

Optimal utilization of functional neuroimaging in epilepsy surgery - A neurosurgeon's perspective

By conservative estimates, there are about a million people with drug-resistant epilepsy in India. Surgery can cure or control epilepsy in a substantial number of people with focal or symptomatic epilepsy. Better understanding of the surgically remediable lesional epilepsy syndromes, improvements in neuroimaging and micro-neurosurgical techniques have contributed to the development of epilepsy surgery programs in many parts of India during the recent years.

Epilepsy surgery can be defined as resection or functional modification of part of the brain with the aim of alleviating seizures and improving the quality of life. Lesion is a volume of altered cerebral tissue detected by imaging techniques, whereas focus is a volume of brain tissue that contains the epileptogenic area or the epileptogenic zone. If pathological substrate containing both 'lesion' and 'focus' is clearly identified and resected, the outcome is successful. However, if there is discordance between the 'lesion' and 'focus' and such resective surgery is not possible, then various types of functional procedures can be performed with the aim to reduce the frequency and severity of epilepsy.

In order to achieve an optimum outcome, it is crucial to identify the ideal surgical candidate who can benefit with various types of resective or functional procedures. This selection is based upon a multimodality evaluation including clinical, scalp EEG, video EEG telemetry, neuroimaging, neuropsychology and psychiatry assessments. Concordance of clinical, EEG and neuroimaging abnormalities correlates with an excellent postoperative seizure outcome. The role of neuroimaging, especially functional neuroimaging will be reviewed in this article from the epilepsy surgery perspective.

NEUROIMAGING

Neuroimaging allows imaging the structure and function of the brain. Magnetic resonance imaging (MRI) of the brain is the most commonly used modality in past two decades for the presurgical evaluation of patients with drug-resistant focal epilepsy. MRI

is essential for the diagnosis of morphological abnormalities like vascular malformations, developmental and foreign-tissue lesions. These cerebral structural abnormalities demonstrable on MRI are highly suspicious of culprit lesion but may not always correlate with the epileptogenic zone. In clinical situations, where MRI brain is either normal or equivocal or demonstrate multiple lesions or lesion too extensive; then epileptogenic zone can be reliably predicted by careful correlation of clinical, EEG and functional nuclear imaging findings from ictal SPECT and Inter-ictal FDG PET.

POSITRON EMISSION TOMOGRAPHY

Interictal FDG PET imaging has been extensively applied in presurgical evaluation of drug-resistant seizures. Primary clinical applications have been correlative with ictal electrophysiologic and structural magnetic resonance findings for the purposes of (1) increasing certainty that the ictal onset zone has been accurately determined by noninvasive studies prior to anterior temporal lobectomy, multilobar resection or hemispherectomy; (2) optimizing selection of intracranial electrode placement sites for ictal monitoring in patients with normal MRI findings or in patients with lesion and focus discordance; (3) prognostication with regard to seizure control, cognitive and other functional effects of epilepsy surgery.

Unilateral mesial temporal lobe hypometabolism on FDG PET is specific and unequivocal finding in case of temporal lobe epilepsy. FDG PET allows further evaluation of the extension of epileptogenic zone (EZ) in cases of temporal lobe epilepsy by providing guidelines for the surgical team regarding the extent of resection in order to minimize the secondary effects on memory and language. There is high agreement between interictal FDG PET and invasive ictal EEG in the localization of the EZ. Invasive ictal EEG evaluation should be performed only if there is disagreement between PET and the set of noninvasive modalities (semiology, ictal EEG, neuropsychological evaluation, MR and SPECT). In this case, PET can guide the localization of the region to be investigated with invasive electrodes.

Detection of regional hypometabolism can guide the extent of resection in lesionectomy, focal corticectomy, multilobar resection, or functional hemispherectomy without prior intracranial monitoring. Normal metabolism or complex regional metabolism bilaterally on FDG PET may provide indirect support for corpus callosotomy. In epilepsies of frontal origin, which are the most prevalent ones among the extra-temporal lobe

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epilepsy, sensitivity of PET is found to be equal to that of MRI in localization of EZ. PET is superior to ictal SPECT mainly in occipital and multifocal epilepsies. Another useful application of PET is the metabolic evaluation of the contralateral hemisphere, especially in cases in which the ample resection of a hemisphere is necessary in children with intractable seizures.

SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

The major strength of brain (SPECT; single photon emission computed tomography) is the ability to perform peri-ictal (ictal or early postictal) studies, making it complementary to FDG PET. Peri-ictal SPECT exploits the fact that focal seizure is associated with transient rise in regional cerebral blood flow (rCBF). Brain SPECT provides the 'snap shot' of phenomenon of transient rise of rCBF, if Tc-99m labeled lipophilic radiopharmaceuticals (ECD/HMPAO) are injected during or immediately (within seconds) of seizure onset. Inter-ictal SPECT is usually performed after a gap of at least one day for comparing it with ictal SPECT. However, accuracy of inter-ictal brain SPECT alone in localization of EZ is low and variable, ranging from 20 to 69.8%. Ictal SPECT studies in patients with typical medial temporal lobe epilepsy will show a characteristic pattern of unilateral global temporal hyperperfusion with relative decreased perfusion in other cortical areas both ipsilaterally and contralaterally. The relative change from the interictal state is often more striking in the lateral temporal cortex than the medial temporal region.

Ictal SPECT findings are very reliable in lateralizing complex partial seizures in temporal lobe epilepsy. Such seizures usually last 90 s or more and provide sufficient time, in a well-organized center to perform the injection of radiopharmaceutical (Tc-99m ECD). In order to obtain good results, the radiopharmaceutical must be injected at the beginning or within the first 30 s of initiation of complex partial seizures. Ictal SPECT demonstrates higher accuracy rates (70.5 to 97%) in localization and lateralization of EZ. Performance of ictal SPECT for localization of temporal lobe epilepsy in pediatric population is equal to adults. The characteristic pattern of focal area of relatively increased cerebral perfusion, usually in the mesial and anterior parts of the temporal lobe with decreased perfusion in the adjacent lateral temporal cortex on ictal SPECT study is regarded reliable finding for localization and lateralization of EZ.

The extra-temporal lobe epilepsy (ExTLE) involves two types of problems in the location of the EZ. First the morphological neuroimaging seldom reveals a single lesion, with a more frequent occurrence of undetectable lesions ("normal" MR), or multiple suspected abnormalities. Second, if MR does not reveal any structural lesion, it is difficult to determine where to apply the subdural grids or strips during invasive EEG evaluation. Ictal SPECT can be useful in this case by indicating functional alterations in the semiologically and electrographically suspected area.

Interictal SPECT is of little localizing value in extra temporal

partial seizures. In cases where there is a large structural lesion, the observation of corresponding hypoperfusion adds little to seizure localization. In the absence of a structural lesion, it is unusual to observe definitive interictal hypoperfusion in the epileptogenic area in seizures arising from the frontal, parietal, or occipital regions. However, interictal studies are crucial in interpreting ictal studies because ictal hyperperfusion in extra temporal seizures is usually more subtle than that observed in temporal lobe seizures. Seizures of extra temporal origin present a challenge to ictal perfusion SPECT studies as they are commonly brief, shorter than temporal lobe seizures, and therefore allow little time for 99mTc-ECD injection. In contrast to complex partial seizures of temporal lobe origin, where diagnostic ictal changes are seen up to 30 s after seizure termination, in extra temporal epilepsies there is little or no persistence of hyperperfusion into the postictal period. Another difference is that ictal SPECT in extra temporal epilepsy cases may highlight regions of spread and the region of seizure initiation may be less prominent. Thus, late ictal injections can be difficult to interpret because there may be a number of hyperperfused regions. The solution to this problem is to attempt to obtain an early ictal study so that epileptogenic focus becomes obvious.

Ictal SPECT is particularly useful in nonlesional extra temporal epilepsies, often revealing discrete neocortical regions of activation not appreciated by video EEG monitoring or MRI. Ictal SPECT can also be applied usefully to the study of correlations between clinical features and seizure onset. For example, clinical and ictal SPECT features have been studied in a series of 14 patients with parietal lobe epilepsy. The images showed focal hyperperfusion in all cases and corresponded with structural lesions that were present in nine. Two main clinical seizure patterns were recognized in association with the SPECT patterns: seizures with sensorimotor manifestations characterized by hyperperfusion in the anterior parietal area and complex partial seizures of the psycho-paretic type associated with hyperperfusion in the posterior parietal region. These two clinical seizure patterns may reflect seizure propagation via association fibers that connect the anterior parietal region to the primary motor, premotor, and supplementary motor areas. However, the posterior parietal region is connected to the cingulate gyrus, insula, and parahippocampal gyrus so that seizure propagation to these structures may well imitate complex partial seizures of temporal lobe epilepsy. Postictal injections in the extra temporal cases are of limited localizing value and provide useful information in only a minority of cases. Moreover, because there may be extensive hyperperfusion late in a seizure in areas of spread, postictal changes can be unreliable. Unlike postictal studies in medial temporal lobe epilepsy, extra temporal cases rarely show postictal hyperperfusion at the focus, nor is extensive hypoperfusion around the focus characteristically present.

SUMMARY

At the present time, MRI, PET and SPECT are useful for localizing the epileptogenic lesion in epileptic patients who

are candidates for resective surgery. MRI and PET may be particularly helpful for differentiating mesial temporal lesions from lesions of the lateral temporal lobe, which could allow some patients to undergo selective surgical resection of either mesial temporal structures or lateral neocortex. In all cases however, localization of a structural abnormality with MRI and a functional abnormality with PET or SPECT requires EEG confirmation of epileptogenicity. In some patients these tests make resective surgery possible without the necessity of depth electrode evaluation, while in others they provide important information that guides the approach to stereotaxic depth electrode placement. The demonstration of focal hypofunction becoming hyperfunctional during a clinical behavior change on PET and SPECT can be regarded path gnomonic of a partial

epileptic condition. In the near future, PET–MRI with dedicated epilepsy protocols may emerge as the preferred neuroimaging modality for the evaluation of patients with complex partial seizures.

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