Outcomes for temporal lobe epilepsy operations may not be equal
A call for an RCT of ATL vs SAH

Gary W. Mathern, MD
John W. Miller, MD, PhD

Correspondence to Dr. Mathern: gmathern@ucla.edu

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An assured way to kindle a lively debate among epilepsy specialists is to ask, “What is the best surgery for medically refractory mesial temporal lobe epilepsy (mTLE)—anterior temporal lobectomy (ATL) or selective amygdalohippocampectomy (SAH)?” Usually, patients with mTLE have seizures arising from epileptogenic lesions such as hippocampal sclerosis or low-grade gliomas involving the lesion and surrounding hippocampus, amygdala, and parahippocampal cortex, although some mTLE cases do not have detectable lesions on imaging. ATL removes the temporal pole to allow access to the lesion and mesial temporal structures (figure, A and B), whereas SAH uses a small temporal neocortical resection to approach and remove mesial structures (figure, C and D). The rationale for SAH has been that it should provide equivalent seizure control because the mesial structures, the presumed source of the seizures, are removed with limited damage of the lateral temporal neocortex and underlying white matter, possibly reducing cognitive functions. Other recent approaches being developed to treat mTLE using the SAH concept include radiosurgery and MRI-guided laser ablation.

SAH is not convincingly superior to ATL in outcome studies. Retrospective cohort studies indicate that seizure-free outcomes correlate mainly with case selection, that is, identifying and removing epileptogenic lesions, rather than the type of resection. Similarly, the strongest predictor of worsening cognitive outcomes with surgery is intact preoperative intellectual ability, not operative technique. These studies have notable methodologic problems, including selection bias and lack of randomization, often with comparison of unrelated and noncontemporaneous surgical cohorts, sometimes performed by different neurosurgeons at different centers.

In this issue of Neurology, Josephson et al. add fuel to this ongoing debate. The authors performed a literature review and meta-analysis of data on more than 1,200, mostly adult, mTLE surgical patients, from 13 studies published from 1997 to 2010 from 5 countries on 5 continents. ATL was more effective than SAH, with 8% more patients with mTLE becoming seizure free after ATL (95% confidence interval 4%–13%). This modest difference achieved statistical significance because of the large sample size. Operative risks for major morbidity were similar with the 2 procedures. Because of differences in testing methods, a meaningful comparison of neuropsychological outcomes was impossible.

The interesting results, but unavoidable limitations, of this study bring to the forefront the need for a well-designed clinical trial to determine definitively the outcome differences between these 2 surgical approaches. This particular meta-analysis is based on nonrandomized data, albeit on a large scale, and is subject to confounding clinical variables and selection bias. For example, seizure-free outcomes after mTLE surgery decline with longer follow-up. Josephson et al. address this potential confounding factor with a subgroup analysis combining studies with similar postoperative follow-up durations, but it would be best eliminated in a randomized controlled trial (RCT). Reporting of seizure outcomes varies among studies; for example, some distinguish between seizure freedom with or without auras, whereas others may not. An RCT would have rigidly defined outcome measures. Similarly, the extent of mesial or lateral resection would need to be strictly standardized among the centers participating in the RCT.

An RCT would need to address the following questions:

1. Is the modest difference in seizure freedom between ATL and SAH, discovered in the meta-analysis, genuine? If ATL is more effective, it could mean that the additional cerebral tissue removed in this procedure contains areas of seizure origination or disconnects such regions.

2. Are there meaningful differences in neuropsychological outcomes comparing ATL with SAH? Do any observed differences in cognitive outcomes depend on whether the resections are in the dominant or nondominant hemisphere? The neuropsychological measures used in the trial would have to be designed to detect impairment of functions referable to temporal neocortex.
3. Are the risks of surgery the same? SAH involves a smaller incision and skull opening and less brain removal than ATL, but does this actually translate into fewer complications, lower mortality risk, or shorter hospitalizations? Such an RCT would certainly be challenging. Because enrolling patients in a randomized surgical trial is difficult, it would need to be international and multicenter, with central oversight of standardized protocols and assessments of MRI volumetric and neuropsychological measures across languages. It might also be difficult to identify centers with enough surgical experience and expertise in both procedures to properly randomize patients.

It is not actually a matter of which of these 2 methods is better, but rather, a question of what their outcome differences are. Even if an RCT confirms a modestly higher efficacy for ATL, convincing evidence of better cognitive outcomes or safety for SAH would nonetheless ensure an important role for this selective procedure in epilepsy surgery. The results of Josephson et al., and the current literature, demonstrate the importance of an RCT for defining the future of temporal lobe epilepsy surgery.

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REFERENCES