Is it time to replace the Wada test?
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Language and memory lateralization usually must be known before epilepsy surgery. Patients whose seizure focus is close to presumed language cortex also require detailed topographic localization of language regions to define safe boundaries for surgical excision. The intracarotid amobarbital, or Wada test, has been the standard for language and memory lateralization, and electrical stimulation mapping the standard for precise demarcation of language cortex.1,2 Both procedures are invasive and have risks and discomfort. The need to replace the Wada test and electrical stimulation mapping with less invasive and more reliable techniques has long been recognized. Alternative approaches include structural MRI, PET activation, event-related potentials, cortical magnetic stimulation, and fMRI.3-7 fMRI, which detects a blood oxygenation level–dependent signal, is a hemodynamic indicator of neuronal activity associated with performance of a task or some other discrete set of events. The Wada test, by contrast, indicates functional lateralization by suppressing neuronal activity on one side and assessing the patient’s ability to perform a task in that context. fMRI has the advantages of excellent spatial resolution and safety of repeated studies, and has seemed a promising noninvasive alternative.7

In this issue of Neurology, Gaillard et al.8 report hemispheric language dominance using an fMRI paradigm of silent naming of items in response to silent reading of item description. The authors found language lateralization in 27/30 patients, bilateral language in one patient, and nonlateralizing results owing to poor activation in only two patients. The fMRI dominance was in agreement with the Wada test in 15/20 patients, with the only disagreement relating to one test suggesting bilateral representation while the other identified one hemisphere as dominant. There were no contradictory lateralizations.

With this paradigm, the authors accomplished three important goals. First, both temporal and frontal language regions were activated. Most fMRI language paradigms have focused on lexical fluency, which tends to produce consistent activation in the inferior frontal gyrus, but inconsistent temporal lobe activation. Given the prevalence of temporal lobe epilepsy among surgical candidates, a paradigm with consistently interpretable temporal lobe activation is essential. Second, the authors’ method is practical for most centers with conventional MRI, but test interpretation will require clinical experience. Third, the paradigm provided consistently interpretable data for individual patients.

Can we now replace the Wada test and direct cortical stimulation with fMRI? In situations where only identification of the hemisphere of language dominance is needed for surgical planning, perhaps. Gaillard et al.8 have extended previous studies with their reading paradigm and methods of fMRI analysis, and have improved fMRI ability to identify temporal language regions in over 90% of patients. As Gaillard et al.8 indicated, the optimal fMRI study may need to involve more than one paradigm, implementing converging operations to determine both lateralization and localization with consistency. A limited fMRI study of that type may be sufficient in patients with a nondominant extrahippocampal epileptogenic zone, particularly in those undergoing lesionectomies. For patients who require excision close to language cortex, a map is needed, identifying cortical regions that may be removed safely and those that need to be spared in order to avoid postoperative deficits. Additional studies are needed before fMRI can be trusted to draw a map. For example, it is not clear that removal or injury of a region activated in an fMRI image with performance of a given task necessarily leads to inability to perform that task.

Most surgery candidates have mesial temporal lobe epilepsy. Lateralizing memory function and identifying patients at risk for postoperative memory loss are functions of the Wada test that fMRI will need to fulfill. There are encouraging reports of mesial temporal activation asymmetries on fMRI that are consistent with epileptogenic zone lateralization.9,10 However, the ability of fMRI to predict postoperative memory function has not been sufficiently investi-
gated. In fairness, the performance of Wada testing for predicting postoperative memory function is not above criticism.1

fMRI will be ready to fully replace the Wada test and electrical stimulation mapping when a paradigm or battery of fMRI paradigms can be validated for identification of language regions that should be excluded from excision, and for prediction of postoperative memory function. We are almost there.

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