Chapter 17: Epilepsy Supplemental Material

Additional Evaluations and Specialized Cognitive Mapping Techniques

EEG

EEG is necessary for classifying seizure type, syndrome, and epileptic zone. Various interictal patterns such as spikes, spike-wave complexes, sharp waves, and polyspikes are considered epileptiform and rarely seen in individuals without seizures. These epileptiform abnormalities occur in up to 98 percent of patients with epilepsy (Noachtar & Remi, 2009). In addition, interictal EEG patterns can provide information about epilepsy syndromes. For example, hypsarrhythmia is the hallmark of infantile spasms, and 3 Hz spike and wave complexes are typical of *absence epilepsy*.

Patients with medically intractable focal seizure disorders may be considered for surgical resection of the seizure onset zone (SOZ). The SOZ may be detected on scalp EEG, through video EEG monitoring (vEEG), intracranial EEG (icEEG), or MEG. The vEEG is conducted over days by videotaping paroxysmal behavior simultaneously with continuous EEG. This is typically necessary for differentiating epileptic from non-epileptic seizures and for surgical localization.

The surgical workup includes examination of the results of long-term video-EEG monitoring, intracranial or stereo EEG, neuropsychological testing, high resolution MRI, and brain mapping methods such as fMRI, Wada testing, MEG, and PET. The goal of the presurgical workup is to localize the seizure focus, determine the most appropriate treatment option, predict likelihood of seizure freedom, and minimize risk for cognitive morbidity.

For patients being considered for surgical intervention for whom the SOZ has not been identified with vEEG, invasive EEG may be conducted where signals are recorded from

surgically exposed cortex through electrocorticography (ECoG) or depth electrodes. Electrodes can be implanted subdurally (grids placed below the dura) or intracortically (with penetrating depth electrodes) as with stereotactic EEG (sEEG). SEEG samples deep structures such as the hippocampus and amygdala and provides more precise localization of the SOZ. Methods like ECoG and sEEG are ideal for brain computer interface applications, which is the next frontier in epilepsy treatment (Herff et al., 2020).

Structural MRI

High resolution MRI will identify underlying etiologies such as malformations of cortical development, neoplastic lesions, focal cortical dysplasias, posttraumatic lesions, vascular malformations (AVMs, cavernous hemangiomas, venous angiomas, strokes), and mesial temporal lobe sclerosis. Mesial temporal sclerosis is the most common identifiable abnormality on imaging in patients with intractable temporal lobe seizures. Temporal lobe atrophy on MRI is associated with greater cognitive impairment at baseline. In addition, hippocampal sclerosis and volume loss prior to surgery predict better seizure and cognitive outcome after temporal lobectomy. Recent studies from the ENIGMA (Enhancing Neuroimaging Genetics through Meta-Analysis)-Epilepsy consortium using structural MRI and diffusion tensor imaging have improved our understanding of disease progression, showing robust structural brain alterations in grey matter and reduced fractional anisotropy in white matter in hippocampal and parahippocampal regions in TLE (Sisodiya et al., 2020).

Presurgical Workup

Thirty to 40 percent of persons with epilepsy fail to respond to medication for seizures and may be a surgical candidate. These patients require the care of a multidisciplinary team including an epileptologist, neurosurgeon, neuropsychologist, neuroradiologist, neurological

nurse, and psychiatrist. The goal of the presurgical workup is to localize the seizure focus, determine the most appropriate treatment option, predict likelihood of seizure freedom, and minimize risk for cognitive morbidity. Evaluations often include long-term video-EEG monitoring, intracranial or stereo EEG, neuropsychological testing, high resolution MRI, and brain mapping methods such as fMRI, Wada testing, MEG, and PET.

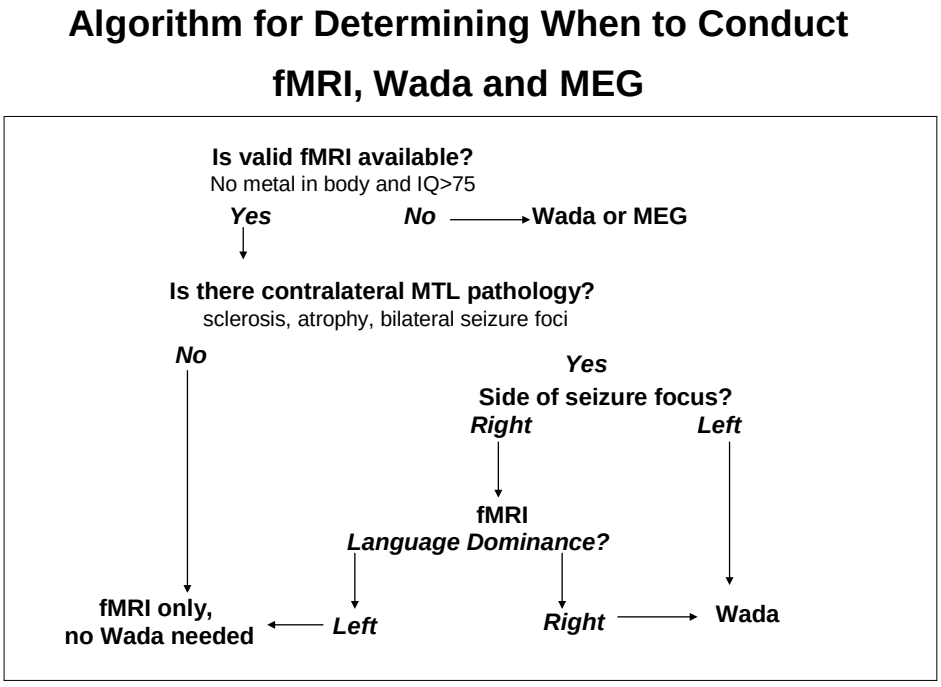
Wada Testing

The Wada test is used to determine hemispheric representation of language and memory functioning through selective anesthetization of each cerebral hemisphere. The technique was first introduced by Juhn Wada in 1949 (Wada, 1949; Wada & Rasmussen, 1960) to determine hemispheric representation of language prior to surgical intervention. Amobarbital or another short acting barbiturate is injected into the internal carotid artery to temporarily anesthetize the hemisphere of surgical interest. This results in a chemically reversible model of the planned resection. During the period of hemianesthesia, language and memory testing of the awake hemisphere is conducted. Memory is typically assessed by exposing the individual to information to be encoded, such as real objects, line drawings, or abstract designs during hemianesthesia. The patient's free recall and recognition for the items encoded during the period when only one hemisphere is "awake" is assessed after the medication effect has resolved. A widely used method for Wada testing was developed at the Medical College of Georgia, and has been well described (Loring, 1992). Wada testing has been empirically validated by studies showing that Wada language and memory scores predict naming (Sabsevitz et al., 2003) and memory (Sabsevitz et al., 2001; Stroup et al., 2003) outcome after dominant ATL, and are related to the functional and pathological status of the hippocampus (Baxendale et al., 1997;

Davies et al., 1999), seizure onset laterality (Alpherts et al., 2000; Baxendale et al., 1997; Loring et al., 2009), and seizure control postoperatively (Lee et al., 2003).

Because of the invasive nature of Wada testing and the availability of alternative mapping methods such as fMRI and MEG, some argue that Wada testing should be only used is specific circumstances (Qadri et al., 2021). An algorithm for determining when Wada is needed to determine the cognitive risks of surgical intervention has been developed (Swanson et al., 2007; See Figure 1).

Figure 1. Algorithm for Determining When to Conduct fMRI, Wada, and MEG



fMRI

For surgical patients, fMRI is considered to be a valid replacement for Wada testing for lateralization of function and for predicting cognitive decline in both language and memory

(Binder, 2010; Massot-Tarrus et al., 2019; Szaflarski et al., 2017). fMRI has the advantage of being noninvasive, requiring no exposure to radiation, and providing not only lateralization but also localization data. fMRI detects task-correlated or event-related changes in blood flow associated with underlying neuronal activity as patients perform various cognitive tasks.

Commonly used tasks for mapping language in epilepsy patients are semantic decision or word generation tasks. The ideal task is active, overt (allowing behavioral monitoring so that performance variables can be examined) and has a perceptual control or contrast task that is matched for difficulty and performance accuracy, thereby eliminating extraneous (e.g., sensory, attentional) processes unrelated to the cognitive function of interest. Laterality indexes (LIs) are calculated based on the number of activated voxels in the left and right hemisphere or region of interest (V_L- V_R/V_L + V_R). These LIs have been found to correlate with results of Wada testing and to predict cognitive outcome after temporal lobectomy. In fact, fMRI laterality indexes predict both language and memory outcome after left ATL (Binder, 2011; Gross, et al., 2022, Powell et al., 2008; Sabsevitz et al., 2003; Sidhu et al., 2015).

Magnetoencephalography (MEG)

MEG involves noninvasively measuring the magnetic fields generated by brain activity (for a review of the method, see Chapter 8). MEG provides a direct measure of neural activity with excellent temporal resolution that is superimposed on MRI to create a magnetic source image. MEG serves two main purposes in the epilepsy evaluation: It is used for more precise identification of epileptiform abnormalities, and for noninvasive functional mapping primarily of language. Because MEG detects magnetic fields induced by intracellular currents and is sensitive to epileptic spikes that may not be seen on surface EEG, it is useful for guiding the placement of intracranial EEG electrodes (Stefan et al., 2011).

There is an emerging literature on the role of MEG in localization of language functions in presurgical epilepsy evaluations. Picture naming and auditory description naming paradigms have been used to lateralize language (Youssofzadeh et al., 2020). Studies have compared MEG lateralization with the Wada testing and found good concordance (e.g., Doss et al., 2009; McDonald et al., 2009) for hemispheric dominance ratings (Papanicolaou et al., 2004). MEG provides information about localization of seizure foci and a noninvasive functional mapping alternative, though more so for lateralization than localization.

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