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CORPUS CALLOSUM STIMULATION AND STEREOTACTIC CALLOSOTOMY IN THE MANAGEMENT OF REFRACTORY GENERALIZED EPILEPSY

PRELIMINARY COMMUNICATION

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SUMMARY — Corpus callosum stimulation produced by chronically implanted electrodes, placed either by craniotomy or stereotactically, failed to control refractory generalized epilepsy in humans and also in experimentally produced penicillin epilepsy in cats. However, the patients that suffered craniotomy, frontal lobe retraction or pneumoencephalograms, without callosal section, showed remarkable improvement of their seizure condition due to these unspecific manipulation effects. Stereotactic anterior callosotomy emerged as a sequel of these functional neurosurgical findings, and as an alternative procedure to preclude undesirable neuropsychological and neurological side effects of split brain syndrome and of brain retraction, associated to conventional callosotomy. Ten patients with various disabling convulsive disorders have undergone this new operation, which showed to be less traumatic and better tolerated than open callosotomy.

Estimulação do corpo caloso e calosotomia estereotáxica nas epilepsias generalizadas refratárias: comunicação preliminar.

RESUMO — A estimulação crônica do corpo caloso, obtida pela implantação de marca-passo e eletrodos implantados, colocados através de craniotomia ou estereotaxicamente, não controla, em humanos ou em animais experimentais, a epilepsia generalizada refratária. Por outro lado, em pacientes craniotomizados, a retração do lobo frontal ou a realização de pneumencefalogramas, sem secção calosa, resultou em importante melhora do quadro convulsivo, em razão de efeitos inespecíficos de manipulação do encéfalo. A calosotomia estereotáxica anterior emergiu como conseqüência desses achados neurocirúrgicos funcionais e como procedimento alternativo para prevenir efeitos colaterais indesejáveis, tanto neuropsicológicos como neurológicos, tais como: 'split brain syndrome' e retração cerebral, associados à calosotomia convencional. Dez pacientes com vários tipos de síndromes convulsivas incapacitantes foram submetidos a esta nova intervenção, que se mostrou menos traumática e melhor tolerada que a calosotomia convencional a céu aberto.

Based on a significant series of 35 micro-surgical EEG guided callosotomies, operated upon under scalp EEG and mesial electrocorticographic monitoring, we have, in previous publications [10,12] described a disruption of the bilateral synchrony after graded section of the anterior portion of the corpus callosum and, in two instances, of a section exclusively of the callosal trunk. During these functional operations, in which the extent of the callosal section was determined by the operative EEG findings, we have also performed callosal stimulation as a part of the intra-operative studies in the latter cases, thus observing that stimulation with pulses of 1 msec duration, 2 to 3 volt amplitude and frequencies in the range of 100 Hz up to 200 Hz were able to modify the spread of the secondary bilateral discharges. Based on this

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operative finding we have tried to reproduce it in cats with experimental penicillin epilepsy [3], and at the same time have selected two patients, who obeyed all our previously reported criteria for callosotomy [10,12], and submitted them to implantation of a chronic stimulation device: a flat 8-lead bipolar platinum electrode which was placed over the anterior convexity of the corpus callosum, and connected to a receiver under the skin of the infra-clavicular region, using the same craniotomy approach as in our previously operated cases [10,12]. The rationale for this operation, in opposition to cerebellar stimulation devices, which seek only stimulation, was to produce a "functional" or non-surgical "interruption" of the callosal fibers, by depolarizing or inhibiting transmission of epileptic discharges from one hemisphere to the other, as an attempt to prevent spread of the epileptic activity and its clinical consequences. Our working hypothesis was to spare the callosal fibers from surgical damage and also to prevent the undesirable sequelae of the "split-brain" syndrome, using a more conservative procedure, whose effects, if not effective, could be immediately reversed. Both cases were operated upon on January 14 and 28, 1986, respectively. No conspicuous adhesions were found between the cingulate gyri in either case, as may usually be observed, and both procedures were carried out smoothly, without excessive retraction over the mesial surface of the brain (Fig. 1).

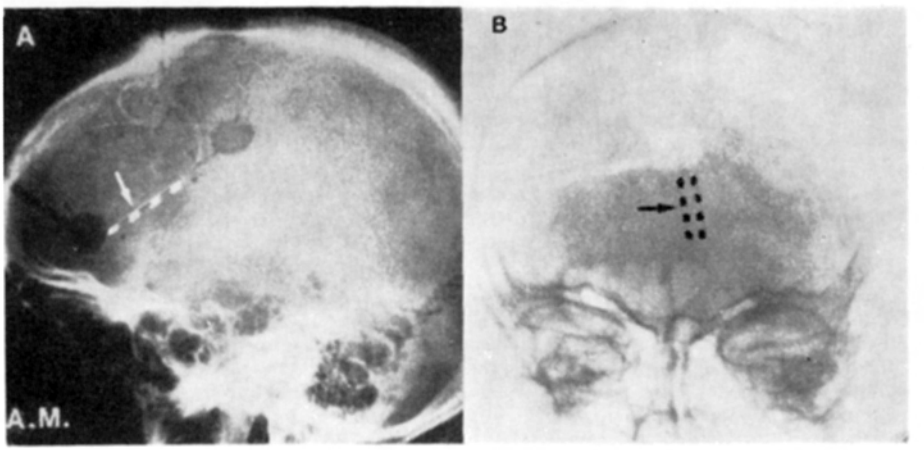

Fig. 1 — Radiographs showing implant of an 8-lead platinum electrode over the anterior convexity of the corpus callosum (arrows): A, lateral view; B, frontal view (Case AM).

SUBJECTS AND METHODS

The post-operative EEG controls of the first operated case (AM), showed surprisingly, a completely different pattern and morphology, with disruption of the previous bilateral synchrony, accompanied by a clinical improvement of the seizure condition. We assumed that this amelioration could be due to the intense callosal stimulation delivered during the procedure, during the testing of the stimulator device. As a consequence of this finding, the second operated case (MTZ), a 17 year-old helmet-wearing boy, initially diagnosed as a typical Lennox-Gastaut syndrome and later on classified as a Doose syndrome (*6*), was not stimulated at all, either during surgery or after the implant, and both were not stimulated again up to the time of this report. The first case (AM), a 23 year old patient, who had been submitted elsewhere to a right Forel-H field stereotactic lesion, as a desperate means to control his multiform seizures, had no significant benefit from that procedure, and at the present time is favourably controlled with medication, after his craniotomy. The second case (MTZ), is 80% free from his major attacks, free of losses of consciousness and atonic fits, doing without his helmet since the time of surgery, discharged and at home and school, controlled with regular amounts of medication. Both cases have been submitted to repeated EEG monitoring, and up to the present time have not shown recurrence of their bilateral synchrony. This stimulating finding of a long-duration unspecific effect of craniotomy on seizures mechanisms, led us to a retrospective evaluation of the magnetic resonance exams of our earlier operated cases, back to 1978 (*1,8*) and also of other published studies (*7,17*). Characteristic MRI findings of T_1 and T_2 images were present, even in the cases where

very gentle retraction was utilized, suggesting that some brain damage of vascular origin might have occurred under the retracted tissue over the right hemisphere mesial cortex: a funnel-like «tornado» — shaped image was observed in the territory of the pericallosal artery, probably representing some of the anatomical substrate of our electrical and neuropsychological (2) findings (Fig. 2).

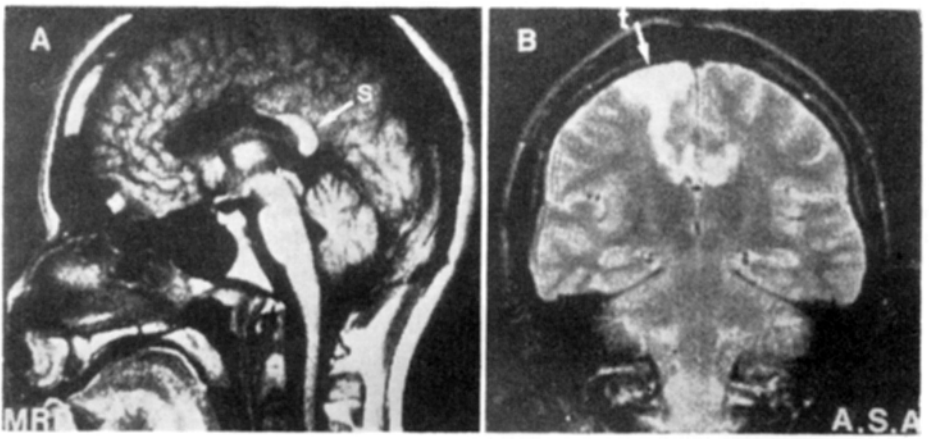

Fig. 2 — Magnetic resonance images of two different cases of craniotomy: A, conventional open callosotomy performed after craniotomy, sparing the splenium (S) (Case MRD); B, tornado-shaped image (t) obtained after craniotomy and retraction of the right mesial frontal lobe (Case ASA).

In order to explain our unexpectedly obtained «sham operation» model, and by-pass its possible mechanisms which, in our opinion, could checkmate our routine callosotomy operations, we decided to create two new rebuttal models: 1. Atraumatic stereotactic implantation of an indwelling electrode for chronic callosal stimulation, thus by-passing the mesial cortices; 2. Graded stereotactic lesion of the corpus callosum, thus preventing cerebral manipulation. However, a new variant came into play during the callosal localization and «repérage» studies: bisynchrony would disappear and the clinical picture would improve after injection of air for the pneumoencephalograms, another unspecific effect reported to affect seizures by early authors: Foerster in 1924, Clovis Vincent in 1933, cited by J. Delay (4), in 1950; Penfield (16), in 1954, has also reported on the therapeutic use of subarachnoid air injections as a deliberate form of treatment for epilepsy. Due to this fact, candidates for stereotactic callosotomy operations were submitted to a PEG before the procedure, in order to determine the duration of the disappearance of the bisynchronies, through repeated EEGs. As an average, this amelioration took 10 to 20 days to regress, and when the clinical picture deteriorated again and the EEG returned to its previous abnormalities, implant or stereotactic callosotomy was undertaken. Only one case (MP) did not show significant amelioration of his severe EEG abnormalities after the PEG, and was submitted to a stereotactic pacemaker implantation, for chronic callosal stimulation.

Model 1 case report (MP) — This was a 17 y.o. helmet-wearing boy with a 16 year history of multiform seizures and severe daily countless absences that gave him the false appearance of being mentally retarded and made him untestable to routine neuropsychological tests. He showed a severe bilateral synchrony and behavior problems, during his periods of awakening from his almost permanent state of absences. No amelioration was obtained from meticulously controlled anticonvulsant medication, during many weeks of hospitalization. No change of his EEG, number of seizures or behavior was noticed after PEG. An indwelling stimulation electrode was implanted stereotactically (Aug. 6, 1986) and after recovery, continuous and wide range voltage and frequency stimulation was delivered to the anterior callosum. Except for transient blockade of his EEG bisynchronous activity and occasional penile manipulation, during the stimulation procedure, no permanent effect was observed from his chronic callosal stimulation. As repeated stimulation did not bring satisfactory results, the indwelling electrode and receptor systems were withdrawn on Feb. 18, 1987 and the patient submitted to an anterior stereotactic callosotomy which brought significant improvement of his absences, behavior, and better control of his multiform seizures (Fig. 3).

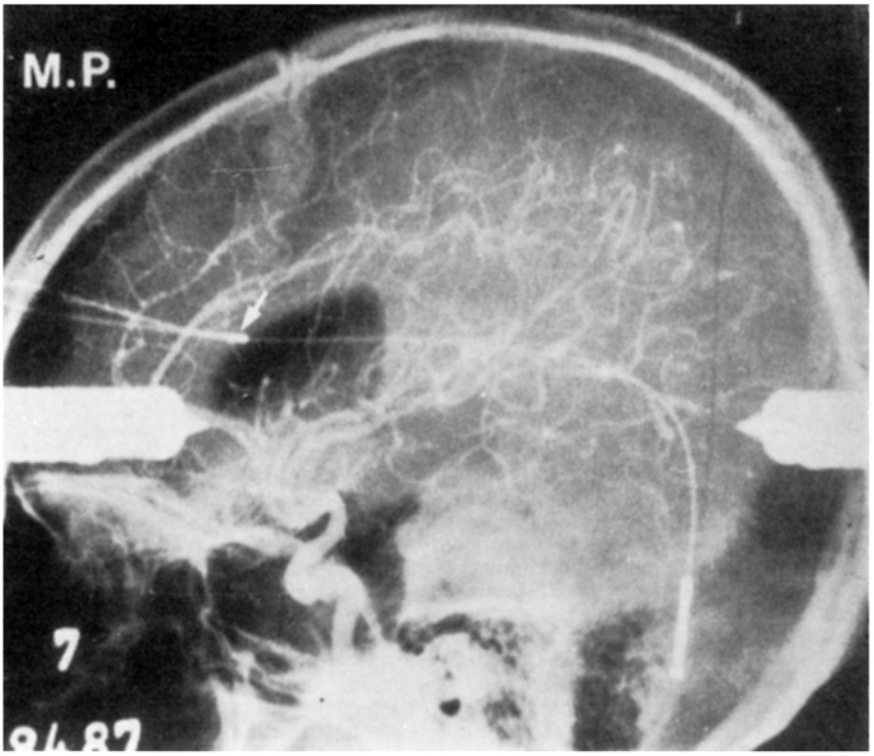

Fig. 3 — Intra-operative stereotactic radioghaph showing implantation of the indwelling electrode for neuroaugmentative callosal stimulation (arrow) (Case MP). Notice combined arteriographic and air studies from which stereotactic coordinates were taken (model-1 operation).

Model 2 case reports — Based on the findings of model-1, and also on our experimental findings in cats (*4*) we have decided not to reproduce the stimulation models, concentrating our efforts on the uprising technique of stereotactic callosotomy, originated in our service as a consequence of the inferential facts reported above. According to this final model, four other cases were submitted to graded stereotactic anterior callosotomy, aiming at prevention of cerebral manipulation (Fig. 4).

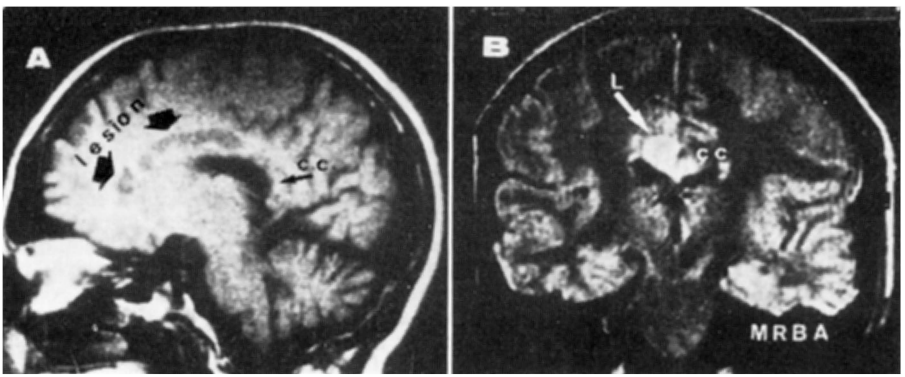

Fig. 4 — Magnetic resonance images (Case MRBA) showing: A, lateral view of three stereotactic callosal lesions (L) surrounded by edema, intact corpus callosum (CC) caudally; B, frontal view showing lesion (L) on right hemisphere.

RESULTS

This descriptive account was howbeit necessary to establish the chaining of events, which led us to propose this atraumatic intervention as a new and reliable surgical treatment for refractory epilepsy. Ten cases have been submitted, up to the time of this report, to stereotactic anterior callosotomy, using radiofrequency and a special side outlet thermocouple electrode. All 5 cases had significant improvement, according to the degree of severity of their preoperative electrographic findings, as we have reported elsewhere (10,12) in our adopted selection criteria. Decrease of their number of seizures and absences, better control with anticonvulsants, improvement of behavior and fewer episodes of consciousness loss were observed. However, more marked results were observed in neurobehavioral findings: differently from craniotomy patients, the stereotactic cases showed less findings in relation to their immediate post-operative disconnection syndrome, no adinamia of the left side of the body, found in patients submitted to open callosotomy (considered as part of the callosal disconnection syndrome), less perseveration and increased attention were also noticed after stereotactic callosotomy. No other formal neuropsychological (7) data could be evaluated due to the extremely low-level of intelectual and cognitive functions of these severely ill patients.

COMMENTS

We soon realized that the present findings would originate many questions yet to be answered. Stimulation of the corpus callosum, either in humans [11] or experimentally [3], has led us to apparently negative results, which forced us to abandon its use for the time being, until more experimental data, if possible in monkeys, as well as other clinical correlations, are established, before we attempt to draw any further conclusions. In our experimental material [3], 12 cats were submitted to callosal stimulation: 2 had direct stimulation after craniotomy and 10 stereotactically. The epileptic activity was produced by topic penicilin, placed over the convexity of the neocortex, after extensive bilateral craniotomies. The results indicated that callosal stimulation was not able to modify the morphology, frequency and synchrony of the epileptic bursts, at least in this model. This might be in agreement with the fact that thalamic and callosal afferents to the cortex do not share the same topographic distribution. Thus, our results are now being rechecked in focal epilepsy models. The most difficult question yet to be answered will be the disappearance of bilateral synchrony and the clinical improvement of seizures in our two patients submitted to a simple placement of a flat electrode over the surface of the anterior corpus callosum. This unspecific effect of craniotomy and frontal lobe retraction has not disappeared in our two patients up to the present time, more than a year and a half after electrode implantation. Conversely, this unspecific effect has not appeared in our single case submitted to insertion of a callosal indwelling electrode, stereotactically placed atraumatically, after a frontal twist-drill hole (Fig. 3). This third case had to be submitted, 6 months later, to a stereotactic callosotomy (after removal of the stimulation electrode), since his clinical picture continued to deteriorate. The MRI scanning finding of a right sided funnel-skaped lesion in the territory of the pericallosal artery in craniotomy cases, may thus represent the anatomical substrate of vascular damage or gliosis under the retracted area of mesial frontal lobe and corresponding callosal fibers, that may account for an unspecific effect of craniotomy and manipulation of brain commisures (Fig. 2).

Another unspecific effect: amelioration after pneumoencephalography, reported by other authors some years ago [4,16], also came into play in our cases to corroborate the fact that other unspecific manoeuvers like subarachnoid air injection [16], reduction of the cerebral mass or resection of brain tissue unrelated to the epileptogenic area [5,13] may reduce seizure activity. The mechanisms that underlie these unspecific findings remain to be elucidated as well. Stereotactic anterior callosotomy was a logical consequence of the findings that followed each other in the models we used, in our endeavour to control generalized refractory epilepsy by a less traumatic and safer functional neurosurgical technique. Experimental demonstration by Marcus and Watson [9], Naquet et al. [15] and Musgrave and Gloor [14], that section of the corpus callosum, even when incomplete, will partially prevent the bilateral synchronization of discharges in cat and monkey has also been demonstrated in our clinical cases, where marked disruption of bisynchrony was found after partial section of the callosum subsequent to craniotomy [10,12]. The introduction of the stereotactic approach to the corpus callosum, in our experience, has produced less neuropsychological findings as compared to previously operated craniotomy cases [2], no disconnection syndrome and no evidence of vascular damage to retracted mesial cortex (as detected by MRI examination), advantages

that were associated to satisfactory seizure control, improvement in behavior and better response to anticonvulsant medication.

We consider that the number of cases operated upon and their follow-up are still limited for further conclusions. However, we feel that we have opened the way to less damaging, more limited and more functional interventions on the cerebral commissures destined to have less side effects to unrelated adjacent structures and other extraneous brain mechanisms. Extensive corroborative technical, electrophysiological, neuro-psychological and neuro-imaging data which have been collected in this ongoing study, will be the subject of future publications. Meanwhile, this new functional neurosurgical approach to the corpus callosum seems worthy of immediate notice.

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