subthalamic P16 potential, and we cannot exclude this possibility from our present results.

Positive–Negative Wave

In previous studies, positive–negative SSEPs with major negativity have been recorded in various thalamic nuclei and in the subthalamic region including the ML,lemniscal radiation and STN. Because the potentials were distributed over a wide recording area and occurred at an equal latency at all recording points, the positive–negative SSEP must be a far-field potential generated by volume conduction from one certain potential generated at one site. Investigators of recent studies have suggested that the potential generated at the cuneate nucleus may partly cause the P13/14 and N18 component of the scalp and subcortical SSEPs. The peak latency of the major negativity of the dorsal column SSEPs recorded from the cuneo-medullary junction is identical to the scalp P13/14. In the present study, most positive–negative SSEPs in the subthalamic region showed no significant potential differences in bipolar recordings, suggesting that they reflect mainly P13/14 and N18.

In bipolar recordings, small negative potentials with a peak latency of 16 msec were recorded in the rostral subthalamic area and at the dorsal border of the STN, which can be a landmark for the dorsal border of the STN. These potentials displayed a tendency for caudorostral increments in amplitudes, and did not show phase reversal. Hanajima et al. have also reported similar negative potentials recorded near or in the STN at similar latencies, which also displayed a tendency toward caudorostral increments in amplitudes. These findings suggest that there is a gradient in the positive (thalamic) to negative (STN) shift that is steep at the ventral border of the thalamus. In the present study, the amplitude of the negative peak was significantly high in the STN. However, the mean peak latency of 16 msec is too short to assume the STN neurons to be a generator because the STN does not receive direct afferent nerve impulses from the medial lemniscal pathway but receives projections from neurons in the primary motor cortex.

Small Notches Superimposed on Subthalamic SSEPs

Several studies have reported small notches superimposed on SSEPs in the thalamus and subthalamic region. In the present study, the amplitude of the small notches superimposed on SSEPs recorded in the posterior subthalamic region was larger at the lower contact located closer to the ML, suggesting that high-frequency components of subthalamic SSEPs may be generated in the lemniscal system.

Conclusions

Our results indicate that the direct recording of SSEPs with DBS electrodes is a practical method for refining stereotactic targets in the subthalamic area. Subthalamic P16 can be a landmark for the ventral ZI. Small negative SSEPs were recorded in the rostral region of the ZI. The small negative potentials may be a landmark for the target of the electrodes for DBS of the STN.

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References


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Address reprint requests to: Mayumi Kitagawa, M.D., Ph.D., Sapporo Azabu Neurosurgical Hospital, North-40 East-1, Higashi-ku, Sapporo 007–0840, Japan. email: kitagawa-jscn@umin.ac.jp.