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Disconnective hemispherectomy for hemispheric dysplasia

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ABSTRACT – Twelve patients suffering from intractable epilepsy and presenting with radiological evidence of diffuse hemispheric involvement of a dysplastic process, were treated by disconnective hemispherectomy, either functional hemispherectomy or peri-insular hemispherotomy. The median age at surgery was 4.5 years old and the interval between seizure onset and surgery, 3 years. All patients underwent a presurgical evaluation that led to the suggestion of disconnective hemispherectomy. Over 70% of patients have remained in Engel's seizure outcome class I since surgery and another 18% have had a satisfactory seizure outcome. There was one unexplained death and one case of early hydrocephalus. Hemispherectomy offers the possibility to improve seizure control in the majority of patients undergoing surgery for extensive dysplastic pathology of the hemisphere. Disconnective techniques reduce the rate of complications in this specific pathology.

KEY WORDS: hemimegalencephaly, peri-insular hemispherotomy, functional hemispherectomy, hemispherectomy, hemispheric dysplasia, epilepsy surgery

Hemispherectomy for the control of pharmacologically refractory seizures is indicated when there is of a diffuse hemispheric pathology that is associated with a hemispheric syndrome, i.e. hemiplegia, hemianopsia. In certain progressive conditions such as extensive Sturge-Weber and Rasmussen's chronic encephalitis, it can be considered prior to the development of maximal deficits. The techniques of hemispherectomy have evolved over the past four decades from the anatomical removal of the hemisphere to different strategies for the removal or disconnection of the hemisphere, all aiming at providing seizure control while reducing the complications associated with the techniques. Disconnective hemispherectomy consists of disconnecting the hemisphere and leaving vascularized brain tissue in the hemispheric compartment. These techniques have been associated with good results in terms of seizure control, with a low complication rate.

In widespread hemispheric dysplasia, seizures are often refractory, raising the question as to the indication for hemispherectomy; clinically, this condition is also accompanied by varying degrees of hemiparesis and hemianopsia, associated with psychomotor retardation in most patients. Hemispherectomy has been reported for the treatment of seizures secondary to diffuse hemispheric dysplasia; some reports indicate a less favourable out-

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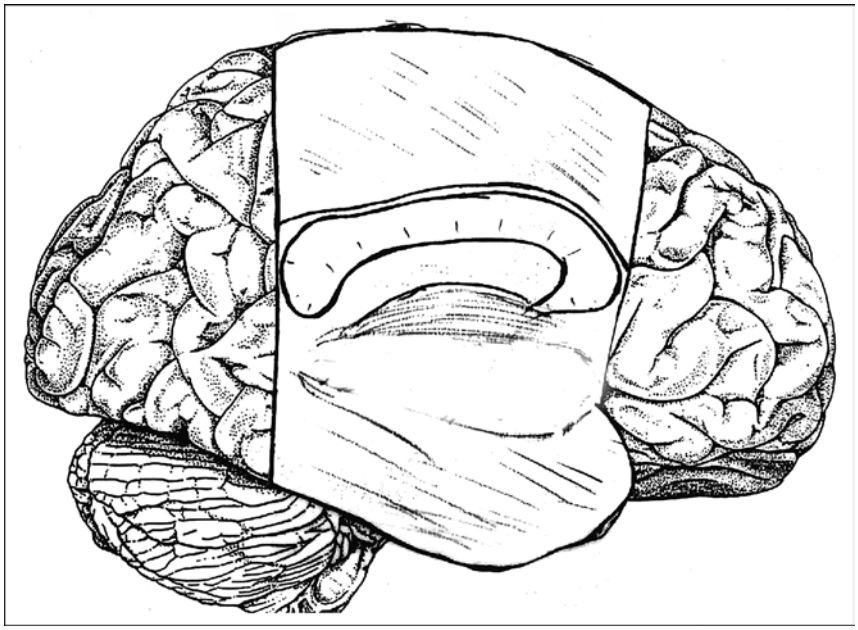


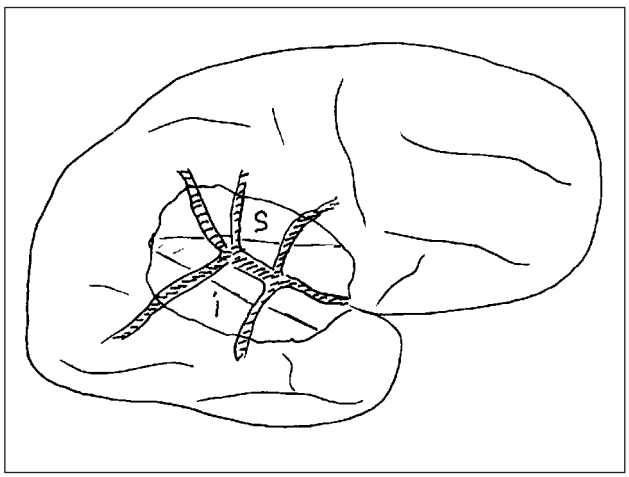
Figure 1. *Functional hemispherectomy (right): schematic illustration.*

come when hemispherectomy is carried out for dysplasia, as compared to other indications, such as infantile hemiplegia, Rasmussen's encephalitis and Sturge-Weber disease. Hemispheric dysplasia consists of a malformation, with or without enlargement, of one hemisphere. In the former instance, it is classified as diffuse migrational disorder and in the latter as hemimegalencephaly. We report our experience of disconnective hemispherectomy in twelve patients suffering from pharmacoresistant epilepsy secondary to extensive hemispheric dysplasia. These entities are encountered isolated or in association with skin lesions, as a part of a neurocutaneous syndrome.

Patients' data and surgical techniques

Patients' data

Twelve patients underwent disconnective hemispherectomy. There were six males and six females. The interval between seizure onset and surgery varied from 0.5 to 19 years, with a median of 3 years. Age at surgery varied from 1 to 20 years old (median 4.5 years). Nine left and three right hemispherectomies were performed. Eight were carried out using the peri-insular hemispherotomy technique and the other four using the classical functional



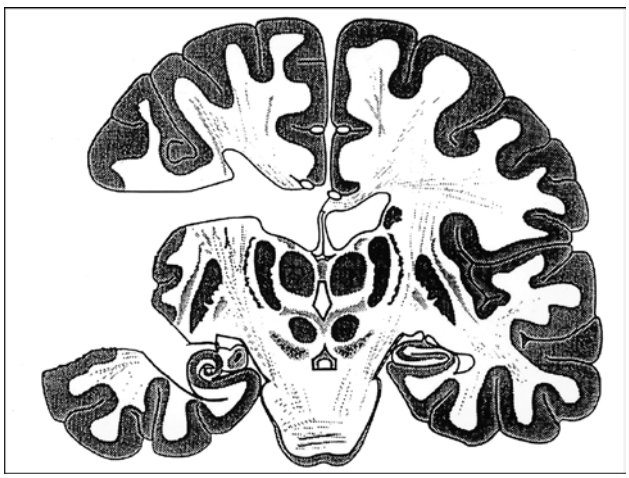


Figure 2. *Peri-insular hemispherotomy (right): schematic illustration.*

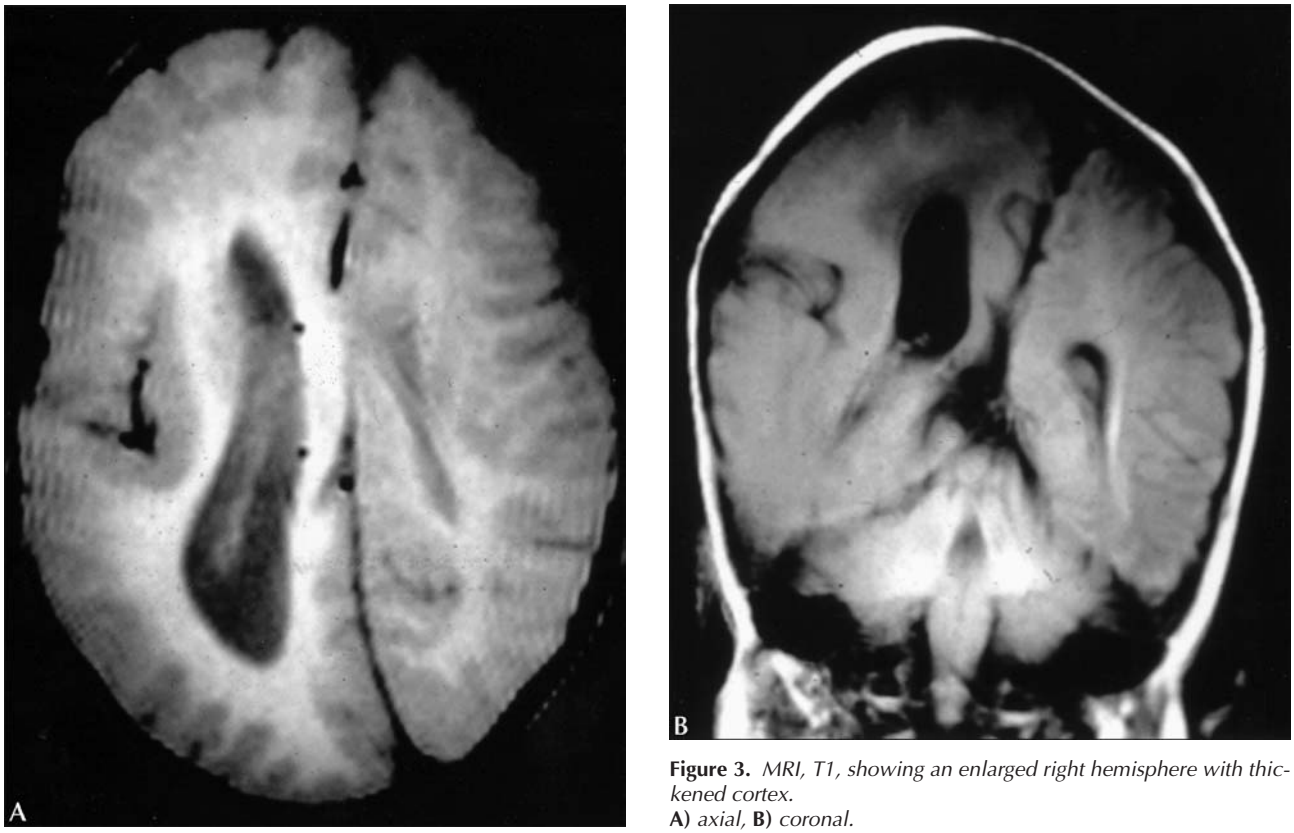


Figure 3. *MRI, T1, showing an enlarged right hemisphere with thickened cortex.*
A) *axial,* **B)** *coronal.*

hemispherectomy technique. Two patients had had previous craniotomies with partial resection. All patients underwent a presurgical evaluation including clinical examination, electroencephalographic seizure recording, MRI, and neuropsychological evaluation. The MRI showed a diffuse pathological process in all patients, this being characterized as hemimegalencephaly in seven patients, and diffuse migrational disorder in the other five. Careful scrutiny of the unaffected hemisphere on EEG and MRI is recommended to detect possible bilateral dysplasia.

Surgical techniques

Disconnective hemispherectomy consists of subtotal anatomical removal of the hemisphere and complete disconnection.

In ***functional hemispherectomy,*** the central convexity and parasagittal tissues are removed, with a temporal lobectomy [1]. The orbito-frontal aspect of the frontal lobe is transected from inside the ventricle to the edge of the sphenoid wing. The fibers entering the corpus callosum through the genu and rostrum, as well as through the splenium, are interrupted so that the frontal and parieto-occipital lobes are disconnected, but left *in situ*, their vascularisation being partially preserved. The insular cortex is removed or undercut.

In ***peri-insular hemispherotomy***, the hemispheric disconnection is made through the removal of the fronto-parieto-temporal operculum, transection of the corona radiata, transventricular callosotomy, amygdalectomy, anterior hippocampectomy, posterior hippocampotomy, resection or undercutting of the insula. In the latter technique, less brain tissue is resected, but complete disconnection of the hemisphere can be accomplished [2].

Morphological features

Macroscopic features

Hemispheric dysplasia involves most of the hemisphere as opposed to multilobar dysplasia, which spares large portions of the hemisphere. Based on the volume of the diseased hemisphere, hemispheric dysplasia is divided in two subtypes; the term "hemimegalencephaly" characterizes the dysplasia where the hemisphere is enlarged, while "diffuse migrational disorder" is not accompanied by enlargement of the hemisphere. In both subtypes, the ventricular system is usually enlarged on the affected side.

On gross examination, the cortical surface may look normal, or show gross gyral abnormalities, these being widened, or having the appearance of small narrow gyri (pachygyri). On cross section, areas of grey matter that are thicker than normal are encountered, and grey matter

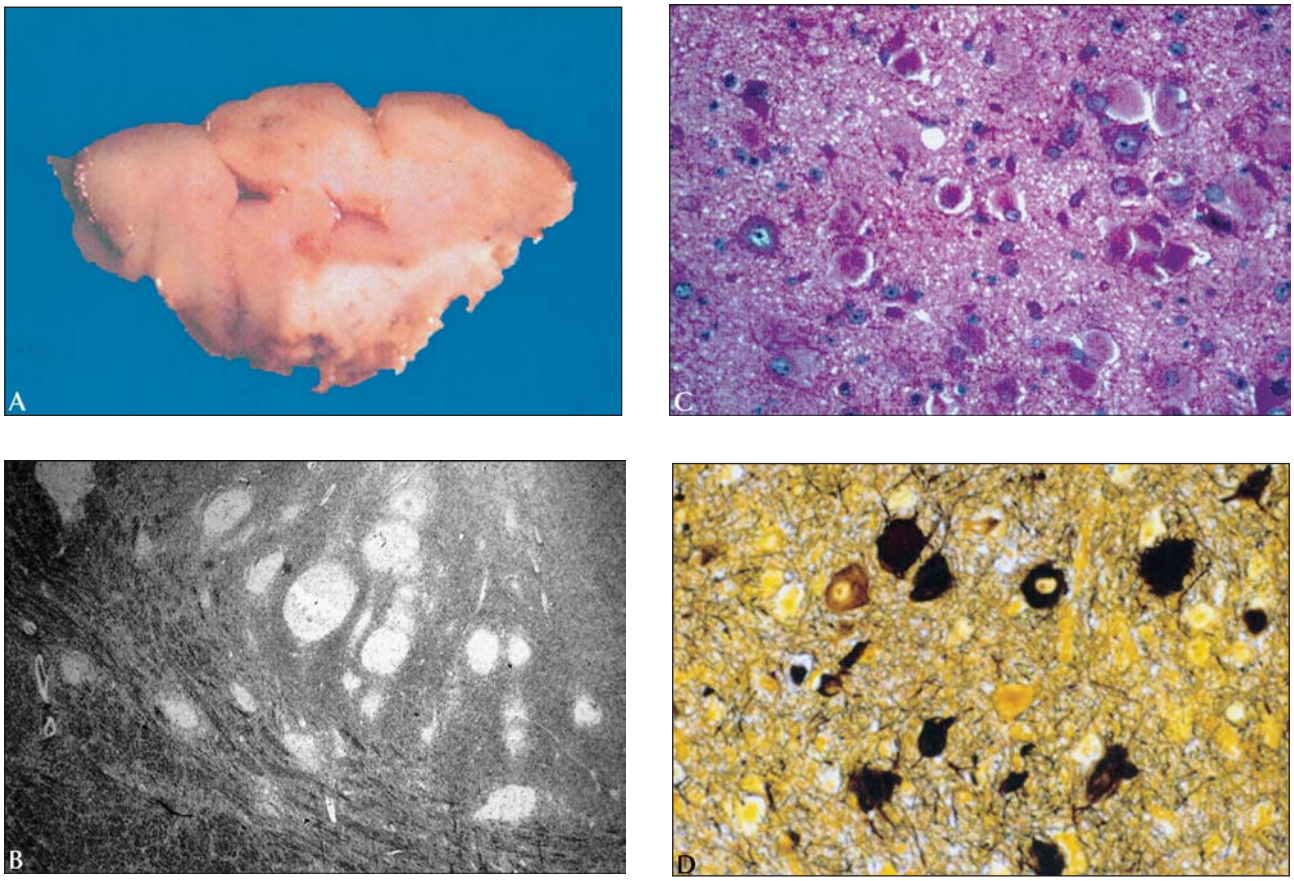


Figure 4. *a) gross findings of thickened cortex with ill-defined areas of palor*
b) Numerous globulous cells isolated or in small clusters. HE × 400.
c) Migrational disorder with many glioneuronal nodules within thin white matter. Luxol Fast Blue × 40.
d) Abnormal cytomegalic neurons. Bielschowsky × 400.

nodules may be found within the usual white matter distribution. Consistency is generally normal.

Microscopic features

There is a wide spectrum of neuropathological findings in hemispheric dysplasia. These findings may vary from case to case, but areas of thick cerebral cortex with abnormal lamination are common. Variable features include the presence of polymicrogyri formations with abnormal layering, or clusters of neurons in the white matter, or glioneuronal foci in the subarachnoid space. Large cytomegalic neurons can be seen within the cortex or the white matter. Other large, globular cells, known as "balloon cells", may be encountered throughout the cortex or the white matter. These may have features of astrocytes, neurons or both, as demonstrated by ultrastructural and immunohistochemical studies. Myelin sheaths in the white matter may be sparse, or may extend to the molecular layer of the cortex.

In summary, the neuropathological findings in hemispheric dysplasia are the result of cellular differentiation, migrational problems and architectural disarray; problems secondary to an aberrant cell death program are also a possibility [3].

Results

Complications

There was one post-operative death occurring in a 5 year-old boy. The child woke up normally from surgery but six hours later presented with sudden cardiac arrest which was not preceded by any other clinical symptoms or signs. Resuscitation was unsuccesful. The autopsy did not reveal any specific intracranial findings or any other cause of death. One patient developed hydrocephalus, which was successfully treated with a CSF diversion. This occurred after the third craniotomy carried out to treat seizures.

Seizure outcome

Seventy three per cent of the patients have remained in Engel seizure outcome Class I since surgery. Eighteen per

cent are in Class II, while 9% have not experienced any significant benefit from surgery (Engel's class IV). The type of dysplasia, whether hemimegalencephaly or diffuse dysplasia, does not appear to influence the outcome; actually, five of the seven cases of "hemimegalencephaly" have remained in Engel's Class I, while three of the four evaluable "diffuse migrational disorder" cases are in Class I. Seizure outcome was also analysed in relation to age at surgery, interval between seizure onset and surgery, sex, type of surgery, side of operation; these variables did not influence seizure outcome.

Discussion

Hemispherectomy for control of refractory seizures is a well established approach in conditions that diffusely involve the hemisphere [4-8]. Extensive hemispheric dysplasia accounts for a large proportion of the hemispherectomy performed for resistant seizures. In our experience with 73 disconnective hemispherectomies, it represents 16% of the etiologies. In a recent survey involving 333 hemispherectomies, it represented 30% of the etiologies; some of the surgical centers involved however dealt only with paediatric epilepsy surgery [9]. In this same report, the subtypes of extensive hemispheric dysplasias were 55% with "diffuse migrational disorder" and 45% with "hemimegalencephaly". In our population of disconnective hemispherectomies for extensive dysplasia, there were fewer "diffuse migrational disorder" cases as compared to "hemimegalencephaly" cases. The subtype of dysplasia does not appear to influence seizure outcome, since seizure outcome following surgery was the same in both groups of dysplasias, in our series as well as in the multicentric report [9].

Seizure outcome following hemispherectomy for hemispheric dysplasia has shown a 56.6%, complete control of seizures in a multicenter analysis. This differs from the results obtained in our series as well as in other series; this difference appears to be related to the way seizure outcome is measured. The multicenter report quotes a "seizure-free" category, while many reports, including this one, refer to Engel's seizure outcome classification. In the latter, there will be some patients who continue to have seizures postoperatively, who will be included along with seizure-free patients. Series using Engel's classification probably have results comparable to the multicenter analysis, rating the completely seizure-free proportion of patients at 56.6%. Overall, seizure outcome does not achieve as good a level as that encountered with strictly unilateral pathology such as infantile hemiplegia, Sturge-Weber or Rasmussen's encephalitis. The early onset and severity of seizures could account for secondary epileptogenesis, but the presence of some dysplastic lesion in the "unaffected" hemisphere should also be considered.

In a multicenter analysis of 99 cases, different hemispherectomy techniques were used. Thirty six per cent of patients who underwent an anatomical hemispherectomy became seizure-free, while this result was obtained in 75% using the Adams modification, 59% using functional hemispherectomy, 42% using hemidecortication and 76% using hemispherotomy, i.e. amalgamating the results with the vertical approach advocated by Delalande or the lateral approach proposed by Villemure [8,9]. When analyzed critically, the difference in seizure outcome as related to technique, may, in great part be due to the indication for hemispherectomy or patient selection. Actually, there are no reasons why seizure outcome following anatomical hemispherectomy should not be as good as that obtained with any other technique; the difference in the results obtained with anatomical hemispherectomy and Adams modification (36% versus 75%) is wide, compared to techniques that are, from a seizure control view point, identical. Removal of the hemisphere, by either technique, cannot result in worse seizure outcome unless patient selection influences the results. It seems fair to say that for the same indication, the different hemispherectomy techniques should have similar results. However, one can put forward some technical pitfalls to account for some of the difference in the results, such as incomplete removal in anatomical hemispherectomy, incomplete disconnection in functional hemispherectomy or hemispherotomy, incomplete removal in hemidecortication. In the latter technique, we can imagine the difficulty of removing all cortical elements parasagittally, under the temporal, frontal and occipital lobes, which could account for residual cortical tissue responsible for the results reported.

Hemispheric dysplasia is a condition that can be diagnosed early based upon the severity of the seizures and the associated neurological deficits. Since these patients are brought to medical attention early in life, the median age at time of hemispherectomy is very young. In the multicenter analysis, the hemispherectomy was carried out at a median age of 1.7 years [9]. In our series, the median age at surgery was 4.5 years, probably reflecting the referral pattern, considering that all patients except two underwent surgery after 2 years of age. It is to be expected that early surgery will become the rule in extensive dysplasia, considering the demonstrated efficacy of hemispherectomy as regards seizure control, and the knowledge that early recognition of the syndrome reduces the negative impact on neurodevelopment.

In comparison to other conditions responsible for intractable epilepsy secondary to diffuse hemispheric damage, i.e. Sturge-Weber, Rasmussen's encephalitis and infantile hemiplegia, the degree of mental retardation is, in general, more pronounced in patients suffering from hemispheric dysplasia. This neurodevelopmental aspect has been studied by Battaglia *et al.* in cases of hemimegalencephaly. Their patients could be classified into two prognostic categories; favourable and unfavourable. It appears as if the morphological changes of hemispheric dysplasia of

the hemimegalencephaly type, as opposed to the diffuse hemispheric type, as well as the severity of epilepsy, are factors of poor cognitive outcome [10]. However, there is no doubt that in both types, the benefit of improving seizure control will have some positive impact on cognitive function and neurodevelopment. Another factor contributing to the poor cognitive development in these patients may be related to the presence of some involvement of the other hemisphere.

In hemispheric dysplasia, as in other indications for hemispherectomy, the choice of the surgical methodology remains based upon training and personal experience. However, there is accumulating evidence that disconnective hemispherectomy, either functional hemispherectomy or hemispherotomy, provides as good a seizure outcome, and with a lower rate of complications, as resective techniques [11]. In hemispheric dysplasia, these disconnective hemispherectomy methodologies give the surgeon the flexibility to resect more or less tissue as he or she is performing the disconnection. It is for example possible, in hemimegalencephaly, to accomplish a hemispheric disconnection by removing more tissue using the functional hemispherectomy approach, as compared to the hemispherotomy approach, which requires less resection. In both instances, similar results should be expected, but in the first, surgery may be made easier as a function of the larger amounts removed. In instances of enlarged hemisphere, peri-insular hemispherotomy may not be easy to perform, but can easily be converted to functional hemispherectomy consisting of a wider resection, which facilitates the surgical orientation.

Conclusion

Hemispheric dysplasia represents a significant proportion of etiologies responsible for intractable hemispheric epilepsy, rendering the patient a candidate for hemispherectomy. Taking into account the early onset of seizures and that these are, in general, difficult to control medically, hemispherectomy is indicated in most conditions of hemispheric dysplasia. The clinical characteristics of this condition are pharmacoresistant epilepsy, with different degrees of contralateral hemispheric deficit, and mental retardation. In some instances, the hemispheric dysplasia is part of a neurocutaneous syndrome. Hemispherectomy is associated with very satisfactory seizure control in most patients, close to two thirds remaining seizure-free after surgery; seizure outcome is thus very worthwhile, although not as good as for other etiologies. Similar observations can be made concerning cognitive development following surgery, which is not as marked as it is with other conditions requiring hemispherectomy for control of seizures. Although all hemispherectomy techniques should have the same results as regards to seizure control, the literature highlights controversies. However, we believe that for identical seizure control, the hemispherectomy technique that provides the lowest rate of complication should be the technique of choice. To this end, disconnective hemispherectomy (either functional hemispherectomy or peri-insular hemispherotomy), would be the most appropriate. □

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