165 Centromedian Thalamic Stimulation for Epilepsy

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Introduction

Sudden onset of generalized seizures that includes loss of consciousness, involvement of global motor activity, and diffuse electroencephalographic (EEG) discharges suggests that convulsive activity is propagated through structures with widespread anatomical and physiological connections. The participation of a neural system with these characteristics in the genesis and propagation of epileptic attacks was proposed some time ago on the basis of clinical observations [1]. Midline and intralaminar thalamic nuclei corresponding to the so-called nonspecific thalamic system [2] meet anatomical and physiological criteria for consideration as an essential part of that neural network [3–9]. While high-frequency stimulation of this system induces cortical EEG desynchronization [10,11], low-frequency stimulation (6.8 Hz) induces cortical synchronization in the form of recruitment of monophasic, long latency, waxing, and waning potentials (recruiting responses, RR) [12–16]. Bilateral stimulation at 3 Hz in these thalamic nuclei or their fiber connections reproduce the clinical and EEG events of a typical absence in cats [17,18] and humans [19,20]. Other experiments have demonstrated the participation of brainstem structures, anatomically linked with the nonspecific thalamic system, in the onset of epileptic seizures in various epilepsy models [21–23].

Although the controversy on the cortical versus subcortical origin of epileptic attacks remains unsolved [11,21–30], there is agreement in that thalamocortical interactions are essential in the development of a variety of seizure types and the propagation of the majority of these [15,24,25,27–30].

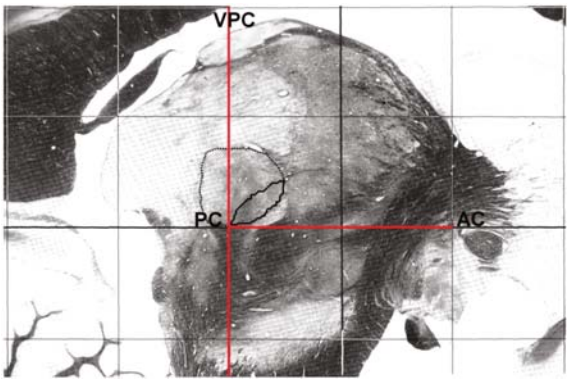
During the past 20 years, we have explored the effects on seizure control as it interferes with thalamocortical interactions using deep-brain electrical stimulation (DBS) of the centromedian thalamic nucleus (CM), which forms part of the nonspecific thalamic system. The CM was chosen as the target, considering its relatively large size (about 1 cm in diameter) and close relationship with the conventional landmarks employed for thalamic stereotactic surgery, i.e., the anterior commissure-posterior commissure (AC-PC) line and the vertical line that touches the anterior border of the posterior commissure (VPC) (*Figure 165-1*).

To date, we have worked on the following: standardizing surgical procedures and stimulation programs [32]; establishing the efficacy and safety of the procedure [33]; confirming correct electrode placement within the nonspecific thalamic system by evoking recruiting responses and EEG desynchronization as described in different animal species [16]; studying the effects of acute, subacute, and chronic electrical stimulation of centromedian nucleus (ESCM) on different seizure types, paroxysmal EEG discharges, and background activities [34,35]; identifying best surgical candidates, and determining predictors in case selection, electrode position, and confirmation, and stimulation parameters associated with favorable outcome of treated patients [36]. Finally, we have worked on describing the effects of ESCM on neuropsychological performance and the quality of life (QOL) patients attain during treatment [31].

Although emphasis has been placed on therapeutic outcome and complications derived from

Figure 165-1

Sagittal section of the thalamus, 10 mm from midline taken from the Schaltenbrand–Wahren anatomical atlas. Red lines indicate anterior commissure-posterior commissure (AC-PC) line and vertical line to posterior commissure (VPC). Centromedian thalamic nucleus (CM) contour is indicated by dashed line and parvocellular subdivision by the continuous line. Stereotactic coordinates provided in the text attempt to place at least two of the four electrode contacts within the parvocellular nucleus. Note that the target is only 1/5 of the total CM area and is located in its more anterior and basal position [31]



ESCM, in performing studies we have had the unique opportunity of exploring, through multiple contact electrodes, the epileptic activity occurring in CM and adjacent structures in hundreds of spontaneous seizures of several types and those that occur under different wakefulness and sleep conditions [19,30,37–41]. Epileptic activity in thalamic and upper mesencephalic areas could also be related in time and wave form with simultaneously recorded scalp EEG activities. In some cases, the relationship of CM paroxysmal activity with that of other subcortical structures could be determined through electrode implantation for localization of epileptic foci before deciding whether the case could be better treated by ESCM [39,40]. These experiences served to analyze and test different hypotheses on epileptogenesis advanced on experimental models of epilepsy and extrapolated to spontaneous seizures in humans [19,42]. They also confirmed the majority of experimental electrophysiological observations on the nonspecific thalamic system [16].

On the other hand, experience with ESCM has provided important information that served to design protocols for clinical trials utilizing electrical stimulation (ES) for epilepsy, and in particular double-blind protocols [36,43,45], parameters and modes of stimulation [31,36], confirmation of target localization [16,31], and plasticity of stimulated tissue [31,43].

Case Selection

Patients selected for ESCM were not candidates for ablative procedures of the epileptic foci because they had evidence of bilateral or multifocal seizure onset, unilateral focus overlapping eloquent areas, or no evidence of focal onset of their epileptic attacks. All patients had a long history of seizures (from 4 to 33 years), with numerous to countless seizures that incapacitated them completely. Seizures were out of control despite adequate doses of the specific anticonvulsants corroborated by therapeutic blood levels.

All treated cases had more than one seizure type; however, these have been grouped according the most prominent seizure and EEG pattern as follows:

Group 1: Focal motor seizures (epilepsia partialis continua or EPC), with frequent generalization in the form of adversive tonic seizures and generalized tonic-clonic convulsions (GTC). They had focal interictal spikes in the central and parietal area, propagated to other ipsilateral areas, and occasionally generalized. Magnetic resonance imaging (MRI) revealed the presence of cortical dysplasia, focal encephalitis, or were normal [46,47].

Group 2: Complex partial seizures (CxP) with frequent generalization as GTC, with surface and/or intracranial bilateral-independent EEG ictal and interictal discharges, bilateral hippocampal sclerosis, or atrophy in MRI associated with memory deficits in the neuropsychological evaluation [36].

Group 3: Tonic seizures with fencing posture, frequently associated with propulsive and retropulsive atypical absences (AA) and GTC. Intracranial studies demonstrated bilateral-independent focal ictal or interictal EEG discharges in mesial frontal regions and no evidence of lesions or dysplasia in epileptic foci in MRI [49].

Group 4: AA and GTC associated with 2.0–2.5 cycles per sec (cps) spike-wave complexes (SKW) and in some cases, with bilateral frontal or temporal interictal spikes. All patients were mentally challenged, some of these since infancy, and others with progressive mental deterioration after onset of seizure history. They were considered as Lennox–Gastaut syndromes. MRI showed signs of regional or hemispheric atrophy, cortical dysplasia, and subependinal calcifications associated with skin stigmata of tuberous sclerosis (symptomatic Lennox–Gastaut syndrome); however, MRI was normal in 56% of cases (idiopathic Lennox–Gastaut syndrome) [31,36].

Patients were evaluated at the Epilepsy Clinic at least 6 months prior to surgery and all were referred from other epilepsy clinics or institutions where they had been treated for >3 years before being considered as refractory to medical treatment. Patients were placed in anticonvulsive regimes, which proved more efficient for seizure control when anticonvulsant blood levels fell within therapeutic range. These regimes were maintained during a 3–6-month preoperative observation (baseline) and throughout at least 1 year with ESCM. Patients and/or relatives were instructed to maintain a meticulous record of the frequency of each seizure type separately. They easily learned to differentiate among GTC, tonic or clonic (Type A), AA (Type B), and focally initiated (Type C) seizures.

Surgical Techniques

Patients (many of these children) are operated on under general anesthesia. Electrodes are implanted by means of a frontal parasagittal approach, and burr holes are centered at 13 mm at each side from midline and immediately behind the coronal suture. This allows to avoid the venous sinus and places the electrodes in a trajectory parallel to midline at a distance of 10–12 mm on each side and at a sagittal angle of 45–60° from the AC-PC line (*Figure 165-1*). Most implantations have been guided by ventriculograms and electrode tips were aimed at the intersection of AC-PC and VPC lines. By using ventriculography, intraventricular symptom-associated blending has occurred very rarely [36], and X-ray films or fluoroscopy nicely confirm the correct position of the contacts after electrodes have been fixed to the skull. More recently, we have employed MRI-computed tomography (CT) image fusion to target CM to avoid venous sinuses and brain and ventricular wall blood vessels in the trajectories of electrodes, particularly those that traverse the ventricular wall. MRI-CT electrodes are implanted with indirect targeting, because the conventional 1.5 T MRI does not permit visualizing the internal medullary laminae of the thalamus that surrounds CM as it unfolds in its posterior end. Coordinates are 11 mm lateral to third ventricle midline, measured from the anterior border of the posterior commissure and contact 0 of tetrapolar electrodes (numbered from 0 to 3) 2 mm above AC-PC level at an angle of 45–60° from AC-PC line.

Sterile scalp electrodes are placed after preparing the skin in a conventional 10–20 system array to be used for electrophysiological confirmation of DBS electrode position. Sterile draping aids in maintaining scalp electrodes in place. Low-frequency (6–8 Hz) bipolar stimulation is delivered through each pair of contacts (0–1, 1–2, 2–3) of DBS using a external electrical stimulator set at a 1.0-ms duration, increasing intensities from 0.2 to 1.0 mA in the search for scalp recruiting responses. Typical RRs are monophasic-negative, long-latency, waxing-waning potentials that may be better analyzed morphologically through

oscilloscopic recordings. These must be distinguished from augmenting and primary evoked potentials (*Figure 165-2a*). Unilateral stimulation typically induced bilateral responses in parasagittal leads of scalp EEG, more prominent in frontopolar regions and ipsilateral to the stimulated site (*Figure 165-2b*).

On the other hand, high-frequency stimulation (60 Hz, 1.0 ms, 0.3–0.8 mA) of CM induces cortical desynchronization and a shift in EEG baseline level (DC-shift), with the same RR scalp distribution [16,36].

These electrocortical potentials are better recorded under awake-relaxed conditions; thus, we formerly performed postoperative electrophysiological confirmation during the first of a two-stage operation with DBS temporally externalized. Recently, we have conducted electrode position confirmation transoperatively; nonetheless, to elicit electrocortical responses the anesthesiologist is requested to situate the patient on a superficial anesthetic plane during the electrophysiological confirmation period and to utilize muscle relaxants and analgesics to maintain the patient relaxed and immobilized.

The aforementioned CM stereotactic coordinates and electrocortical responses attempt to place at least two DBS electrode contacts within the nucleus's parvocellular subdivision of the nucleus, that is, the most lateral, anterior, and ventral part. Outside this subdivision, ESCM is much less effective in controlling seizures [31,36,42] (*Figure 165-3*). Thereafter, electrodes are connected to internalized pulse generators

Figure 165-2

(a) Electrocortical potentials induced by centromedian thalamic nucleus (CM) stimulation and analyzed in oscillographic recordings: recruiting responses (RR) (*top*) are monophasic, 32–36-ms latency-negative potentials with maximal amplitude in frontal (F4) leads. They must be differentiated from augmenting responses (*midline*), which are positive-negative potentials elicited by stimulation of magnocellular CM subnucleus and better recorded in central (C4) leads. Also from primary (*bottom*), evoked potentials elicited by stimulation of specific sensory ventroposteromedial-ventroposterolateral (VPM-VPL) thalamic nucleus or posterior subdivision of CM and recorded in parietal (P4) leads. (b) Distribution of recruiting responses in scalp electroencephalogram (EEG): these are more prominent in ipsilateral frontopolar regions. RR on the left were elicited through externalized electrodes, and RR on the right were elicited through internalized pulse generators [36]

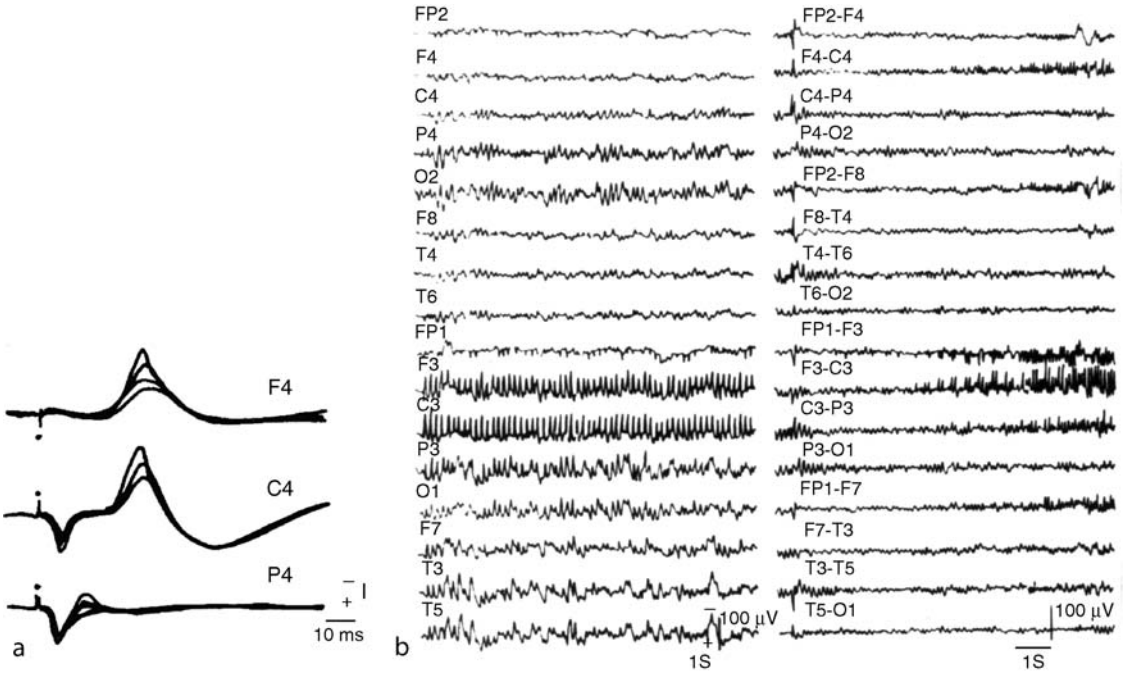
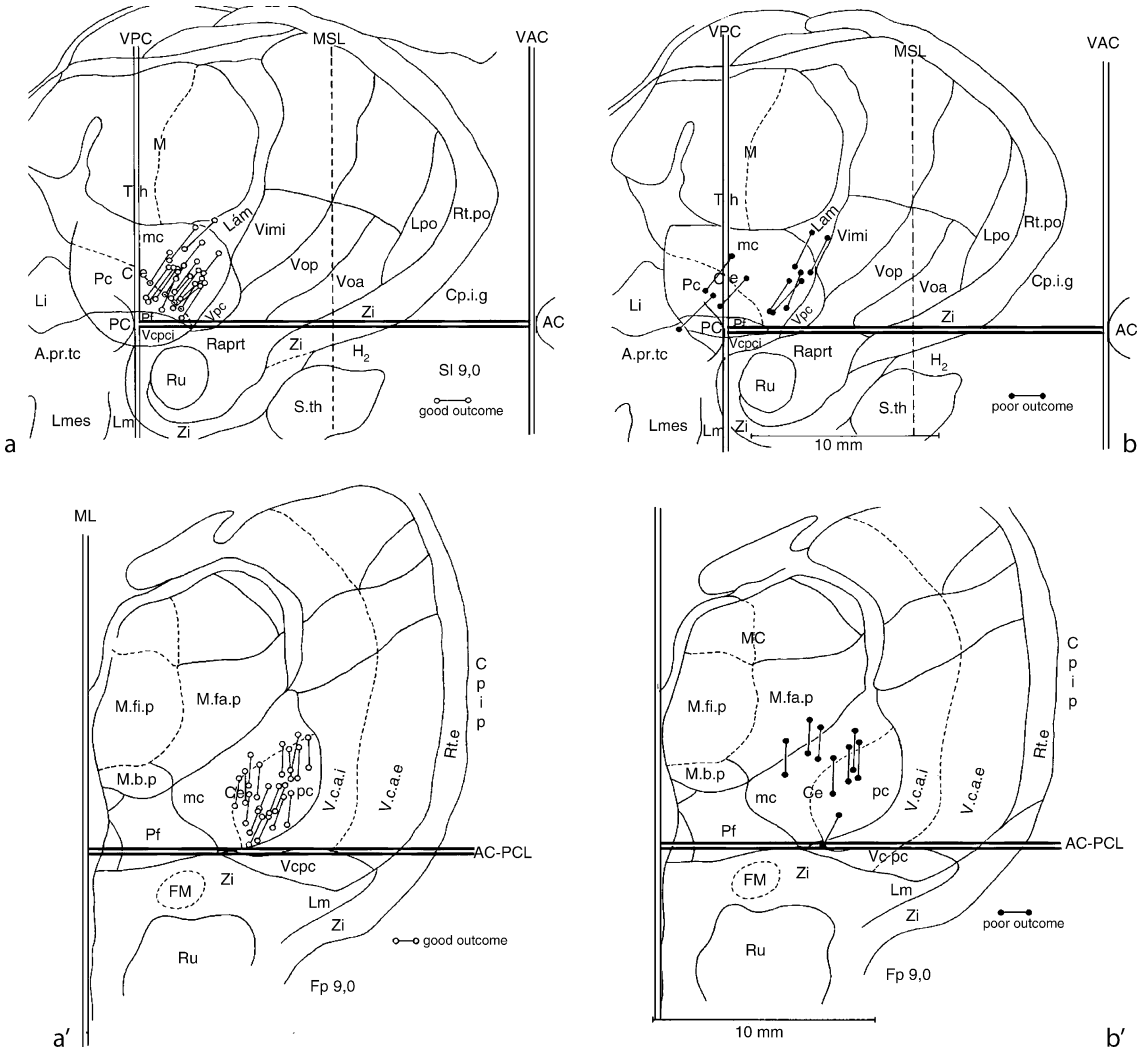


Figure 165-3

Plotting of pairs of electrode contacts used for chronic bipolar electrical stimulation on sagittal (SI 9,0) and frontal (Fp 9,0) sections of the Schaltenbrand–Wahren anatomical atlas. (a) and (a′): plotting of cases with >80% decrease of seizures (good outcome). (b) and (b′): plotting of cases with <80% improvement (poor outcome). Note that while electrodes are grouped in the anterolateral part of centromedian thalamic nucleus (CM) (parvocellular area) in cases with good outcome, electrodes are dispersed toward more posterior, superior, and medial regions of CM (magnocellular, internal medullar laminae, and parafascicularis) in poor-outcome cases. *AC*, anterior commissure; *PC*, posterior commissure; *VPC*, vertical line posterior commissure; *ML*, midline; *Ce*, centromedian nucleus; *mc*, magnocellular; *pc*, parvocellular; *Mfip*, fibrosus posterior; *Lam*, lamina medullaris; *Lm*, medial lemniscus; *M*, territorium medialis thalami; *Pf*, parafascicularis; *Pu*, pulvinar; *Raprl*, prelemniscal radiations; *Vci*, ventralis caudalis internus; *Vce*, ventralis caudalis externus; *Vcpc*, ventralis caudalis parvocellularis; *Vimi*, ventralis intermedius; *Vop*, ventralis oralis posterior



(IPG) placed in subcutaneous subclavicular pockets through extension cables.

Because the most frequent complications by far of the procedure comprise neurostimulator hardware-induced skin erosions, the following precautions are recommended: (1) Scalp incision must be a skin flap at least 2 cm away from burr-hole edges and skull-fixation devices; (2) Low-profile extension cables should be placed and immobilized by a stitch under muscular fascia behind mastoid bone, and (3) Place the IPG away from subclavicular incision and

fixed to pectoralis muscle with stitches. In children and slender patients, it is better to place the IPG below muscular fascia at abdominal wall and ensure that the extension cable is loosened in gentle loops below IPG, as it will be required to straighten as the child grows.

Chronic Stimulation

A cycling mode of stimulation was initially adopted to avoid electrical current overcharge and damage to stimulated tissue [32]. With time, we have observed that cycling mode is as effective as continuous stimulation for seizure control. Therefore, we continue to use cycling mode that saves IPG battery to the point that it may last from 3 to 9 years.

On the other hand, while adjusting the stimulation parameter to treat movement disorders is a relatively easy task, ES adjustment for treating epilepsy is more complicated. We have recently adjusted ES for seizure control not to exceed the 4 $\mu C/cm^2$/phase, according to the following formula [44]:

$$\text{Charge density } (\mu C/cm^2/\text{phase}) = \frac{\text{amplitude (mA)} \times \text{pulse width (ms)}}{\text{cathodal electrode area } (cm^2)}$$

A charge density ca 2–3 $\mu C/cm^2$/phase corresponds to 50–80% of that necessary to induce RR or DC-shift [31].

Follow-Up

Patients were interviewed every 1–3 months for the first year and every 6 months thereafter. Different seizure-type calendars were updated and stored in a database. After 1 year of ESCM, anticonvulsants could be adjusted according to response to ESCM and tolerance to medication.

EEG and neuropsychological evaluation were repeated every 3 months for 1 year and every year thereafter. In view of the mental- and cognitive-function deterioration of treated patients, neuropsychological evaluation consisted mainly of evaluating abilities by means of scales and QOL questionnaires standardized and validated for our population [31,35].

During the same EEG sessions, stimulation parameters delivered by IPGs and electrode impedance were revised. Also, electrocortical responses to test reactivity to ESCM of stimulated tissue were elicited by setting IPGs parameters at 6–8 Hz, 450 µs, 6–10 V for RR and 130 Hz, 450 µs, 7–10 V for DC-shift (*Figure 165-2*). These precautions confirmed correct stimulation of CM, not only from the neurostimulation hardware standpoint, but also from the physiological response of stimulated tissue [36].

Some patients underwent a double-blind randomized trial of ESCM in which one half of these would have stimulation turned OFF between months 6 and 9 and the other one half, between 9 and 12 months. Because ESCM induced no objective and subjective sensations, patient and examiner remained unaware of the maneuver and the IPG stimulation-parameter code and reading was maintained in secret by a third party, the maneuver was considered valid.

Significance in seizure reduction for total seizure number and for each seizure type was evaluated through Student *t*-test and for neuropsychological and QOL scales by Wilcoxon test.

Results

Effect of ESCM on Seizure Control

Group1: EPC included five children aged 3–7 years who were tested subacutely (for 3 months) with electrodes externalized through a connector cable away from skull burr hole. During the first month, a significant decrease ($p < 0.01$) in GTC and tonic adversive seizures was observed. By the end of

3 months, four patients were seizure-free and their electrodes were explanted. In the remaining patient, the stimulation system was internalized and seizures disappeared in 2 months and remained so for 8 months, when the stimulation system required explantation due to multiple skin erosions. Explantation was followed by progressive reappearance of seizures and the patient was finally treated with subpial transection.

Group 2: Sixteen patients with CxP seizures who were not candidates for surgical ablation because they had evidence of bilateral independent foci were treated by ESCM. They had no significant decrease in CxP seizures during the first year, but both GTC and tonic seizures decreased or disappeared during that time ($p < 0.001$). However, an evaluation at 3 years showed significant decrease of even CxP seizures ($p < 0.01$) that persisted for periods up to 16 years [36,42].

Group 3: Six patients with tonic seizures and AA and evidence of bilateral interhemispheric foci had significant reduction of AA ($p < 0.001$). However, no patient in this group became seizure-free.

We consider the results of ESCM for these three groups of patients satisfactory and certainly competitive with those reported in other trials involving electrical stimulation of different structures for seizure control [49–51]. Nevertheless, ESCM in children <7 years of age with EPC has been abandoned in view of frequent skin erosions along the neurostimulator-hardware trajectory and in older children and adults due to the promising results with ES of epileptic foci in eloquent areas. This is also true for patients in Groups 2 and 3; Group 2 cases are being studied and treated with stimulation of hippocampus [45], whereas persons in Group 3 are being administered treatment with cortical interhemispheric stimulation (See chapter K-13).

During the past 7 years, we have used ESCM solely in cases with generalized seizures of Lennox–Gastaut syndrome and have treated 25 patients with long-term (>3 years) follow-up. Lennox–Gastaut syndrome is one of the most severe forms of childhood epilepsy, characterized by drug-resistant GTC and AA, EEG generalized 2.0–2.5 per sec spike-wave complexes, and mental retardation. Over 80% of patients continue to experience seizures throughout adulthood [52]. Selected patients have been >8 years of age and weighed 25 kg. They experienced a severe to extreme epileptic condition and were completely disabled. Some of these had retardation in neuropsychological condition noticed in early childhood, while others became mentally retarded after seizure onset.

ESCM in cases of individuals with Lennox–Gastaut syndrome resulted in global improvement of seizures of 83%, with 15.4% of patients becoming seizure-free. Most important was improvement in their QOL, particularly in cases of persons who experienced mental deterioration after seizure onset; these regained abilities and some are living a normal life, seizure-free and OFF medication [31].

Other surgical procedures have been proposed to treat Lennox–Gastaut syndrome, such as corpus callosum section (CCS) and vagal nerve stimulation (VNS). The degree of significant improvement in seizure occurrence has been reported for 60.9% [53], and for 72% [54] of patients in the most optimistic outcomes for CCS. The latter is particularly efficient in controlling drop attacks and some varieties of atypical absences, but not to date to a great extent for GTC [53,55]. VNS in Lennox–Gastaut syndrome has induced a global seizure reduction of 27–64% with no patient rendered seizure-free [56]. To our knowledge, there are no reports of DBS in other areas for treating this specific syndrome.

Predictors in Seizure Control with ESCM

Although Lennox–Gastaut syndrome GTC and AA have been the best indications for ESCM,

certain cases responded better than others (global improvement range, 30–100%). Conversely, ESCM is less effective in CxP seizures: we continue to achieve seizure reduction from 52 to 98.6% in different patients and secondary GTC disappear in the majority of patients. Therefore, we have searched for other predictors related with favorable outcome, and have observed that stereotactic position corresponding to parvocellular area of CM and typical RR elicited through contacts used for therapeutic stimulation correlate with better outcome ($p < 0.001$). Other variables such as age, sex, length of seizure history, seizure frequency, stimulation parameters (amplitude and frequency, 60–130 Hz), or continuous versus cycling mode of stimulation did not significantly modify outcome [31,36].

ON/OFF Stimulation Condition

Because epilepsy is a condition with frequent spontaneous fluctuations in seizure occurrence that are related with a number of factors (stress, drug intake, menstrual periods, and concomitant diseases, among others), evaluation of any therapy by means of a double-blind protocol is desirable. We have evaluated a group of patients in a double-blind protocol designed to interrupt stimulation for 3 months beginning at day 60 (range, 60–90 days) in one half of these, and from 90 to 120 days in the remaining one half. Patients were assigned to each group by lottery number. A cross-sectional analysis of total seizure number and each seizure type separately was performed among baseline, the 3-month period preceding the double-blind maneuver, and the 3-month OFF stimulation period. Significant differences were found between baseline and ON and OFF period ($p < 0.001$) for total seizure number and each seizure type: GTC and AA ($p < 0.001$) and focal seizures ($p < 0.05$). Nonetheless, no significant differences were found between the period ON and OFF stimulation (*Figure 165-4a*). We conclude that there was a residual effect of ESCM that outlasted the 3-month OFF stimulation period [36].

More recently, we analyzed the spontaneous OFF stimulation periods that occur either when the IPG battery charge depletes or when we have been required to explant neurostimulation systems because of skin erosions. In the former, we have observed that seizures reappear when the battery is depleted, although these do not reach baseline levels. Seizures decrease rapidly after the IPG is replaced and stimulation reinitiated. More interesting is that as the stimulation period is extended, recurrent battery depletions are accompanied by less and less recurrence in seizures and that these are controlled more rapidly after reinitiating stimulation (*Figure 165-4b* and *c*). In cases of explantation, seizures slowly increase for months and eventually may – although not always – reach baseline levels. We have witnessed the case of a child with symptomatic Lennox–Gastaut syndrome who became seizure-free and OFF medication during 5 years with ESCM; this was accompanied by normalization of EEG recordings and the return of the child's mental condition to normal after being completely deteriorated. This patient was explanted after 5 years due to skin erosions, and after 2 years only occasional 2.0–2.5 EEG spike-wave complexes without clinical manifestations have been found. This adolescent is living a normal life at present [31].

All these observations suggest that long-term ESCM induces plastic changes in the stimulated tissue that maintains a residual antiepileptic effect. Thus, new studies evaluating therapeutic trials of electrical stimulation in epilepsy place the double-blind maneuver at the beginning of stimulation period, and one half the patients initiate stimulation immediately, while stimulation is delayed for 1–3 months in the other one half [43–45].

The Role of CM in the Genesis and Propagation of Epileptic Activity

Simultaneous recording from scalp, electrode in CM, and other intracranial electrodes used for diagnostic purposes prior to ESCM was decided as treatment to provide information on the role of CM

Figure 165-4

(a) Cross-section of 3-month follow-up epochs indicating baseline (BL), 3 months ON stimulation, and 3 months OFF stimulation (3–6 to 6–0 months after the onset of electrical stimulation of centromedian nucleus [ESCM]). Note that 3-month periods OFF stimulation are not accompanied by seizure return to basal level (BL). (b) Long-term follow-up in two cases in patients in whom implantable pulse generator (IPG) batteries depleted twice and were replaced. Note that initial improvement reached a plateau after 4–5 months, while subsequent reinitiation of ESCM arrows was followed by an immediate amelioration. (c) One case was explanted after 8 months of ESCM and followed up for several months. Seizure increased OFF stimulation but for months did not reach BL levels [31,33,36]

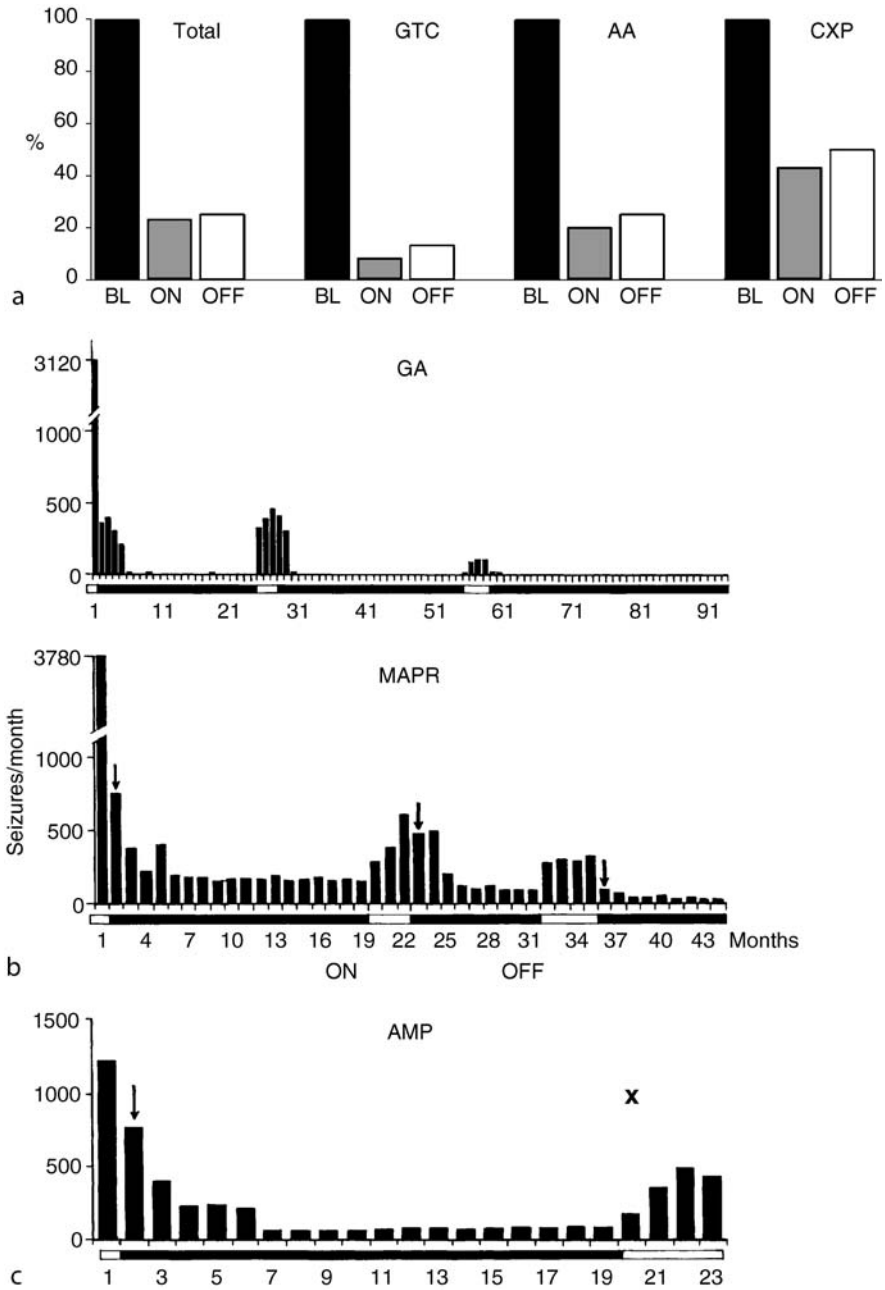
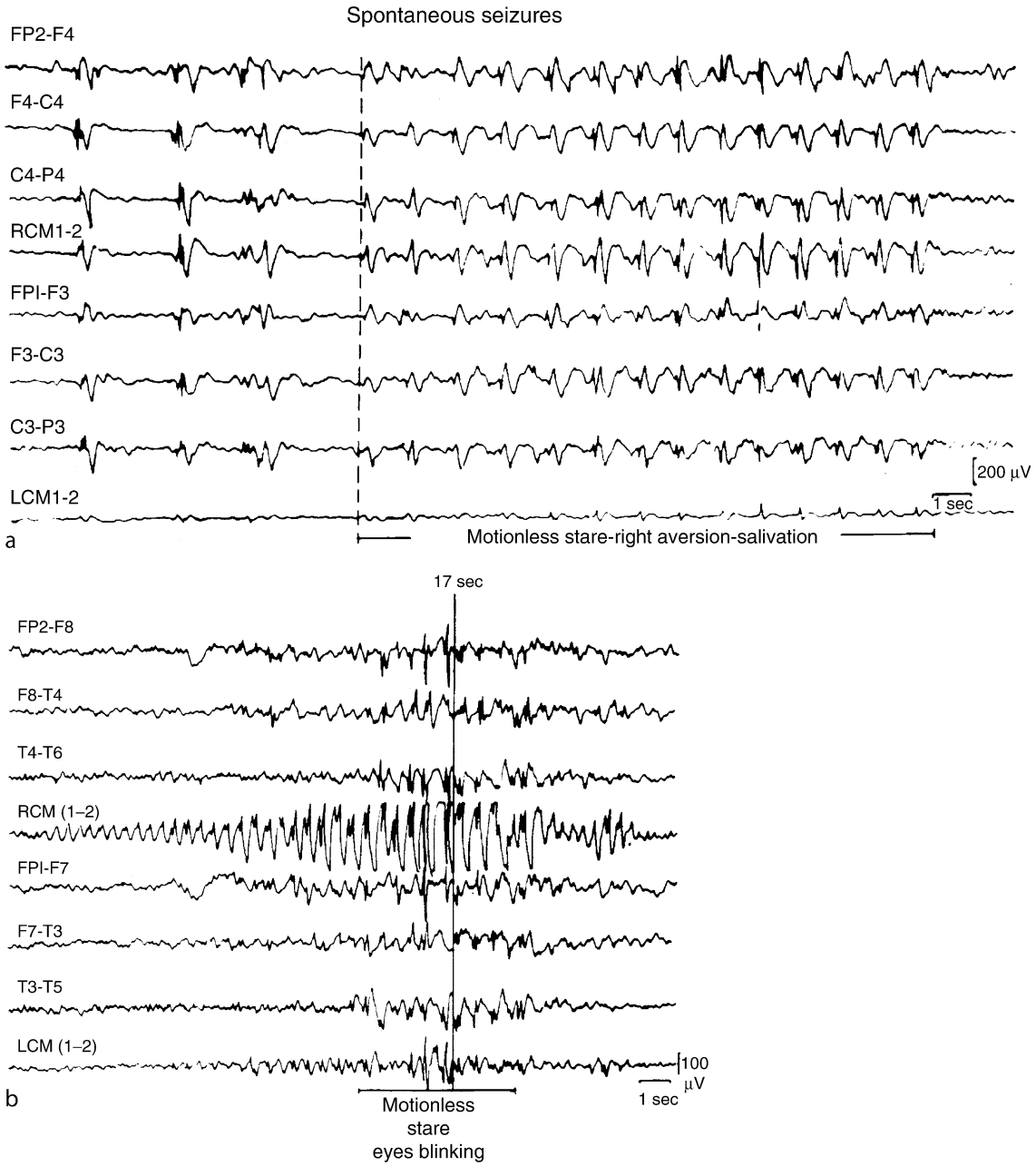


Figure 165-5

EEG recordings from right and left centromedian thalamic nucleus through implanted deep-brain electrical stimulation and simultaneously from intracranial or scalp electrodes. (a) Spike-wave complexes recorded from scalp EEG and thalamic electrodes in a case with Lennox–Gastaut syndrome. Paroxysmal discharges appear to occur simultaneously. (b) Spike-wave complexes recorded during a typical absence. Paroxysmal discharges initiated in right CM (RCM) many seconds before left CM (LCM) and scalp [19]



in different seizure patterns. Intracranial electrodes were placed mainly along hippocampus amygdala axis, underneath temporal or frontal lobes, or at each side of interhemispheric frontal areas.

1. EPC focal jerks were accompanied by cortical discharges that did not propagate to CM unless focal motor seizures involved the neck in a contraversive movement or at

GTC onset. Under these circumstances, repetitive bursts of polyspikes appeared in CM [41]. Cortical and CM spikes increased in amplitude, while muscular jerks decreased during slow-wave sleep. Both EEG and muscular spikes decreased to disappearance during paradoxical sleep.

2. Cortical and temporal spikes increased during CxP without concomitant discharges in CM. When CxP evolved to GTC, delayed polyspikes and comb-like activity appeared in CM [47].
3. In cases of supplementary motor cortex foci, tonic seizures were accompanied by nearly simultaneous onset of cortical and CM paroxysmal discharges; also in AA, CM and cortical spike-wave complexes were simultaneous [40,48] (*Figure 165-5a*).
4. In AA of the Lennox–Gastaut syndrome, spike and wave complexes appeared to occur simultaneously in CM and cortex. However, when the spike component of the EEG complexes exhibited a single negative spike, peak latency presented 35 ms before in CM and in upper mesencephalon than in cortex [40].
5. Typical absences occurring in young adults showed unilateral EEG spike-wave complexes anticipating (by 6–13 ms) the same complexes in contralateral CM and scalp [38] (*Figure 165-5b*). Bilateral simultaneous high-amplitude 3-cps stimulation in CM induces generalized 3-cps spike-wave complexes accompanied by typical absences and motor arrest, as described many years ago in cats [17] (*Figure 165-6*).

Figure 165-6

Three-cycles per sec (3 cps) spike-wave complexes induced by simultaneous stimulation of right and left CM (RCM-LCM) at 3 cps, 2.0 mA, 1.0 ms, while the patient was performing a task (pressing a button in response to a flash). During stimulation, the patient presented a typical absence-and-stop to respond to flashes that lasted precisely for the time of stimulation [16]

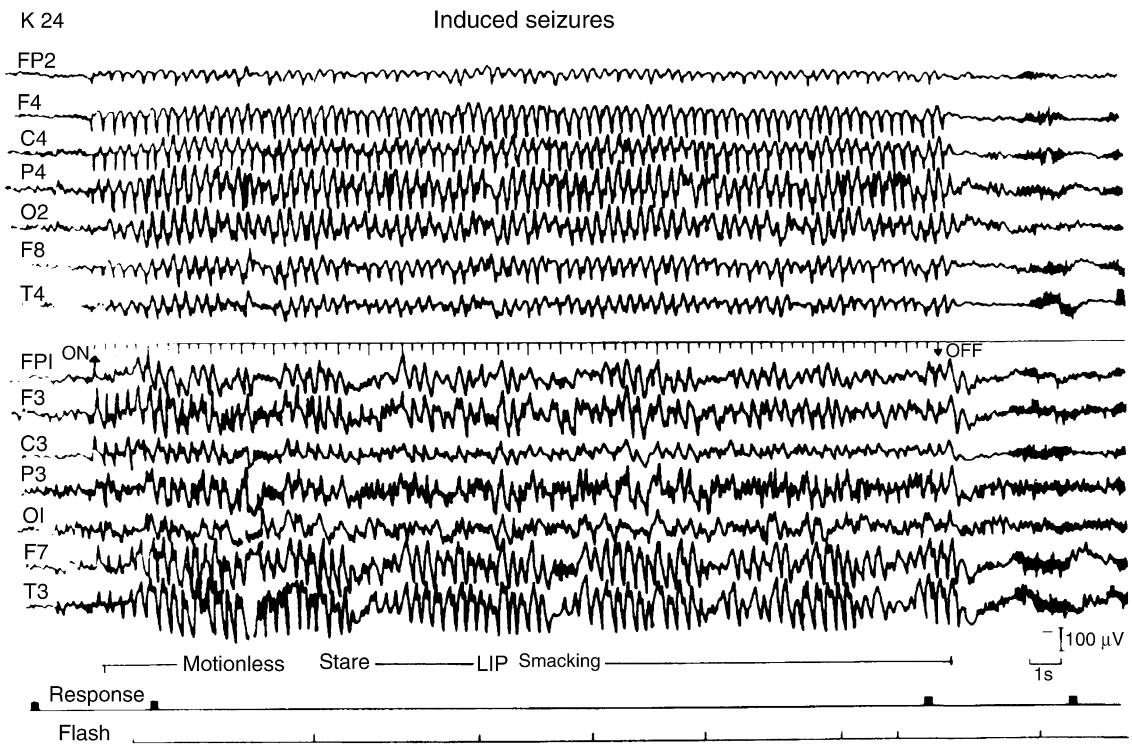
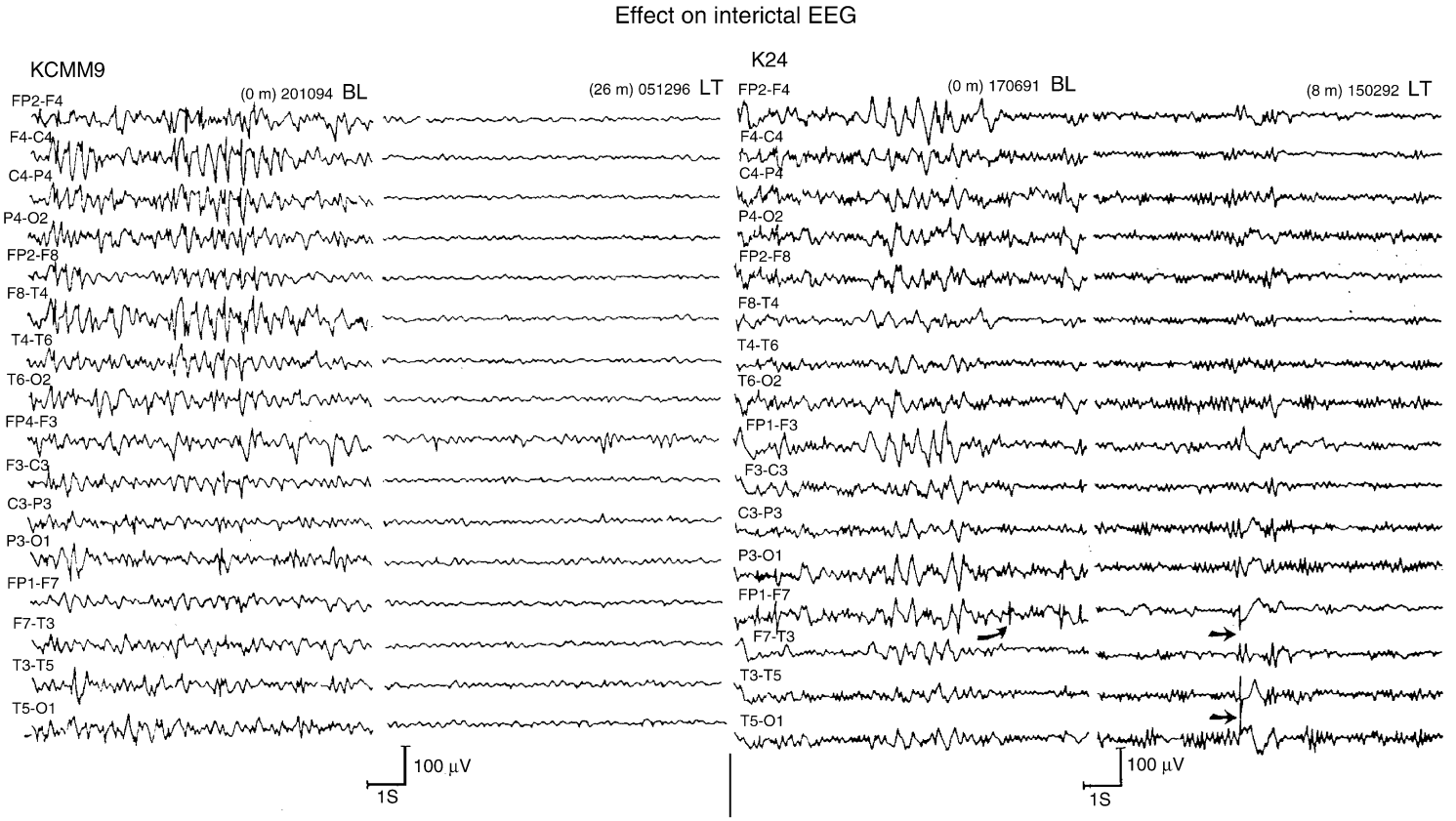


Figure 165-7

Effect of chronic ESCM on EEG generalized spike-wave complexes in a case of Lennox–Gastaut syndrome (*left*) and on secondary synchronous discharges (*right*) of a patient with complex partial seizure (CxP) and focal spikes on left temporal leads (*arrows*). After chronic ESCM, spike-wave complexes and secondary synchronous discharges disappeared, but focal spikes persisted



6. Myoclonic seizures frequently occur with no concomitant paroxysmal discharge in scalp, cortex, CM, or upper mesencephalon.

These observations correlate well with the effect of ESCM on different seizure types, with the exception of EPC. In fact, ESCM stimulation in CxP seizures interferes with generalization in the form of GTC seizures, but much less so in focal interictal spikes (*Figure 165-7*). ESCM decreases adversive tonic and AA secondary to epileptic foci in supplementary motor cortex and AA of Lennox–Gastaut syndrome, while it exerts no effect on myoclonic epilepsy.

CM recordings and acute and chronic stimulation provide evidence that the nucleus – and perhaps all nonspecific thalamic nuclei – may be the origin of spike-wave complexes associated with typical absences. They probably play an important role in the genesis of atypical absences associated with Lennox–Gastaut syndrome 2.0–2.5 spike-wave complexes, most likely in a thalamic-cortical interplay. They participate in the propagation of epileptic activity focally initiated in the cortex, at least in frontal and temporal lobes. In contrast, they do not participate in the genesis or propagation of myoclonic jerks that may originate in brainstem [42].

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