Bifocal cortical electrical stimulation for pain by interdural implantation of the electrodes

Report of 4 cases

DAMIANOS E. SAKAS, M.D., THEOFANIS N. FLASKAS, M.D., IOANNIS G. PANOURIAS, M.D., AND NIKOLAOS GEORGAKOULIAS, M.D.

Department of Neurosurgery, Medical School, University of Athens, Evangelismos General Hospital, Athens, Greece

Chronic electrical cortical stimulation (ECS) is an evolving therapy for alleviating treatment-refractory chronic pain syndromes. In this report, the authors describe a modified technique of ECS that involves resection of dural strips and interdural placement of the electrodes as a patch, and bifocal stimulation by implanting 2 electrode strips, that is, one over the motor and one over the sensory cortices.

The technique was used in 4 patients with treatment-refractory pain syndromes: a 76-year-old woman with poststroke central pain, 2 women, (71 and 73 years old) with trigeminal pain, and a 44-year-old man with phantom limb pain. All 4 patients experienced a sustained significant improvement in the intensity of pain and have gained a substantially improved functionality and quality of life. An important finding in these patients was the constancy of impedance within a narrow values range throughout the postoperative period. For the cases, the follow-up exceeds 24, 15, 12, and 9 months. The factors affecting the efficacy of ECS are discussed. In the authors’ opinion, interdural implantation of the electrodes holds the promise to improve the efficacy and consistency of ECS compared with the standard epidural or subdural implantation without increasing the risk of the procedure. The technical considerations and the potential therapeutic advantages of the interdural bifocal approach are discussed.

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KEY WORDS • cortical stimulation • deafferentation pain • interdural electrode • poststroke central pain • surgical technique • trigeminal neuralgia

Since the first application of epidural electrical motor cortex stimulation for treating central deafferentation pain in 1991, the method has been used to alleviate various refractory pain syndromes. Alternative therapeutic approaches of ECS have been the implantation of the electrodes subdurally, inside the central sulcus, or the stimulation of the sensory cortex. It is hypothesized that motor ECS acts by modulation of the sensory input at the thalamus, while sensory ECS acts by modulating the disorganized cerebral zone that surrounds the deafferented sensory cortex.

Several parameters have been examined for their potential role in the efficacy of ECS such as bipolar versus monopolar stimulation, the positioning of the electrode (perpendicular or parallel to the central sulcus), the precision in positioning the electrode, the electrical stimulation algorithms, the nervous system plasticity, and the thickness of the intervening dura or the CSF layer. Various methods have been investigated to achieve maximum accuracy of cortical targeting, eliminate the risk of electrode migration, and minimize interference of the dura in the therapeutic effect.

In the presented cases, the standard ECS technique has been modified in 2 respects: the electrodes are implanted interdurally, that is, in a patchlike fashion, and are placed not only over the motor but also over the sensory cortex. Hence, the stimulation can be offered either as unifocal, that is, single motor or sensory, or bifocal stimulation, that is, simultaneous stimulation of both motor and sensory cortices. To the best of our knowledge, this particular protocol for ECS has not been previously reported.
Bifocal interdural electrical cortical stimulation

Case Reports

Study Design and Clinical Assessment

All patients had a thorough clinical and laboratory investigation and were examined repeatedly pre- and postoperatively by an independent neurologist and a psychiatrist; the pain intensity was scored on the VAS pre- and postoperatively during all programming sessions. The imaging studies included brain MR imaging, spectroscopic analysis of both thalami, tractography of corticospinal axes, and functional MR imaging (both motor and sensory). Postoperatively, the patients were evaluated both on and off stimulation and during stimulation with different parameters, in random order, and on separate days. The patients, the neurologist, and the psychiatrist were unaware of whether the stimulation was on or off or which program was on at any time. The patients received no other treatment during the study period. The postoperative follow-up was made at 3-month intervals.

Summary of Cases

Case 1. In 2003, this 76-year-old woman suffered an ischemic stroke in the right thalamus; initially, this caused numbness on the left side of her body. Over the next few months, this complaint was replaced by allodynia in the same body area. Gradually, the problem evolved into a continuous torturing, rather burning pain of the left hemisoma with fluctuations of intensity from 7 to 10 on the VAS. The pain was less severe in the morning, but it worsened throughout the day, particularly during body movements or during periods of emotional stress. The clinical examination was unremarkable. Somatosensory evoked potentials of the left arm (median nerve) and the left leg (posterior tibial nerve) were consistent with a right thalamic stroke lesion. Over the next 4 years, the medical treatment included morphine, barbiturate, gabapentin, and ketamine; these proved effective only for brief periods. The pain remained unabated, and the patient developed severe depression.

Case 2. This 71-year-old woman presented with a 20-year history of medically refractory left trigeminal neuralgia more pronounced in the distribution of the first division. In 2000, she was offered left trigeminal nerve microvascular decompression at another unit. The pain remission was immediate but transient. Over the next few years, the patient developed incapacitating pain with attacks and remissions on the left side of her face. The pain was severe, radiating to the top of the head, making daily activities such as chewing, swallowing, or speech insufferable. On examination, both light touch and pin prick sensation were abolished in the distribution of all branches of the left trigeminal nerve. The patient presented with the first symptoms of phantom limb syndrome in the form of burning pain and dysesthesias. Epidural cervical cord stimulation was offered 6 years earlier, in 2003, but with poor analgesic effect, and the system was removed 5 months later. Over the past 6 years, all appropriate analgesic and psychiatric medications and their combinations were offered but with minimal benefit.

Anesthetic Technique

All patients were underwent surgery under general TIVA with propofol and remifentanil. Anesthesia was induced with a loading dose of remifentanil 34 ng/ml in continuous infusion followed, after 5–8 minutes, by propofol 5.5 μg/ml as induction dose. After endotracheal intubation, no muscle relaxants were administered. Anesthesia was maintained with remifentanil 5–6 ng/ml and propofol in a range between 2.5 and 3.0 μg/ml to obtain a steady level of anesthesia. During the period of evoked potentials recording, no further administration of drugs in bolus was necessary to maintain a steady anesthetic state. At the end of the surgical procedure, all patients were awakened within 15–30 minutes from the end of TIVA, and none of them had cardiovascular or respiratory complications in the recovery room.

Surgical Procedure

All patients underwent a preoperative brain MR imaging (T1 3D axial sequence with 0.9-mm slice thickness) covering the head from the skull base up to the air. Paramagnetic skin markers (fiducials) were placed on the patient’s head prior to MR imaging, as guidance points, for intraoperative registration. Surface match utility was also used to decrease the registration error less than 0.2 mm. Segmentation of the MR image was performed, and the 3D model of the patient brain was created. In the operating room, each patient was placed in the lateral decubitus position and the head was turned 90° toward the side of the pain and securely affixed in a vacuum headrest. The projection of the central fissure on the scalp was
defined by craniometric landmarks (Haughton-Taylor lines) and neuronavigation guidance (Omnisight Excel, Radionics). A U-shaped skin incision of 6 cm on each side and a 4 × 6–cm craniotomy with 4 bur holes centered on the central sulcus were performed. The size of the craniotomy was large enough to accommodate two 28 × 6–mm electrode arrays, that is, one over the motor and one over the sensory cortex (Lamitrode, Advanced Neuromodulation Systems). Then, a U-shaped linear incision of the dura was made at least 0.5 cm apart from the craniotomy edges to preserve sufficient dura mater for wound suturing and watertight closure of the dura. The dural flap was reflected and the central sulcus, and the motor and sensory cortices were identified (Fig. 1). The intraoperative neurophysiological mapping of the motor cortex was performed using the stimulator and monitoring system Avalance XT & Twister (Langer Medical). A cortical stimulation probe was used to deliver stimulation train pulses with a frequency of 5.3 Hz, pulse width of 200 μsec, and 1 msec interval of a 5-train stimulus up to 8 mA intensity. Muscle responses were recorded with needle electrodes from the muscle bellies of the contra-lateral hemisoma (frontalis, masseter, thumb, upper and lower eyelid, upper and lower lip, and calf). The mapping of the motor cortex was performed in an orientation parallel to the central sulcus starting from the face representation area and proceeding toward the area of trunk in 3-mm intervals. Once this was completed, the mapping was repeated in the opposite direction, that is, from the area of trunk to the area of face.

In the dural flap, 2 dural strips, similar in size and shape to each of the two 8-polar strip electrodes, were resected exactly over the cortical motor and sensory representation areas of the face and arm and trunk. The strip electrodes were positioned in the place of the resected dural strips, in a patchlike fashion and were sutured to the edges of the dura in a position parallel to the central sulcus. The entire dura flap was reversed to its original position and sutured with many stitches back to the edges of the surrounding dura (Fig. 2). A groove was made in the inferior aspect of the craniotomy to allow the passage of the electrodes. Synthetic dura (TISSU DURA, Baxter International, Inc.) and glue (DuraSeal, Confluent Surgical, Inc.) were applied on top of the patient’s dural flap to ensure watertight closure and eliminate the risk of CSF leakage. The bone flap was repositioned firmly in place with 4 absorbable plates (INION, Inion Oy). The bur holes were sealed with bio cement (PALACOS R+G, Heraeus Medical GmbH) to prevent CSF pulsation and any compromise of the scalp. The scalp was closed in the standard fashion. The 2 electrodes (Lamitrode, Advanced Neuromodulation Systems) were tunneled and connected to an implantable pulse generator (Eon Neurostimulation System, Advanced Neuromodulation Systems) that was inserted in the subclavicular region. The function of the generator was verified intraoperatively, and the parameters of the stimulation that caused muscle contraction were noted. The entire procedure required 3 hours to be completed.

Postoperative Course

A lateral scalp radiograph verified the correct location of the strip electrodes (Fig. 3). Antiepileptic therapy and antibiotics were given prophylactically for 1 month and 2 days, respectively. No intra-, peri-, or postoperative seizures related to mechanical irritation of the cortex by the interdurally placed electrodes were noted. During the trial stimulation period, however, the patient in Case 1 developed a brief episode of focal seizures of the left hand when stimulation amplitude increased above 8 mA. This adverse effect was induced by stimulation intensities

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**Fig. 1.** Intraoperative view of the central sulcus, the motor and sensory cortices, the intact arachnoid membrane, and the reversed dural flap.

**Fig. 2.** Intraoperative image showing the interdural placement of the 2 strip electrodes and the closure of the dura.
the impedance values remained constant within a narrow range from 480 to 520 Ω. Bipolar stimulation with the electrode over the motor cortex functioning as the cathode (negative contact) and the electrode over the sensory cortex functioning as the anode (positive contact) offered a further considerable reduction in pain intensity, thus making the patient pain free. The most effective stimulation parameters were frequency 120 Hz, pulse width 150 msec, amplitude 4–5 µA, and cyclical mode stimulation (15 minutes on and 1 hour off). At the latest follow-up 15 months postoperatively, the patient has regained a normal quality of life without taking any analgesic medication.

In Case 3, single motor ECS started on the 3rd postoperative day but was discontinued after 2 days due to the appearance of mild weakness and loss of dexterity in the left hand. The patient’s symptoms subsided after appropriate adjustments of stimulation settings. Single motor cortex stimulation was then offered for the next 5 days and offered a 60% improvement in pain relief. Single sensory ECS was offered for the following 5 days. The left-hand weakness and loss of dexterity had further considerable improvement, whereas the pain improved by 30% on the VAS. Bifocal motor/sensory stimulation was commenced 15 days after the operation. This offered substantial additional improvement; the pain intensity was reduced by 80%, and the residual mild hand weakness resolved completely. Notably, the impedance remained again constant within a narrow range from 480 to 550 Ω throughout the entire programming period. The best result was obtained with the following stimulation parameters: amplitude 3 mA, frequency 66 Hz, pulse width 350 msec, and cyclical mode stimulation (30 minutes on and 1 hour off). At the latest follow-up at 12 months, the reduction in pain intensity has remained at 80%.

In Case 4, single motor ECS started on the 2nd postoperative day. The phantom limb pain improved by 60% and became restricted at the hand only. However, on the 5th postoperative day, motor ECS was discontinued due to severe dysarthria and persistent dysesthesias on the right side of the patient’s body. Subsequently, single sensory ECS was administered for 5 days and offered an 80% overall improvement. Again, however, the undesired dysesthesias persisted despite many adjustments of stimulation parameters. On the 10th postoperative day, bifocal stimulation was commenced. This offered a 90% improvement in the pain sensation over the entire arm area that was previously affected by the phantom limb pain while minimizing the side effects of unifocal ECS. The best analgesic effect was achieved when changing polarity so that to stimulate only the upper part of the motor and sensory cortices where the hand area is represented. The most effective stimulation parameters were amplitude 3.5 mA, pulse width 250 msec, frequency 180 Hz, and cyclical mode stimulation (40 minutes on and 1 hour off). Notably, the impedance remained again constant within a narrow range from 500 to 550 Ω. At the latest follow-up 9 months postoperatively, the patient, for the first time after his injury, has been experiencing a virtually pain-free daily life and has become again happy and optimistic about the future.

In the presented 4 cases, the improvement in pain in-
Rationale of the Reported Technique

Case 2, 70%; Case 3, 60%; and Case 4, 60%. The improvement in pain intensity by single sensory ECS was as follows: Case 1, 40%; Case 2, 20%; Case 3, 30%; and Case 4, 80%. The improvement rate of combined motor/sensory stimulation was Case 1, 80% (face, 90%; arm, 70%); Case 2, 100%; Case 3, 80%; and Case 4, 90%. In summary, in the presented series, single sensory ECS offered 32.5% improvement in pain intensity, single motor ECS 57.5% and combined motor/sensory ECS 87.5%. The highest possible benefits resulted from combined stimulation of the motor/sensory cortices.

Discussion

Rationale of the Reported Technique

Motor cortex stimulation has proved to be an effective alternative treatment in alleviating intractable pain syndromes. Most ECS approaches, however, have been associated with either lack of consistency or reduction of efficacy in the long term. In an effort to achieve maximum accuracy of cortical targeting, eliminate the risk of electrode migration, and minimize the interference of dural thickness in the therapeutic effect, we selected to implant the electrodes interdurally, that is, in a patchlike fashion. Furthermore, given the small number of pain sufferers who are considered candidates for ECS, we decided to implant electrodes over both the motor and sensory cortices to be able to offer either unifocal (exclusively motor or sensory) or bifocal (combined motor and sensory) stimulation. Such an approach would allow us to have as many stimulation options as possible and, in the long term, to identify which types of pain respond better to which type of stimulation.

Technical Considerations

It is important to verify by neuronavigation and neurophysiological monitoring, throughout the procedure, that the approach is centered on the central sulcus, and to perform meticulous watertight wound closure to prevent CSF leakage and potential infection. In our experience, TIVA with propofol and remifentanil appears to provide the most favorable anesthetic and neurophysiological properties for cortical mapping. These drugs have a very short half-life, allowing intraoperative monitoring of motor system and early postoperative neurological evaluation, without increasing the risk of anesthesia-related side effects. The interdural technique appears to be inherently safer, more stable, and more precise than subdural placement because, in the former, the electrode is anchored by sutures at the edges of the dural opening; this minimizes pressure on the brain and the risk of electrode migration, subdural hematomas, or seizures. Notably, in all cases, we found that the values of impedance remained constant within a narrow range compared with the epidural stimulation procedures in which, in our experience, the impedance values can vary quite widely. This possibility of offering stimulation with higher accuracy and long-term efficacy compared with epidural ECS outweighs the modest additional technical effort and time needed for the interdural approach.

In the presented approach, in addition to the interdural anchoring of the electrode, we also implanted the electrodes over both the motor and sensory cortices in 1 procedure. This made it feasible to investigate the efficacy of not only unifocal (either single motor or single sensory stimulation) but also of bifocal (combined simultaneous motor and sensory stimulation). Sensory ECS has been tried in a much smaller patient population than motor ECS because of the uncertainties with respect to its efficacy. Our technique allows us to explore the efficacy of sensory stimulation in various pain syndromes; notably, if sensory stimulation proves ineffective, the attending physician can revert to either single motor ECS or to combined motor/sensory ECS without subjecting the patient to further surgery. Bifocal interdural ECS could prove particularly helpful in patients like those in Cases 1 and 4 in whom single motor cortex stimulation offered small improvement, and sensory cortex needed to be stimulated as well for alleviating pain. It should be pointed out that the patient in Case 4 had received cervical chronic spinal cord stimulation for 5 months 6 years ago, had negligible improvement, and requested removal of the device. Hence, the present very good response of this patient to bifocal ECS supports the suitability of interdural bifocal stimulation for phantom limb pain.

Conclusions

Nowadays, new noninvasive techniques such as transcranial magnetic stimulation and transcranial direct current stimulation are expected to provide new indications for the therapeutic use of ECS by implantable electrodes. These developments make pressing to readdress the issue of what is “the most appropriate interface” of the electrode with the brain, that is, “with or without” the presence of the dura. The presented interdural placement of electrodes is a feasible, safe, and effective technique for ECS. The above technique allows the following: comparable safety to epidural ECS, stability of impedance because variations due to the interference of the dura are no longer present and higher accuracy in implanting the electrode over the selected cortical area. The potential advantages of interdural ECS that should be further evaluated include the following: minimal risk of electrode migration due to its secure anchoring with multiple stitches in the surrounding dura, easier postoperative programming of stimulation and optimization of clinical benefit in fewer follow-up sessions, improved clinical efficacy, and longer battery life due to the lower intensity of electrical current needed to achieve therapeutic effect. In our opinion, it is imperative to open this field for further investigation. Studies are needed to evaluate and confirm the clinical and surgical advantages of interdural unifocal (motor or sensory) or bifocal (combined motor/sensory) over the standard epidural ECS and assess the potential role of this new technique in the therapeutic armamentarium for intractable central pain syndromes.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
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Author contributions to the study and manuscript preparation include the following. Conception and design: Sakas. Acquisition of data: Sakas, Flaskas, Panourias. Analysis and interpretation of data: Sakas, Flaskas, Panourias. Drafting the article: all authors. Critically revising the article: Sakas, Panourias, Georgakoulas. Reviewed final version of the manuscript and approved it for submission: all authors. Administrative/technical/material support: Flaskas, Panourias, Georgakoulas. Study supervision: Sakas.

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