MRI Studies in Epilepsy

Jerome ENGEL, Jr. (*)

ÖZET

Epilepside MRI Çalışmaları

Nörolojide görüntüleme yöntemlerindeki büyük ilerlemeler son yıllarda epilepsi tanısında devrim yaratmıştır. Hernekadar EEG temel tanı gereci olma özeliğini, PET ve SPECT gibi fonksiyonel görüntüleme yöntemleri önemli ama sınırlı yararlarını korusalar da MRI ile yapılan strüktürel görüntüleme birçok merkezde giderek daha kolay uygulanabilir olmakta ve önemi artmaktadır. Yeni yüksek rezolusyonlu tarayıcılar kolaylıkla hipokampal skleroz veya fokal yerleşimli displastik dokular gibi cerrahi rezeksiyona uygun semptomatik epilepsinin en sık rastlanan patolojik yapılarını kolaylıkla tanımlayabilirler. Bu gelişmeler rutin epilepsi tanısının giderek daha doğru konmasını ve daha az masraflı olmasını sağlamaktadır. Ancak bu durum cerrahi öncesi hazırlıkların çok pahalı olması nedeniyle kullanımı kısıtlı olan epilepsi cerrahisi için kısmen geçerlidir.

Anahtar kelimeler: *epilepsi, cerrahi, MRI*

SUMMARY

Major advances in neuroimaging have revolutionized the diagnosis of epilepsy in recent years. Although EEG remains an essential diagnostic tool in this disorder and functional imaging techniques such as PET and SPECT continue to have limited, although important, applications, structural imaging with MRI is becoming increasingly accessible and important in most major centers.

New high resolution scanners easily identify most common pathological substrates of symptomatic epilepsy, including hippocampal sclerosis and subtle localized areas of dysplastic tissue that are often amenable to surgical resection. With minor, relatively inexpensive modifications, functional MR might also become feasible for clinical evaluation of patients with epilepsy.

These developments promise to make routine epilepsy diagnosis more accurate and, in some ways, more cost-effective. This is particularly true for surgical treatment of epilepsy, which has been greatly underutilized, in part due to the expense of pre-surgical evaluation.

Key words: *epilepsy, surgery, MRI*

Advances in neuroimaging have revolutionized the practice of neurology, and have had a profound effect on approaches to diagnosis of epileptic conditions. Structural neuroimaging, particularly *magnetic resonance imaging (MRI)*, has enjoyed much wider application than functional imaging, due to the relatively greater ease of operation and consequent increased throughput of the former. Recent developments now permit MRI to be used for functional imaging as well (fMRI), and this technique may be available for routine clinical applications soon. Standard MRI, and perhaps fMRI, could become indispensable diagnostic tools in neurology in general, and in epileptology in particular, with capabilities for cost-effective implementation in developing, as well as developed countries.

Neuroimaging plays an important role in differential diagnosis of epilepsy, particularly when structural lesions can be used to distinguish between a neurological and a psychogenic condition, or between a primary (idiopathic) and a secondary (symptomatic) epileptic condition, and also to diagnose specific diseases and syndromes such as *cysticercosis* or *tuberosclerosis*. Neuroimaging has its greatest impact on management of epilepsy, however, when an underlying treatable cause is revealed. Usually this is a structural lesion that can be surgically removed. Surgically remediable epileptic conditions today include more than those due to discrete lesions such as solitary neoplasms, congenital cysts, vascular malformations, and localized infectious processes. A variety

(*) Departments of Neurology and Anatomy & Cell Biology and the Brain Research Institute, UCLA School of Medicine, Los Angeles, California, USA
Adress correspondence to: Jerome Engel, Jr., M.D., Ph.D. Reed Neurological Research Center 710 Westwood Plaza, Los Angeles, CA 900024-1749

of syndromes have now been identified that respond poorly to antiepileptic drug treatment and may be associated with progressive deterioration, but can be successfully treated by surgical resection of epileptogenic brain tissue [1]. Patients with surgically remediable epilepsies deserve early surgical intervention, which offers the best chance of seizure remission and a normal behavioral outcome. MRI is often key in establishing the diagnosis of a surgically remediable syndrome in time to maximize surgical results. MRI is also important in the presurgical evaluation of patients with difficult to diagnose epileptic conditions, although the impact on outcome may not be as dramatic as occurs with the surgically remediable syndromes. The establishment of MRI facilities throughout the world should make safe and effective surgical treatment for epilepsy available even in developing countries, which would reduce the human, as well as financial, cost of this disorder.

The remainder of this paper will concentrate on the use of MRI studies for planning specific types of resective surgical treatment for epilepsy.

Anteromedial temporal resection for mesial temporal lobe epilepsy (MTLE): MTLE is the prototype of a surgically remediable sydrome [2,3]. This disorder is characterized by medically refractory complex partial seizures associated with unilateral, or predominantly unilateral, hippocampal sclerosis. Seizures characteristically begin late in the first decade of life and usually become intractable by mid to late adolescence. Patients have often experienced prolonged febrile convulsions prior to onset of habitual seizures, and a family history of epilepsy is common. The interictal EEG reveals unilateral or bilaterally independent anterior temporal spikes, and there is a characteristic sphenoidal ictal EEG onset [4]. A material-specific memory deficit on neuropsychological testing and hypometabolism of the involved temporal lobe on interictal *positron emision tomography with 18F-fluorodeoxyglucose* (FDG-PET) help to confirm the electrographic localization and lateralization [5]. Interictal localized hypoperfusion of the temporal lobe can also be seen on *single photon emission computed tomography* (SPECT), and a characteristic pattern of hyper- and hypoperfusion occurs on ictal and postictal SPECT [6]. With the advent of high resolution MRI, however, most patients with MTLE can now be identified by obvious atrophy of one hippocampus on thin-cut T1 coronal images and increased signal of that hippocampus on T2 images [2,7].

Although ictal recordings are still necessary for diagnosis of MTLE in most patients, the finding of hippocampal atrophy on MRI can greatly simplify the presurgical evaluation process, reduce the need for expensive FDG-PET and invasive recording in most cases, and permit cost-effective early identification of surgical candidates. Postoperative results reported by a large number of epilepsy centers over the past decade indicated that 70 % of patients with medically refractory complex partial seizures of all causes who undergo a standard anterior temporal lobectomy, or amygdalohippocampectomy, can expect to become seizure free, while less than 10 % experience no improvement [8]. More recent unpublished data from a number of centers suggest that results of anteromedial temporal resection for MTLE, based in part on evidence of hippocampal atrophy on MRI, may be closer to 80 % seizure free.

Hemispherectomy and large multilobar resections for diffuse unilateral and secondary generalized epilepsies: There are a variety of surgically remediable syndromes in infancy and early childhood characterized by diffuse dysfunction of one hemisphere, catastrophic unilateral or secondary generalized seizures, and profound developmental delay. Patients presenting with this clinical picture and MRI-documented syndromes such as *hemimegencephaly*, *Rasmussen's encephalitis* and *Sturge-Weber syndrome*, who already have hemiparesis with a useless hand, can benefit greatly from hemispherectomy [9]. Almost 70 % of such patients can expect to become seizure free with consequent reversal of the developmental delay and improved function of the hemiparetic side, although manual dexterity is invariably lost [8]. Subtotal hemispherectomies can also be performed, for instance to preserve vision when occipital cortex appears normal on MRI and/or FDG-PET.

Large areas of focal cortical dysplasia limited to one hemisphere can sometimes be detected in infants and young children who have been given the diagnosis of a secondary generalized epilepsy, such as *infantile spasms*, with or without clinical or EEG focal features. These localized developmental disturbances were initially identified with FDG-PET and confirmed by attenuation of normal and abnormal electrographic activity during intraoperative electrocorticography (ECoG) [10]. Now, however, they can be seen after the age of one as white matter aberrations on T2 MRI [11]. Large multilobar resection of dysplastic cortex, usually involving temporal, occipital and parietal lobes, eliminates seizures in approximately 70 % of patients with this disorder, most of whom experience reversal of developmental delay and minimal, if any, postoperative motor impairment.

Localized resections for medically intractable partial seizures: Apart from MTLE, which is presumably due to hippocampal sclerosis, and the catastrophic seizure disorders due to diffuse hemispheric abnormalities described in the previous section, partial epilepsies can be classified as *lesional*, due to discrete structural abnormalities such as neoplasms, cysts, vascular malformations, and localized dysplastic processes, or as *cryptogenic*, indicating that the disorder is secondary to a localized pathological substrate that has not been identified. Lesional partial epilepsies are usually neocortical and can be treated surgically, either by removal of the lesion alone (*lesionectomy*), or by excision of the lesion and adjacent epileptogenic cortex [12,13]. Both require identification of the structural abnormality, best accomplished with MRI, and electrographic verification that seizures are originating in this area.

It is important to note here that not all structural lesions identified by MRI in patients with partial epilepsy are responsible for the habitual seizures. In all cases, epileptogenicity of the lesion must be demonstrated electrophysiologically. Venous angiomas and cavernous hemangiomas are the most common non-epileptogenic lesions encountered in patients with epilepsy, but caution is also advised when solitary lesions are encountered that suggest conditions commonly associated with multifocal pathology, such as cysticercosis and tuberous sclerosis. Epileptogenicity can often be established by scalp EEG recordings demonstrating interictal spikes and ictal onset in the vicinity of the structural lesion. The boundaries of cortical excisions are usually determined by interictal spikes recorded during intraoperative ECoG, or by mapping of interictal and ictal discharges recorded extraoperatively using chronically implanted subdural or depth electrodes [14,15,16].

When epileptogenic lesions are adjacent to essential primary cortex, functional mapping is also necessary to determine the location of motor, sensory, language, and other cortical areas that cannot be damaged in the resection process. For lesions within primary cortex, lesionectomy can sometimes result in elimination of seizures, without introducting additional neurological deficit. For lesions adjacent to primary cortex, cortical margins can be take up to, but not including, essential cortex. In these situations, *multiple subpial transection* of primary cortex has been reported to relieve seizures without producting neurological deficits [17]. Functional mapping can be accomplished during intraoperative ECoG, or be performed extraoperatively with subdural grid electrodes or depth electrodes, depending upon whether the cortical area to be explored is on the surface or in the depth of the brain, respectively [18].

When MRI fails to reveal a structural lesion, and history provides no clue to an etiology, patients with cryptogenic medically refractory partial epilepsy can still be considered surgical candidates if electrophysiological studies demonstrate a well-localized epileptogenic region based on identification of the site of ictal onset and maximal interictal spike activity, usually obtained with chronic intracranial electrode recording [14,15,16]. The presurgical evaluation and approach to surgical resection or multiple subpial transection for cryptogenic partial epilepsy is the same as for lesional partial epilepsy, with the exception that lesionectomy is obviously not a surgical option. However, there is rarely confirmatory localizing information from tests of focal function deficit such as PET and neuropsychometric evaluation [19].

Although only approximately 45 % of patients with medically intractable partial seizures can expect to become seizure free following localized resection, postoperative outcome for those with lesional epilepsy is almost as good as the outcome achieved by temporal lobe resection in patients with MTLE [8]. On the other hand, limited resection is much less likely to eliminate epileptic seizures in patients with cryptogenic partial epilepsy. This may be due to the increased risk of false localization of the epileptogenic region when MRI fails to demonstrate a structural lesion, or it may be due to the specific pathophysiologic process underlying cryptogenic epilepsy, which could be diffuse or multifocal. Possibilities for the pathological substrates of this disorder include: **1)** lesions such as those causing lesional partial epilepsy, which are too small to be detected by MRI or even by screening histopathological analysis of surgically resected or post mortem brain tissue; **2)** cortical cell loss and synaptic reorganization similar to that occurring in hippocampal sclerosis, which are not revealed by routine histopathological procedures; and **3)** one or more pathophysiological processes that are unique to neocortex and have yet to be elucidated. Cryptogenic partial epilepsy is a major frontier for research in the field of epilepsy surgery, and MRI should play a major role in this pursuit.

Future applications of MRI in surgical management: Three dimensional reconstruction of MRI can help identify subtle lesions, particularly cortical dysplasias. MRI is being used with increasing frequency for depth electrode implantation, and reconstructed images are providing exceptionally detailed visual aids for neuronavigation in the oparating room, permitting discrete removal of lesions deep to the surface, with minimal cortical disruption [20]. Functional information can be superimposed on these images with coregistration techniques; essential primary cortical areas adjacent to an epileptogenic region, identified by activation PET [21] or magnetic source imaging (MSI) [22], as well as the epileptogenic region itself, identified by interictal and ictal epileptiform abnormalities recorded with intracranial EEG recording or MSI can be used to plan the surgical excision. Magnetic resonance arteriography (MRA) [23] can also be coregistered on the reconstructed image so that major vessels can be avoided during either depth electrode implantation or surgical resection. The most exciting new development, however, is the use of fMRI to localize primary essential cortical areas, which could replace the need for intracranial recording, PET or MSI for this purpose [24]. The spatial resolution of fMRI is at least as good as that of either PET or MSI. More importantly, fMRI is a dynamic technique with a temporal resolution that is theoretically in the millisecond range. Consequently, it might also be possible to map the onset and propagation patterns of ictal discharges with fMRI in order to definitively localize the epileptogenic region. Such an approach would be particularly useful in patients with cryptogenic partial epilepsy, where no structural lesion is present to guide the investigation.

Preliminary studies have already demonstrated the ability of fMRI to identify discretely localized changes in deoxyhemoglobin during repeated partial seizures [25]. Techniques are currently being developed to record EEG simultaneously with fMRI mapping of ictal events [26]. Further improvements are still needed in order to account for movements that might occur during ictal studies, if fMRI is to become useful for presurgical evaluation of most seizure types that are treated surgically. Ultimately, however, this noninvasive technique should prove more cost-effective than diagnostic procedures currently used for presurgical evaluation of medically refractory partial epilepsy. Theoretically, functional mapping and localization of ictal discharge could be accomplished at any center with an MRI scanner, making it feasible to create epilepsy surgery centers in many areas where this treatment modality is now prohibitively expensive.

ACKNOWLEDGMENTS

Original research reported by the author was supported in part by Grants NS-02808, NS-15654 and GM-24839, from the National Institutes of Health, and Contract DE-AC03-76-SF00012 from the Department of Energy.

REFERENCES

1. **Engel J Jr, Shewmon DA:** Overview: Who should be considered a surgical candidate? In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press, 1993; pp 23-34
2. **Engel J Jr:** Recent advances in surgical treatment of temporal lobe epilepsy. Acta Neurol Scand 1992; 86:71-80
3. **Wieser HG, Engel J Jr, Williamson PD, Babb TL, Gloor P:** Surgically remediable temporal lobe syndromes. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press 1993; pp 49-63
4. **Risinger MW, Engel J Jr, Van Ness PC, Henry TR, Crandall PH:** Ictal localization of temporal lobe seizures with scalp/sphenoidal recordings. Neurology 1989; 39:1288-1293
5. **Engel J Jr, Henry T, Risinger MW, Mazziotta JC, Sutherling WW, Levesque MF, Phelps ME:** Presurgical evaluation for partial epilepsy: relative contributions of chronic depth electrode recordings versus FDG-PET and scalp-sphenoidal ictal EEG. Neurology 1990; 40:1670-1677
6. **Rowe CC, Berkovic SF, Austin MC, McKay WJ, Bladin**

PF: Patterns of postictal cerebral blood flow in temporal lobe epilepsy: Qualitative and quantitative analysis. Neurology 1991; 41:1096-1103

7. Cascino GD, Jack CR Jr, Parisi JE, Sharbrough FW, Hirschorn KA, Meyer FB, Marsh WR, O'Brien PC: Magnetic resonance imaging-based volume studies in temporal lobe epilepsy: pathological considerations. Ann Neurol 1991; 30:31-36

8. Engel J Jr, Van Ness P, Rasmussen TB, Ojemann LM: Outcome with respect to epileptic seizures. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press 1993; pp 609-621

9. Shields WD, Duchowny MS, Holmes GL: Surgically remediable syndromes of infancy and early childhood. In Engel J Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press 1993; pp 35-48

10. Chugani HT, Shields WD, Shewmon DA, Olson DM, Phelps ME, Peacock WJ: Infantile spasms: I. PET identifies focal cortical dysgenesis in cryptogenic cases for surgical treatment. Ann Neurol 1990; 27:406-413

11. Sankar R, Curran JG, Kevill JW, Rintahaka PJ, Shewmon DA, Vinters HV: Microscopic cortical dysplasia in infantile spasms: Evolution of white matter abnormalities. AJNR (in press).

12. Cascino GD, Boon PAJM, Fish DR: Surgically remediable lesional syndromes. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven press 1993; pp 77-86

13. Fried I, Cascino GD: Lesional surgery. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press 1993; pp 501-509

14. Arroyo S, Lesser RP, Awad IA, Goldring G, Sutherling WW, Resnick TJ: Subdural and epidural grids and strips. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, 2nd Edition. New York: Raven Press 1993; pp 377-386

15. Ojemann GA: Intraoperative tailoring of temporal lobe resections. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, Second Edition. New York: Raven Press 1993; pp 481-488

16. Oliver A, Awad IA: Extratemporal resections. In J Engel Jr, ed: Surgical Treatment of the Epilepsies, Second Edition. New York: Raven Press 1993; pp 489-500

17. Morrell F, Whisler WW, Bleck TP: Multiple subpial transection, a new approach to the surgical treatment of focal epilepsy. J Neurosurg 1989; 70:231-239

18. Ojemann GA, Sutherling WW, Lasser RP, Dinner DS, Jayakar P, Saint-Hilaire JM: Cortical stimulation. In J Engel Jr, ed: Surgical treatment of the epilepsies, 2nd Edition. New York: Raven Press 1993; pp 399-414

19. Henry TR, Sutherling WW, Engel J Jr, Risinger MW, Levesque MF, Mazziotta JC, Phelps ME: Interictal cerebral metabolism in partial epilepsies of neocortical origin. Epilepsy Research 1991; 10:174-182

20. Drake JM, Ratke JT, Hoffman HJ: ISG viewing Wand system. Neurosurgery 1994; 34:1094-1097

21. Woods RP, Mazziotta JC, Cherry SR: MRI-PET registration with automated algorithm. J Comp Asst Tomography 1993; 17:536-546

22. Gallen CC, Sobel DF, Schwartz B, Copeland B, Waltz T, Aung M: Magnetic source imaging. Present and future. Investigative Radiology 1993; 28(suppl 3):S153-S157

23. Awad IA, McKenzie R, Magdinec M, Masaryk T: Application of magnetic resonance angiography to neurosurgical practice: A critical review of 150 cases. Neurological Reserach 1992; 14:360-368

24. Jack CR Jr, Thompson RM, Butts RK, Sharbrough FW, Kelly PJ, Hanson DP, Riderer SJ, Ehman RL, Hangiandreou NJ, Cascino GD: Sensory motor cortex: Correlation of presurgical mapping with functional MR imaging and invasive cortical mapping. Radiology 1994; 190:85-92

25. Jackson GD, Connelly A, Cross JH, Gordon I, Gadian DG: Functional magnetic resonance imaging of focal seizures. Neurology 1994; 44:850-856

26. Ives JR, Warach S, Schomer DL: A technique for recording a patient's EEG during an echo-planar magnetic resonance imaging scan. Electroenceph Clin Neurophysiol 1994; 90:56P