Resecting without detecting the lesion in extratemporal lobe epilepsy?

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Nonlesional extratemporal lobe epilepsy (ETLE) often persists following resection of the site of ictal onset, localized with definitive intracranial EEG recordings.[1,2] In lesional ETLE, however, lesionectomy with resection of a single electrophysiologically defined ictal onset (ictogenic) zone often stops seizures immediately and permanently.[1,2] In temporal lobe epilepsy (TLE), a single ictogenic site can be resected, either with an accompanying lesion or in the absence of an MRI-detected lesion, and is a highly efficacious epilepsy therapy.[2] Efforts to increase surgical efficacy in nonlesional ETLE have focused on localization by functional imaging to substitute for lesion localization by structural imaging.

In nonlesional TLE, an ancillary functional imaging abnormality is generally used to confirm scalp ictal EEG localization for surgical planning, but even without imaging abnormalities, intracranial EEG recordings can support efficacious resection. Both extracranial and intracranial EEG recordings have spatial sampling limitations. No safe and tolerable set of scalp, subdural, and intracerebral electrodes can sample all possible sites of ictal onset. Brain MRI examines the structure of the entire brain, however. It might well be assumed that finding a lesion on MRI serves mainly to add full brain spatial sampling to the specificity of ictal EEG localization in planning surgery of lesional TLE and of lesional ETLE. A whole-brain functional imaging abnormality may serve as a surrogate for an MRI lesion in planning surgery of nonlesional TLE, using glucose metabolic maps of PET, ictal perfusion maps of SPECT, *N*-acetylaspartate maps of magnetic resonance spectroscopy, and other imaging techniques.[3,4] Many of these studies assist in refining hypotheses regarding ictal onset zones or eloquent cortex, but none of these techniques provides localizing information that adequately substitutes for the finding of a lesion in planning efficacious surgery for nonlesional ETLE, comparable to application of functional imaging in nonlesional TLE.[1,4,5]

Ictal SPECT is unique among functional imaging techniques in its ability to map localized dysfunction that is generated by seizure states, as opposed to mapping interictal dysfunction or to mapping persisting biochemical abnormalities. The whole-brain field of view offered by ictal SPECT solves the spatial sampling problem of extracranial and intracranial ictal EEG. The demands of prompt radioligand injection during seizures and numerous associated technical issues require great effort and precise attention to sources of artifacts. On comparing ictal and interictal brain blood flow maps, normal variations in resting interictal blood flow are a source of potential error in ictal–interictal difference mapping with SPECT. In this issue of *Neurology*®, Sulc et al.[6] provide a rigorous validation of improved ictal–interictal perfusion difference mapping using appropriate statistical analyses in refractory partial epilepsies. They found that statistical parametric mapping of ictal vs interictal cerebral perfusion increases the specificity of ictal hyperperfusion maps to the site of resection that will be efficacious in seizure control for nonlesional TLE but does not do so for nonlesional ETLE.[6] In other words, they found that optimized localization of ictal hyperperfusion was associated with excellent surgical outcome in MRI-negative TLE, but surgical outcomes were relatively poor in nonlesional ETLE despite planning with optimized localization of ictal hyperperfusion.

It is disappointing but perhaps revealing that improved statistical parametric SPECT mapping of the ictogenic zone does not much enhance surgical planning in nonlesional ETLE. Based on several decades of studying a mechanistically diverse set of functional imaging techniques that have considerable utility in planning resection for MRI-negative TLE, it appears that none of these techniques provides similarly useful localizing information for MRI-negative ETLE. Are TLE and ETLE fundamentally different in the mechanisms by which epilepsy may or may not persist after the currently active site of seizure initiation has been removed?

In lesional TLE, an MRI-detected epileptogenic lesion usually is located in or near the electrophysiologically defined ictogenic zone[7]; the epileptogenic–ictogenic site often can be resected to stop seizures immediately and permanently. In MRI-negative TLE, no epileptogenic lesion can be found, but

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localizing a single ictogenic zone permits this site to be resected efficaciously, seemingly as if an unseen (MRI-negative) epileptogenic lesion had also been removed. In lesional ETLE, the electrophysiologically defined ictal onset zone is distant from the epileptogenic lesion more often than occurs in lesional TLE[7]; perhaps resection of both sites acts to halt seizures that have been initiated at the ictogenic zone and to prevent the lesion from generating new ictogenic zones. If the epileptogenic site in a patient with MRI-negative ETLE is distant from the ictogenic zone, it might be expected that resecting only the current site of ictal onset will not prevent the undetected epileptogenic site from generating new ictogenic zones, however. Numerous other explanations could account for the relative inefficacy of epilepsy surgery in MRI-negative ETLE, of course. Nonetheless, the etiologic importance of a causative lesion must be strongly suspected whenever a candidate lesion can be found. By this line of reasoning, one might expect that detecting previously unseen lesions will enhance planning of efficacious surgery in ETLE. The observations of Sulc et al.[6] encourage further development of ultra-high-field MRI and new MRI sequences likely to better detect subtle ablative and dysplastic lesions and also disturbed white matter morphology that may be associated with subtle cortical lesions,[8–10] in addition to improving functional imaging applications, to better evaluate the full range of refractory epilepsies.

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