169 Stimulation of the Hippocampus and the Seizure Focus

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Introduction

Neuromodulation has been used as an alternative nonlesional surgical procedure for patients with intractable epilepsy. Several targets for such modulation have been proposed. Cerebellar [1–3], centromedian thalamic [4–6], vagal nerve [7–9], anterior nucleus of the thalamus [10] and subthalamic nucleus [11] stimulation have all shown variable degrees of efficacy in decreasing either primary or secondary generalized seizures.

Regardless of the chosen target, neuromodulation has proved to be very well tolerated by patients. If adverse effects occur, there are options in changing stimulation parameters such as decreasing intensity, frequency, or changing stimulated contacts. Another advantage is that there is no deterioration of neurologic functions. On the contrary, improvement in the performance of ability scales of patients with Lennox-Gastaut Syndrome who have undergone chronic stimulation of the thalamic centromedian nuclei have been reported [12].

The above mentioned targets are stimulated with the purpose of influencing seizure propagation or the excitability of large cortical or subcortical areas; they are not directed to the epileptic focus itself. As a result, their effect on partial seizures has been limited. Our experience, as well as other Epilepsy surgery clinics [13,14] is that 70% of referrals for epilepsy surgery are patients with focal onset of epileptic discharges in mesial temporal lobe. Even though ablative surgery in these cases has demonstrated to be very efficient in reducing or eliminating seizures [15–19], there are a number of patients in whom there is a high risk of neurologic sequelae, for example patients with epileptic focus localized in dominant hippocampus have high risk of memory deficit [20,21] and [22]; which is even higher in resection of bilateral hippocampal foci can produce amnesia [23].

In these patients, a reversible nonlesional method such as neuromodulation is a very attractive option.

Rationale for Using Hippocampal Stimulation

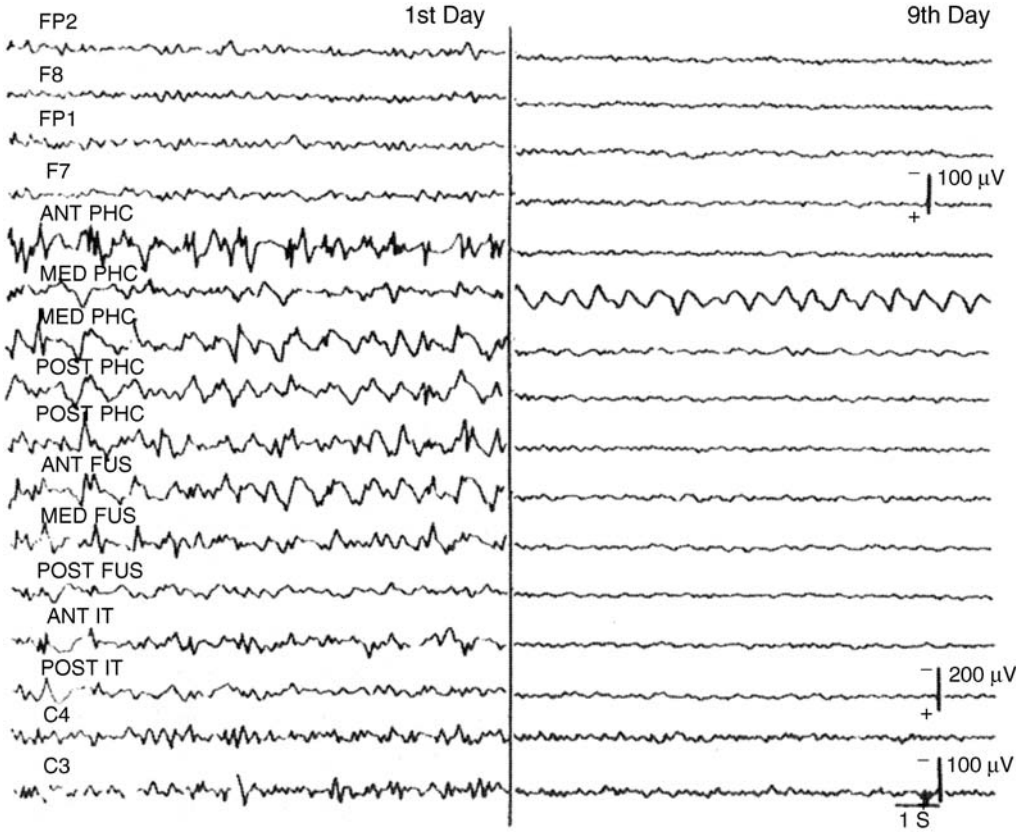
Susan Weiss and her group [24] observed that low level direct current inhibits amygdala kindling in rats. The rats were implanted with depth electrodes in the temporal lobe amygdala and were intended to be used for electrical stimulation in a kindling paradigm to produce seizures and afterdischarchges. She applied simultaneous continuous 1–5 μA DC current delivered through the same depth electrode and observed that this stimulation disrupted epileptogenesis. In fact, these rats could not be kindled and instead, they showed an increase in the threshold to induce afterdischarges. This antiepileptic effect was named *quenching*. We performed initial study based on Weiss's observations an in ten patients with intractable mesial temporal lobe epilepsy, candidates for temporal lobectomy, in whom diagnostic hippocampal electrodes or basotemporal grids were implanted

for epileptic foci localization. Once the epileptic focus was detected, patients underwent a 3 week trial of continuous 130 Hz, 300 μA, 450 μs pulse width, electrical stimulation. Thereafter, patients underwent temporal lobectomy. In seven out of ten patients, seizures stopped after 6 days of stimulation and EEG showed a significant reduction of interictal spikes (*Figure 169-1*). Our conclusion was that electrical stimulation of epileptic focus arrested epileptic seizures within a period of days [25]. Those patients had no MRI evidence of mesial temporal sclerosis, whereas those areas that did not improve have. This was not realized in the first report and failure in improvement was attributed to other factors such as failure to reach the precise stimulation target.

To have been able to perform a temporal lobectomy after the stimulation trial permitted us to study the epileptic tissue under light microscopy. The surgical specimens of stimulated temporal lobes were compared with specimens from other ones obtained from epileptic patients who underwent diagnostic electrode implantation,

Figure 169-1

The effect of subacute stimulation on electroencephalogram background activity. Two 10 s samples of maximal paroxysmal EEG activities in records performed on day 1 and day 9 of stimulation. Recordings were made from surface right and left fronto-temporal (FP2, F8, FP1, F7), central (C4, C3) and left subdural anterior (ANT), medial (MED) and posterior (POST) parahippocampal (PHC), fusiform (FUS), and inferior temporal gyri (IT). All EEG recordings were referred to ipsilateral ear lobe electrodes (A2 and A1). On day 1 there was a large number of interictal spikes and slow waves in all subdural recordings, which were more prominent in the anterior parahippocampal gyrus where the seizures initiated. After 9 days of subacute stimulation of the epileptic site, both spikes and slow waves disappeared. In addition a monomorphic delta activity appeared in the medial parahippocampal region (immediately posterior to the stimulated region)



but were not stimulated. The pathologist was asked to report differences between the adjacent brain tissue to electrode contacts used for stimulation and those that were not stimulated in the same patient [26]. The histopathology abnormalities consisted in diffuse, moderate gliosis and cell loss of cortical layers I and II, increase in mononuclear inflammatory cells in the subarachnoid space and meningeal thickening of the cerebral tissue attached to the electrode grid. Similar abnormalities were found in depth electrode trajectories, most likely in relation to body reaction to the presence of the silastic sheet of the electrodes. The pathologist was unable to determine which contacts of the grid or area of the trajectory of the hippocampal electrodes had been stimulated. Therefore, seizure reduction in the stimulated patients was related to electrical stimulation and not to microlesions induced by the implanted electrodes.

We performed neurophysiologic tests such as producing epileptogenic afterdischarges, as Weiss et al. used [26], recovery cycle tests, as well as SPECT studies to try to explain the mechanisms through which the stimulation produced its antiepileptic effect [25,27,28,29)]. We compared basal conditions with 3 weeks stimulation conditions (previous to lobectomy).

Producing hippocampal afterdischarges by using acute local electrical stimulation is a technique used to evaluate the susceptibility of cerebral tissue to present clinical and electroencephalographic epileptic responses. For this purpose, we applied short (10 s) trains of high frequency (130/s) 1.0 ms duration square pulses and increasing intensities every 5 V to the site of the EEG epileptic foci. The threshold (μA) and duration of afterdischarges were measured. *Figure 169-2* shows the afterdischarge obtained in basal condition (previous to subacute hippocampal stimulation) in the upper record. An 88 s afterdischarge consisting of fast-frequency recruiting EEG spikes initiated at the contiguous hippocampal amygdaloidal region, which propagated to the other parasagittal and lateral regions bilaterally, was elicited by acute 8 s stimulation at 560 μA. This afterdischarge was accompanied by a clinical complex partial seizure (epigastric sensation, behavioral arrest, right adversion of the head, left hand exploratory automatisms). The lower record shows the response obtained in the same patient after 560 h of subacute hippocampal stimulation. We had to increase stimulation intensity to 5,300 μA to elicit only a few spikes in the area, with no propagation and no accompanying symptoms.

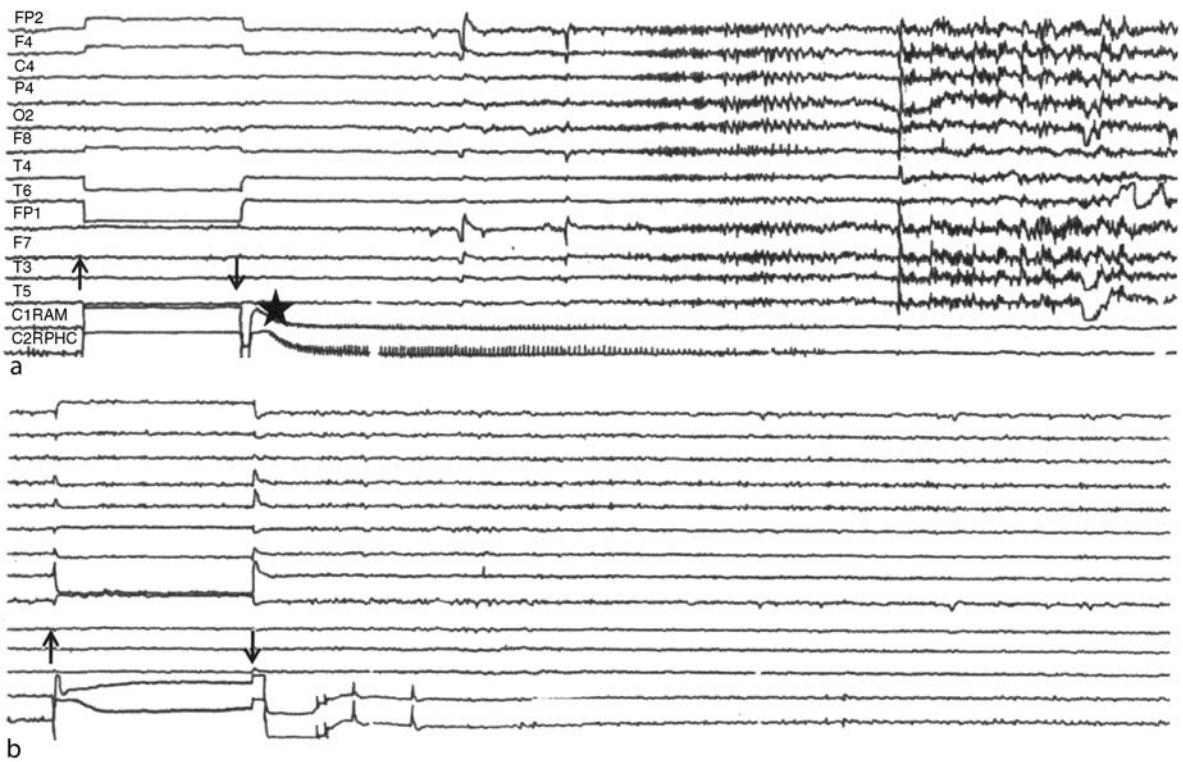
The recovery cycle test (*Figure 169-3*) is an electrophysiological technique that evaluates changes in neuronal excitability. It consists of the application of a pair of pulses with identical physical characteristics to evoke a response, applied at different interstimulus time intervals. As shown in *Figure 169-3a*, when we stimulated the amygdala and recorded the hippocampus in basal condition, the paired pulses had similar amplitudes when the interstimulus interval between the first (conditioning) and the second (test) response was over 100 ms. As the stimulus interval shortened, the amplitude of the test response decreased (refractory period). When compared to the recovery test obtained from the same patient after sub acute hippocampal stimulation, the test response never reached the amplitude of conditioning response suggesting an inhibitory effect (*Figure 169-3b*).

Single photon emission computed tomography (SPECT) is used to evaluate the regional cerebral blood flow (rCBF) perfusion as and indirect evidence of hyper or hypo metabolic neuronal dysfunction. *Figure 169-4a* shows the basal SPECT in a patient with left temporal epilepsy demonstrating hypoperfusion in the corresponding area. *Figure 169-4b* in same patient after sub acute hippocampal stimulation shows a further decrease in (rCBF) in the stimulated hippocampal area.

Compared to basal conditions, the results after the hippocampal stimulation showed that afterdischarges were blocked, paired pulses diminished

Figure 169-2

Effect of subacute stimulation on afterdischarges in patient KG 111: 2A shows the threshold and duration of the afterdischarge produced by acute stimulation of the right anterior parahippocampal gyrus with 8 s trains of rectangular pulses (130/s and 1.0 ms) before initiating subacute stimulation. Threshold stimulation of 600 μA produced an 80 s afterdischarge initiated in the amygdala PHC region close to the stimulation site (indicated by the star), which spread 10 s later to the right and left fronto-temporal scalp regions. The afterdischarge was accompanied by symptoms of a spontaneous complex partial seizure. 2B shows that after 560 hrs of subacute stimulation, the threshold for the afterdischarge increased to 5,300 μA and its duration decreased from 80 to 8 s, with no clinical symptoms. (Arrows indicate ON and OFF for the 8 s trains to obtain afterdischarges)



their amplitude and SPECT showed decreased rCBF in the stimulated area. Moreover, determination of benzodiazepine receptor binding measured by autoradiography was used to evaluate the activity of GABA system receptors, indicative of neuronal inhibition of the stimulated hippocampal region. There was an increase of hippocampal benzodiazepine receptors density in those patients who had undergone hippocampal stimulation compared to non stimulated tissue, obtained from temporal lobectomies in epileptic patients who had not undergone subacute stimulation [29].

Chronic Hippocampal Stimulation

Patient Selection

In our experience, 30% of intractable temporal lobe epilepsy patients undergo bilateral hippocampal electrode implantation for diagnostic purposes before performing a temporal lobectomy. From this group of patients we selected nine for chronic electrical stimulation of the hippocampal foci [30]. We settled the criteria for selection according to the following parameters:

Figure 169-3

Effect of subacute hippocampal stimulation on recovery cycles of the amygdala hippocampal evoked responses. 3a shows basal condition, note that paired pulses had similar amplitudes when the interstimulus interval between the first (conditioning) and the second (test) response is 100 ms. As the stimulus interval shortened, the amplitude of the test response decreased. 3b shows the recovery test obtained from the same patient after sub acute hippocampal stimulation, the test response never reached the amplitude of conditioning response

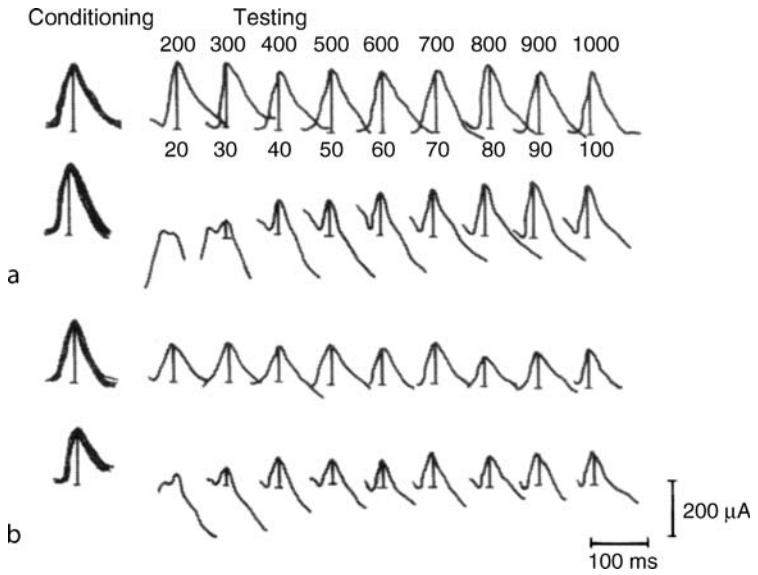
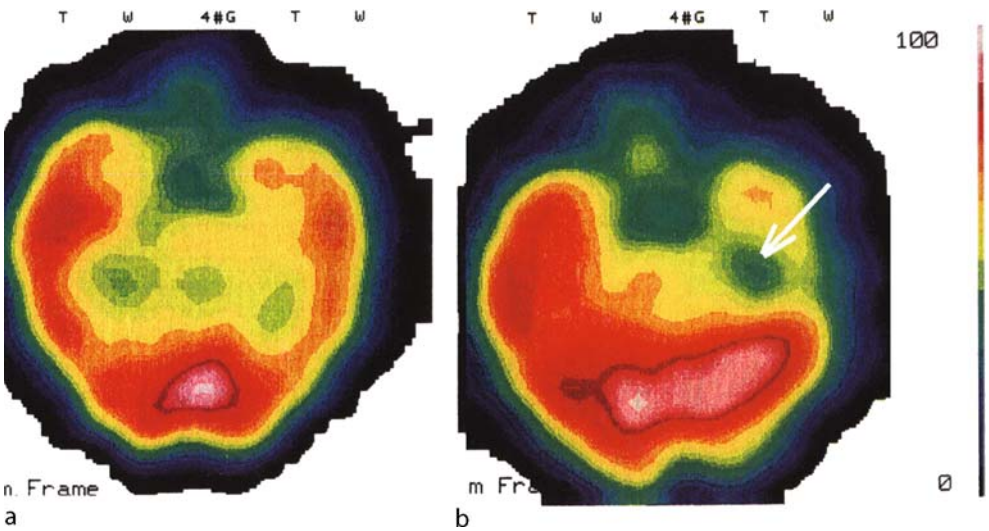


Figure 169-4

SPECT studies of same patient before (a) and after (b) 360 hrs of subacute electrical stimulation. Note that there was a relative hypoperfusion of the left epileptic hippocampus compared to that of the right hippocampus in basal conditions. Arrow shows that the hypoperfusion is more evident in the left hippocampus after 360 hrs of subacute stimulation



1. Four patients with bilateral hippocampal epileptic foci which were confirmed with depth EEG recording of several seizures arising independently from both hippocampuses. These patients would have been rejected for bilateral ablative surgery because of the resulting severe amnesia [22].
2. Epileptic focus localized on dominant hippocampus. It has been established by several authors that temporal lobectomies affect verbal memory when ablative surgery is performed in dominant hemispheres [21,22], so as a result, either they are rejected as surgical candidates or limited resections are performed with the consequent seizure persistence and elevated risk of memory loss. Three patients with left hippocampal foci with neuropsychological tests showing left dominance were included.
3. Two patients with right hippocampal foci were also included, one of them because she had bilateral hippocampal sclerosis in MRI imaging and the other because there was independent interictal activity in the left hippocampus.

The group consisted of 6 males and 3 females, ages ranging from 14 to 43 years, with seizure onset between 3 and 16 years of age, seizure number varied from 15 to 70 seizures per month (average 28). The study protocol for epilepsy surgery was followed [5]. All of them had complex partial seizures; seven had secondary tonic clonic generalized seizures. All were right handed. According to the neuropsychological tests battery that was applied (*Table 169-1*) [31–35] and [36], six patients had mild memory impairment in neuropsychological tests and three of them had severe abnormalities. Serial EEGs were abnormal with bitemporal paroxystic epileptic activity and secondary bilateral synchrony. The magnetic resonance studies were normal in five patients, three had left hippocampal sclerosis and one had bilateral hippocampal sclerosis. All patients had undergone several trials of antiepileptic drugs without obtaining seizure control and were willing to participate and sign the informed consents. The study was reviewed and approved by the Scientific and Ethical Committee of the General Hospital of Mexico.

Table 169-1

Neuropsychological tests battery used to evaluate patients. Notice that special interest was centered in memory and language dominance. All tests used were standardized for Spanish speaking patients

Test	Function
Dichotic listening test	Language dominance
Neuropsi Attention and Memory Battery	
Rey verbal learning	Verbal memory
Digit Counting	Verbal memory
Logic memory	Verbal memory
Visual reproduction	Non verbal memory
Wind Mill visual spatial Bezarez Test	Non verbal memory

The Committee agreed on an aleatory (randomized by lottery number) double-blind maneuver with an initial 1 month OFF period in one half of the subjects; the other half initiated stimulation immediately after stimulation system internalization.

Surgical Procedure

The selected patients had a 3 month seizure baseline for reliable seizure calendars and afterwards were hospitalized to undergo diagnostic depth electrode implantation. The surgical procedure was performed in two stages. In the first stage an eight contact, spaced 0.7 mm from center to center, were implanted from an occipital approach. The stereotactic frame was fixed under general anesthesia and the patient was placed in ventral *decubitus* to have a double contrast enhanced CT scan. Two and a half mm CT axial sections were

taken to be fused with preoperative MRI sections taken the day before surgery. On the fused image, virtual trajectories that traversed the entire hippocampus, avoiding blood vessels and ending in the basal part of the temporal lobe amygdala were planned. Those trajectories had a lateromedial angle of 10–15°, starting 26.0–30.0 mm in the skull entrance and ending 22.0–25.0 mm lateral to the midline. It is important to mention that the estimated center of the planned burr holes averages 3.0 cm lateral to the midline. Therefore, about 10.0 cm distance between the pins that will fix the posterior part of the skull is required. This has to be taken into consideration when placing the stereotactic frame.

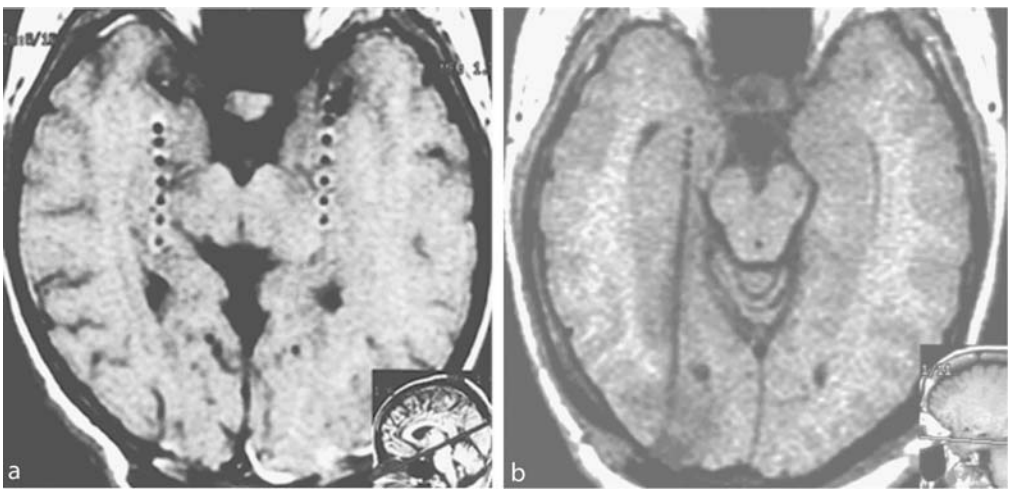
An occipital horseshoe shape incision is performed, leaving a distance of 2 cm between the estimated edge of the 14 mm diameter burr holes, the electrodes fixation device and the edge of the incision. This is to avoid skin erosions over the implanted electrodes. Diagnostic electrodes are left externalized for EEG localization of the epileptic foci. A post operative MRI will confirm the exact position of each contact of the electrodes (*Figure 169-5a*).

Once the electrode position was verified, antiepileptic drugs were tapered and continuous recording for seizure detection was performed. After localizing the epileptic focus, we performed the neurophysiologic testing. This testing consisted in stimulating the pair of selected contacts for chronic stimulation at low (6 Hz) and high (60 Hz) frequencies to elicit electrocortical responses. This test had two purposes, first, to set the amplitude parameter for long term stimulation (50% of the amplitude needed to obtain electrocortical responses) and to record scalp responses in the ipsilateral temporal leads to monitor long-term stimulation (see below).

Antiepileptic medication was reinitiated and the patients underwent the second surgical stage. The stereotactic frame was replaced under general anesthesia and CT scan was repeated. This CT study was fused with the post operative MRI with the diagnostic electrodes in place. Four contact electrodes (for deep brain stimulation) with a 3 mm distance from center to center of adjacent contacts were implanted for long term therapeutic stimulation. They were directed to the previously identified epileptic focus with at

Figure 169-5

MRI axial images with bilateral diagnostic 8 contact hippocampal electrodes position (5a) and final position of the permanent therapeutic 4 contact electrode (5b) placed where the epileptic focus was localized. Contacts 2 and 3 are currently being stimulated



least two contacts within the epileptic site (*Figure 169-5b*). Afterwards the pulse generator was implanted and connected to the depth stimulation electrode.

Double Blind Maneuver

Five patients had an initial 1 month OFF according to the aleatory selection and four patients initiated stimulation immediately. Patients and medical personnel that collected seizure calendars were unaware whether pulse generator was ON or OFF as previously explained.

Bipolar stimulation was performed choosing the pair of contiguous contacts which covered the area where the epileptic focus was localized. In case of bilateral foci, bilateral hippocampal stimulation was used. The parameters for chronic stimulation of the hippocampus were the following:

Cyclic stimulation: 1 min trains of square pulses with 4 min interstimulus interval

Charge density adjusted to 2–4 μC/sq cm/phase

High frequency: 130 Hz

Pulse width: 450 μs

Amplitude of 300 μA which equals 50% of the amplitude needed to obtain electrocortical responses.

According to the formula referred by Velasco et al. [3], the charge density for these parameters is <3.0 μC/cm^2/phase. In patients with bilateral foci, parameters were the same but alternating 1 min stimulation on one side with a 4 min interval between right and left sides. The stimulation parameters used are within a safe nonlesional range [3,37].

Follow Up Protocol

Follow up in all patients was at least 18 months (18–84 months) after initiating hippocampal stimulation. Seizure calendars were collected once a month; EEG and neuropsychological tests were performed on months 6, 12 and 18 after stimulation onset. Neurophysiologic tests to assess the viability of the stimulated tissue to electrical stimuli were carried out every 6 months. The internalized pulse generators were programmed with a transcutaneous computer to stimulate through the selected contacts for therapeutic stimulation using 8 Hz pulses, 6–8 V 450 μs to induce electrocortical responses, EEG recording referred to ipsilateral ear; responses are seen in the ipsilateral temporal leads.

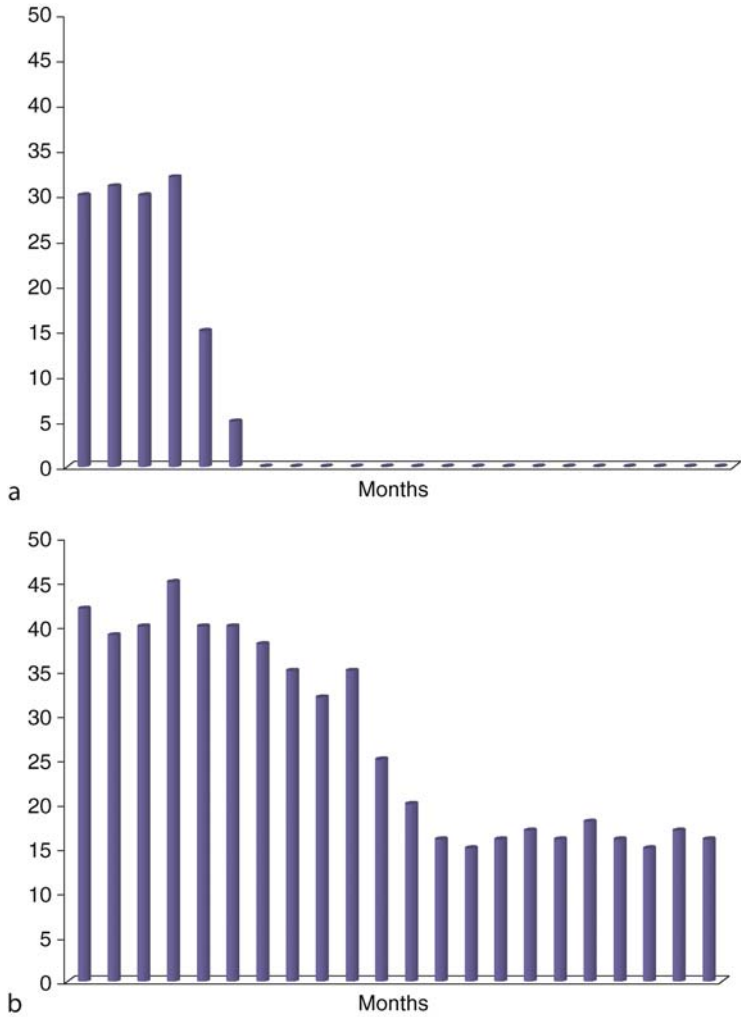
Results

The postsurgical control MRIs showed no evidence of hemorrhage or edema, all patients tolerated the surgical procedure well. None of the patients had side effects with the stimulation parameters employed, as a matter of fact; they were unaware of device activation which permitted us to have a double blind ON OFF protocol.

Impact on seizure number: *Figure 169-6* shows the seizure graphs of two patients as examples of the response to stimulation. Significance of seizure reduction was determined by Student's T test. Although all patients improved, there were two types of responses. One of them is shown in *Figure 169-6a*. The graph shows the seizure number per month (individual bars), the first three bars show the baseline seizure count followed by the OFF bar which indicates the first month of the double blind protocol during which this particular patient had the stimulator OFF. The following 18 bars show the seizure counts during 18 months follow-up. Observe the immediate decrease in seizures as soon as stimulation was initiated (ON). It is also outstanding how the patient was seizure free after 2 months of stimulation and remained so during the whole follow-up. A total of five

Figure 169-6

Seizure counts per month of patients KG111 (a) and patient KG 112 (b). First three bars correspond to the 3 months basal condition. OFF indicates the initial double blind month with implanted electrodes but pulse generator turned off; ON indicates when chronic therapeutic stimulation is initiated. Note that both patients had a seizure decrease but there is a difference in their response. ''A'' had no hippocampal sclerosis in her MRI and had an immediate seizure decrease. She remained seizure free from month 3 on. ''B'' had a slower response which was not significant till month 8 of therapeutic stimulation. He remained with a 60% seizure reduction throughout follow-up



patients had this type of response, four of them remained seizure free and one had occasional brief complex partial seizures. The seizure reduction for these patients beyond month 3 was highly significant ($p < 0.0005$).

Figure 169-6b shows another type of response. Note that the difference in the number of seizures per month between 3 months baseline, 1 month OFF stimulation, the stimulation onset and first 8 months follow-up is not significant.

After this time, there is a seizure reduction but not as significant as the previous group of patients ($p < 0.05$), this reduction was maintained, but none of the patients became seizure free.

A retrospective review of all patients showed that the difference between the two groups of patients was that those who had a better and faster response, had normal MRIs and those who had a modest response, had evidence

of hippocampal sclerosis shown in the MRI studies. Stimulation parameters in both groups were similar. Conceivably, sclerotic tissue may have higher impedance and therefore, those patients with mesial temporal sclerosis should have been stimulated with higher density charge. Or maybe, the smaller response is due to the disruption of the normal histology of the tissue.

ON-OFF protocol: According to the aleatory double-blind maneuver with an initial 1 month OFF period that was authorized, five patients underwent an OFF period after deep brain stimulation system implantation. The other four patients initiated stimulation immediately after neurostimulator implantation. This study design was based in the preliminary subacute studies where we had observed a significant seizure reduction after day 6 of therapeutic stimulation. As already mentioned, patients who responded to subacute stimulation in the study had no evidence of hippocampal sclerosis by MRI. In contrast, the double blind protocol included both patients with normal MRI and with evidence of mesial temporal sclerosis, so we did not realize that there would be a retarded response in patients with mesial temporal sclerosis. For this reason, the results of double blind protocol are difficult to analyze. We can say that all patients who underwent an initial OFF period, showed either no changes in seizure number when compared with baseline in four patients and seizure increase in one patient. From four patients who went ON electrical stimulation immediately, three had a modest non significant seizure decrease (two of them had mesial temporal sclerosis); one patient had a 90% seizure decrease. Regardless of having or not mesial temporal lobe sclerosis in MRI, all patients had a significant lower seizure count by the end of the 18 months follow-up compared with baseline.

Neuropsychological impact: Our main concern and reason for including these patients was the high risk of memory deficit with temporal lobectomy due to either bilateral hippocampal foci or left side (dominant hemisphere) localization. All patients had some degree of memory loss in the baseline stage, probably due to the long seizure history and poor medical treatment response. When stimulation started, no patient had a memory decline and after 18 months stimulation, and there was a trend to improve in both verbal and non verbal memory evaluations. The small number of patients studied does not permit statistical analysis.

After the initial publication in 2000 of our first report on hippocampal stimulation, a series of studies using hippocampal stimulation for the control of mesial temporal lobe epilepsy [38,39] and [40] have been published. Results have varied for a number of reasons: considering evidence of hippocampal sclerosis in MRI an inclusion criteria, when we have described above that these patients do not have the same seizure reduction than patients with no sclerosis. Skipping the first surgery where diagnostic eight contact electrodes are implanted and thus possibly missing the exact location of the hippocampal focus could also explain different results.

Regardless of the differences in seizure reduction, all studies agree that stimulation of the hippocampus is a safe method with no evidence of tissue damage, all studies use stimulation parameters within a safe nonlesional range, and more importantly, all authors agree that there is no deterioration in memory function.

We can conclude that stimulation of the hippocampus is a safe, nonlesional alternative for patients with complex partial seizures, with or without secondary generalization who are not candidates for resective surgery. Other inclusion criteria might be considered, for example, patients with previous temporal lobectomy who develop or have residual contralateral intractable seizures. More studies have to be performed to clarify a number of questions. What if we use other stimulation parameters for the sclerotic hippocampus? What happens if, instead of

stimulating a hippocampal sclerotic tissue, we stimulate the parahippocampus to avoid seizure propagation? We should also conduct multicenter studies to validate the neuropsychological findings. Even though patients with mesial temporal lobe epilepsy are the most frequently referred ones for surgery, could other types of partial seizures be treated with stimulation? We will address the last question in the next part of this chapter.

Stimulation of the Motor Cortex for the Treatment of Supplementary and Primary Motor Cortex Seizures

Ablative surgery of epileptic foci located in the supplementary motor or the primary motor cortices has been performed in several epilepsy surgery centers [41–44,45]. Though results vary within each center, the outcome in seizure reduction varies from 65 to 100%. Most of the cases are patients who have lesions such as cortical dysplasia, cavernomas and gliosis; very few non lesional cases are included. The main problem with these surgeries is that there are a number of neurological sequelae, i.e., paralysis, paresis, apraxia, aphasia and mutism. There were also complications due to the surgical procedure itself. No wonder the epileptologists have a great concern when they have to operate these patients. If the patient has no evidence of a lesion in the MRI, this concern is even greater. With all this considered, we decided to evaluate the possible anticonvulsive effect of stimulating the epileptic foci located in the motor area in two patients with non lesional intractable epilepsy, one of them in the supplementary motor area and the other in the primary motor area.

Both had severe seizures despite multiple antiepileptic drugs and were candidates for intracranial grids for foci detection. The two patients were studied following the Epilepsy Surgery Protocol of the General Hospital of México. The study was reviewed and approved by the Scientific and Ethical Committee of the General Hospital of Mexico. Patients were willing to participate and signed the informed consents. The selected patients had a 3 month seizure baseline to collect reliable seizure calendars. Neuropsychological evaluation was performed and QOL scales were applied. Afterwards patients were hospitalized to undergo diagnostic depth electrode implantation. Two diagnostic 20 contact grids were implanted through frontal craniotomies.

Patient I: 17 year old male with refractory supplementary motor seizures. Perseverance and verbal aggressiveness were present. Surface EEG showed frontal parasagittal epileptic activity. MRI was normal. Bilateral 20 contact grids were implanted in right and left SMA (*Figure 169-7a*). Ictal depth EEG showed spontaneous seizure onset located at contacts 3, 2 and 9 of right grid.

Patient II: 24 year old female with left primary motor seizures and progressive loss of motility of the left side of the body and face. Surface EEG showed slowing in right frontal area, MRI was normal. Two 20 contact grids were implanted in the upper and lower right motor cortex. Ictal EEG showed seizure starting in contact 10 of the upper grid (*Figure 169-8b*).

Daily depth recording was performed without AEDs and ictal EEG activity was obtained. Once the epileptic focus was detected, patients reinitiated AEDs. Grids were explanted and replaced by a four contact, 1cm diameter, plate electrode localized over the epileptic focus (*Figure 169-7b*) for chronic stimulation. The position of the electrodes was fixed by suturing them to the *dura matter* using nylon stitches in each end of the electrode. In the case of primary motor cortex, electrode was fixed to the *dura* in the convexity; in the case of supplementary motor cortex focus, the electrode was fixed to the cerebral falx. Thereafter, electrode was connected to a DBS system. Stimulation was started with

Figure 169-7

Diagram of diagnostic 20 contact grid on right interhemispheric cortex (7a) and sagittal MRI showing definite 4 contact electrode position. Contacts 2 and 3 where epileptic focus was located are currently being stimulated

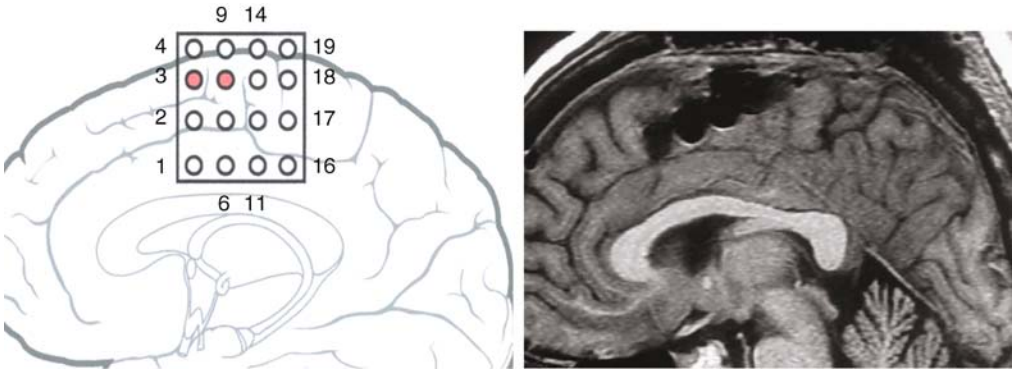
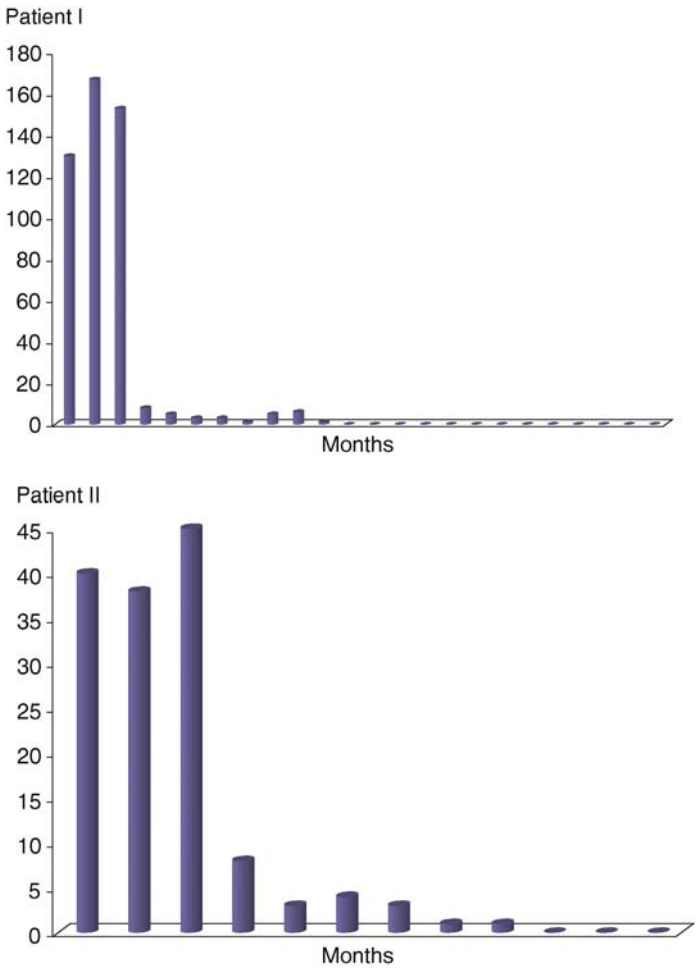


Figure 169-8

Graphs seizure reduction for patient 1 who had supplementary motor area seizures (a) and for patient 2 who had primary motor area seizures (b). Both had an immediate seizure decrease; patient I became seizure free from month 8 on and patient 2 became seizure free from month 7 on



the following parameters: bipolar continuous stimulation between contacts that covered the epileptogenic zone, 130 Hz, 350 μA and 450 μs.

Both patients had a seizure reduction which was observed from the beginning of the stimulation of the epileptic focus. Patient I became seizure free from month 8 on and has remained so for 14 months and patient II from month 7 with no seizures for 3 months. Motor function was preserved, no adverse effects were observed and patients are unaware of stimulation. QOL scales improved in both patients.

We present two cases where results are dramatic and encourage us to continue attempting to stimulate the motor cortex too. We are sure we will face other challenges, as for example, having a huge epileptic area with multiple foci for which there are no grid type electrodes available for cortical stimulation. Would we need several electrodes, could they be connected to a single pulse generator, would we need a specially designed electrode? All these questions point to the need of a near collaboration between clinicians and biomedical engineers to design better hardware for stimulation that can be well tolerated by the patient and avoid skin erosions or other problems such as lead breakage [30,46] Another goal to achieve is to decrease costs so more patients have the opportunity to try this alternative surgical method.

Many questions and challenges arise, and to be able to answer them, a multidisciplinary group is mandatory with collaboration of basic scientists, neuropsychologists, epileptologists and neurosurgeons.

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