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Epilepsy Surgery and Nuclear Medicine

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ABSTRACT

One of the major indications of brain scintigraphy is guidance for determination of the epileptic focus prior to epilepsy surgery. Although there are several methods for localization of epileptic focus previous studies have shown that removal of the focus that is indicated by single photon emission tomography (SPECT) or positron emission tomography (PET) increases the success of the surgery and good prognostic indicator. In this chapter we wanted to summarize the information from the literature about radionuclide approach for localization of the epileptic focus; benefits, indications, prognostic information and methods.

Keywords: Epilepsy Surgery; Epileptic Focus; SPECT; PET

INTRODUCTION

Epilepsy surgery is a relevant approach in the treatment of epilepsy and sometimes only choice for the patient. Considering the high mortality and morbidity associated with status epilepticus [1] and antiepileptic drugs [2] and success of surgical procedures [3] increase in surgery rates is inevitable. There are some localization methods for the definition of the epileptic focus. Among these methods there are invasive methods like invasive EEG and noninvasive methods like MRI. However any of these methods can truly indicate epileptic focus in all patients. Radionuclide methods are brain SPECT with Tc-99m hidroksimetilenpropilenaminoxime (HMPAO) or Tc-99m ethylenecistein dimer (ECD) and PET/CT with different radiopharmaceuticals especially F-18 florodeoxyglucose (FDG). The scintigraphy might be performed in different phases; interictal (without seizure), ictal (at the time of seizure) and postictal (just after the seizure). Previously consideration of ictal and interictal SPECT with additional MR information was considered the best diagnostic approach. However some of the patients do not have structural anomaly on MR or might have conflicting results in tests or bilateral disease ect thus the interictal PET is the most preferable method in this area recently because of easy of the method and high diagnostic accuracy. Many different radiopharmaceuticals are present for PET but the most available one is F-18 FDG.

MATERIALS AND METHODS

The aim of this chapter is firstly to provide brief information about the following subjects;

1. Definition of epilepsy surgery
2. Indications of epilepsy surgery
3. The preoperative tests before epilepsy surgery
4. Nuclear medicine tests

The importance of diagnostic Nuclear Medicine procedures, indication, applications in special circumstances will be discussed and some important issues will be highlighted.

RESULTS

The Definition

The epilepsy surgery is the surgical removal of epileptogenic focus from the brain which aims to control epilepsy and to obviate ideally or at least decrease the number and severity of the epileptic seizures and thus increase the quality of life of the patient and decrease the risk of adverse effects related to the/or severity of seizures and antiepileptic drugs.

The Indications

There are two prerequisites for epilepsy surgery; presence of uncontrolled epilepsy and resectable epileptic disease. The definition of uncontrolled epilepsy is a little bit conflicting but

contains at least twenty seizures in two years time despite appropriate antiepileptic treatment with two different antiepileptic drugs [4,5].

The respectability is important and a necessary issue. The lesions that may be associated with good outcome after epilepsy surgery are listed below; mesial temporal lobe epilepsy, low grade tumors, vascular pathologies, postinfectious or posttraumatic changes, cortical developmental malformations, the lesions without MR findings especially [3].

Mesial temporal lobe epilepsy is the most common type which is characterized by hypocampal atrophy and sclerosis [3].

Preoperative Tests

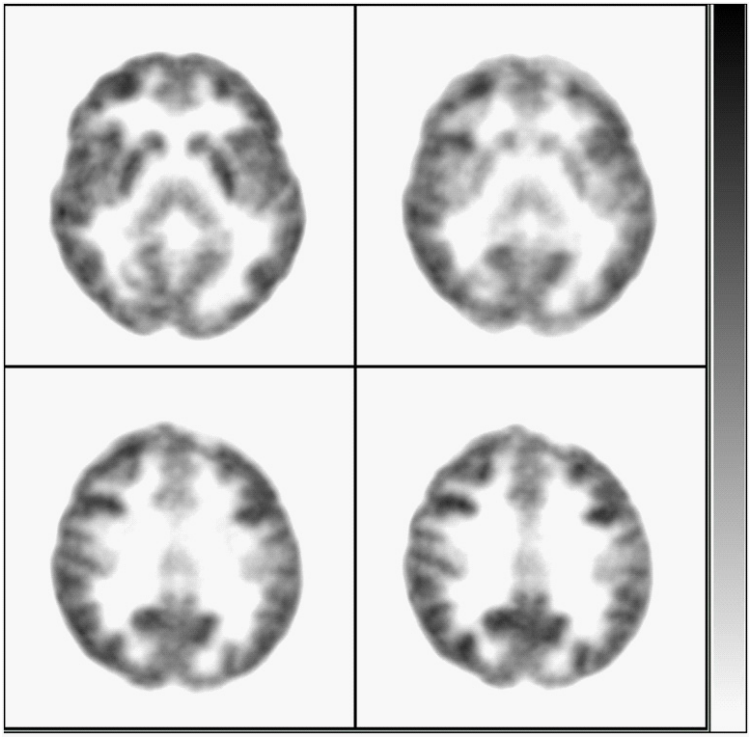
Long term video electroensephelography, high resolution MR and neurophysicological tests are mandatory methods and optional methods are PET and SPECT, functional MR, MR spectroscopy, magnetoensephalography and Wada test [3]. MR findings help to localize the seizure onset zone [6].

Nuclear Medicine Tests

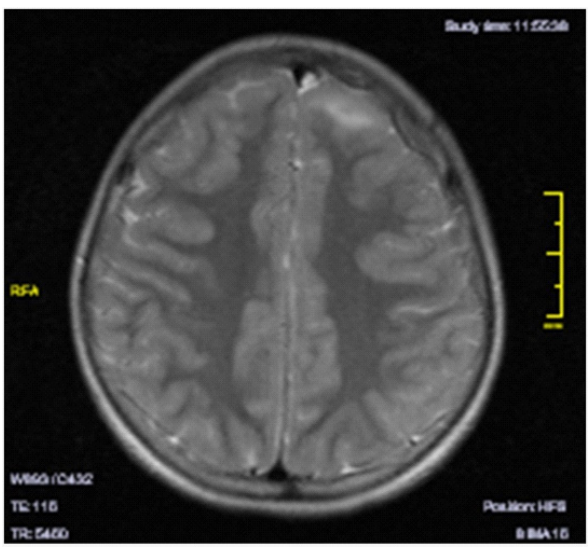
SPECT and PET are nuclear medicine methods which are considered for localization of the epileptic focus prior to the surgery. The radiopharmaceuticals used in the SPECT imaging are Tc-99m HMPAO and Tc-99m ECD. F-18 FDG is the most available radiopharmaceutical for PET imaging however there are other radiopharmaceuticals like F-18 flumazenil (FMZ) which indicates a more restricted region of abnormality than FDG [7].

PET has higher sensitivity for temporal lobe epilepsy (60-90%) especially for the patients with hypocampal atrophy (100%). However in extratemporal lobe epilepsy the sensitivity of PET is only 50% [8,9]. In MR negative temporal lobe epilepsy patients who comprise the 16% of the whole group of temporal lobe epilepsies PET is a suitable and informative imaging method according to long term outcome results [10]. Previous reports have clearly indicated the importance of PET imaging in patients without MR pathology [11]. Another radiopharmaceutical F-18 FCWAY has shown to be more helpful than FDG in MR negative patients [12].

PET has been shown to change the patients' management in 53% of the patients previously and this ratio was 73% in another series [13,14]. Another approach in preoperative determination is the combination of interictal PET information with interictal scalp EEG which has shown to be associated with improved outcome after surgery [15]. Additionally the size of the area of the hypometabolism on PET imaging has found to be associated with outcome previously [16] (Figure 1).



1 (a)



1 (b)

Figure 1: 14 years old male patient experiencing unconsciousness especially at night with following tonic clonic seizure for 13 years. His EEG findings were bilateral hemispheric involvement with left temporal lobe. FDG PET images (Fig.1) shows hypometabolism on left frontal lobe consistent with the cortical dysplastic region in MR. The patient underwent surgery and pathology revealed diffuse astrosytoma WHO grade ll.

The most common structural anomaly in patients with temporal lobe epilepsy is hippocampal sclerosis [7] and most reliable predictor of favorable outcome [17]. It has been documented by Van Paesschen et al. [18] that hippocampal sclerosis is associated with ictal hiperperfusion and interictal hypoperfusion on SPECT Additionally propagation pathways might be observed in approximately 1% of the patients in different areas like frontal lobe [19,20]. Analystic semiquantitative methods like substraction ictal SPECT coregistered to MR (SISCOM) have shown significantly higher localization rates (39 vs 88%) [21]. Combination of SPECT and invasive EEG data have revealed good outcomes after surgery in 83% of the patients who were MR negative [22]. In another study it has been shown that multimodal neuroimaging may obviate the need for invasive EEG and reduce the resection size [23]. FDG PET might reveal epileptic zone as a focal hypometabolic area in focal cortical dysplasia patients with and without abnormality in MR [24]. In patients who has refractory epilepsy and needs repeat resective surgery neuroimaging studies are considered necessary in especially patients with conflicting results in other studies [25,26]. However in patients who did have well established ictal scalp EEG and concordant MR data PET might not reveal any new information although in patients with normal MR and inconclusive EEG findings PET has high predictive value for good postoperative outcome [27,28]. The success of PET is reduced in patients with bilateral temporal disease compared to unilateral disease and in that situation additional deep EEG is advised [29]. In patients with suspicion of additional extratemporal disease PET might exclude or confirm it [30] (Figure 2).

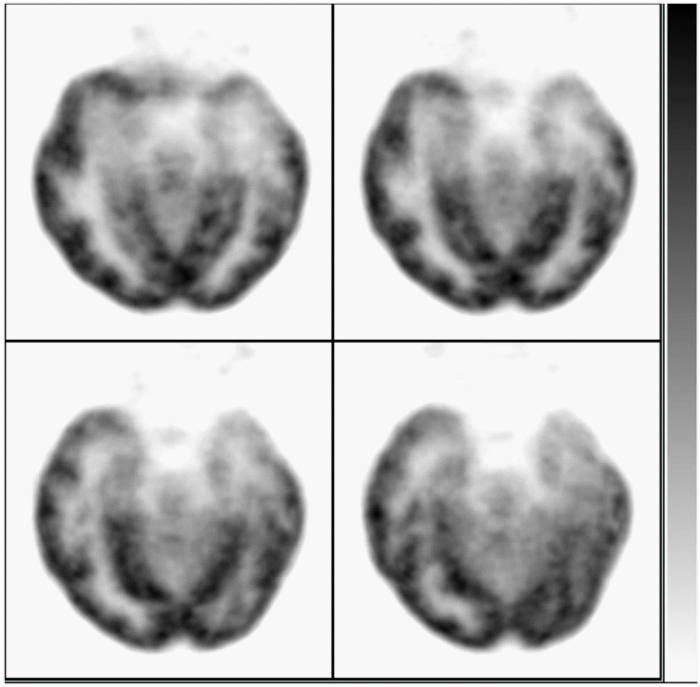


Figure 2: 28 years old male patient with history of complex partial and secondary generalized tonic-clonic seizures for 14 years. EEG findings supported left temporal pathology

and MR images shows left hippocampal sclerosis. Interictal PET images (Fig. 2) demonstarates left temporal hypometabolism and surgery confirmed left hippocampal sclerosis. The patient was free of seizures after operation (Engel l).

Ictal SPECT analysis needs a challenging workup in order to perform the injection at the seizure onset time. Generally it may not be possible at all times. It needs a special team in order to catch out at the seizure time usually bed side trained staff if it is possible. Previous studies have shown that the sensitivity of ictal SPECT significantly drops when the injection is performed more than 20 minutes after seizure onset [31,32]. The interpretation criteria is the at least %15 difference compared to contrlateral side. The greater asymmetry is related to increased chance of becoming seizure free after surgery [33]. The ictal SPECT has a sensitivity of 97-100%; postictal SPECT 75-77% and interictal SPECT 43-44% [34].

There are two radiopharmaceuticals for SPECT imaging those are Tc-99m HMPAO and Tc-99m ECD. Although Tc-99m ECD seems to have superiorities over Tc-99m HMPAO like more linear extraction in higher flow rates and longer in vivo stabilization time (providing longer time for performing acquisition) the sensitivity rates of Tc-99m HMPAO is higher [34].

F-18 FDG PET has comparable sensitivity to ictal SPECT according to the previous studies especially in extratemporal lobe epilepsies (ETLE) [35,36]. In some recent studies it has been showed that PET/MR imaging might provide additional information compared to PET only interpretation [37]. Additionally C-11 flumazenil PET may be a choice for the patients for identification of epileptic foci however in patients with normal MR study FMZ PET might reveal more false results than FDG [38,39]. In characterization of the responsible tuber in multiple tuberous sclerosis C-11 alphamethyl L tryptophan PET in interictal period is a promising tool [40]. In patients with epileptic focus located in parietal or occipital lob ictal SPECT may be superior to PET [41]. However in patients with normal MR PET has found to be superior to ictal SPECT [42]. Since the epilepsy surgery promises high success rates (around %72 in ten years follow up) [43] the surgery is clearly efficient for the patients. The statistical analytical methods like statiscal parametric mapping (SPM) seems to yield additional information. However there are conflicting results about SPM analysis some researchers have reported better performance and some of them have not [44-47]. Additionally it has been observed that visual interpretation by experienced observers gained approximately %15-20 more favorable results than inexperienced observers [48]. In the study by van 't Klooster et al. it has been observed that repeat analysis of the PET scans by the same observer gains increased diagnostic yield [44].

It has been suggested by Feng et al. [49] that successful resective surgery might be achieved by PET in case of MR negative TLE without invasive EEG comparable to the patients with hippocampal sclerosis.

Chandra et al. have compared ictal SPECT and PET in patients with TLE and ETLE and concluded that the sensitivity of SPECT was higher than PET for ETLE (60% vs 33%) but lower

for TLE (66% vs 84%) [50]. Additionally they have observed that the outcome after surgery is better when the results of PET/SPECT and MR/EEG are concordant [50]. Perissinotti et al. [51] have compared SISCOM, FDG PET and MR based on postoperative results and concluded that SISCOM (67% of the patients (36/54)) achieved better results than PET (57%) and MR (39%). It has been suggested previously that since the SISCOM point out the cerebral blood flow changes it has capacity to show the seizure onset zone and FDG PET localizes the functional deficit zone [52]. Perssinotti et al. [51] also have concluded that when all the imaging studies point out the same region the outcome of surgery is more favorable. The main indications of SISCOM in mesial TLE are inconclusive clinical symptamatology, not characteristic EEG pattern, bilateral temporal lobe seizures, in patients with dual pathology in MR and patients with nonlesional epilepsy; in ETLE these are the suspicion of neocortical ETLE, nonlesional epilepsy discordant study results, multiple cortical dysplasia, nerocutaneous syndromes, multilobar or bilateral disease, previous history of operation, for localization of subdural electrodes and infantile epilepsy [53].

MR changes related to the epilepsy in TLE is usually mesial temporal sclerosis which is usually associated with atrophy and gliosis of hippocampus and reduction in size and hyperintensity of hypocampus on T2 weighted and FLAIR sequences [53]. The removal of temporal anteromedial structures or amygdalohippocampectomy usually produces remission of the seizures in approximately 80% of the patients [54]. MR might be insufficient in special circumstances like in focal cortical dysplasia which is the most common cause of pharmacoresistant epilepsy in infancy to show the epileptic focus [55].

The sensitivity of PET in ETLE is between 45-92 % according to previous reports [53,56]. The most common cause of this low sensitivity is small size of the lesions [53,57,58]. PET changes the treatment plan in approximately 50-70% of the patients [53,59]. The indications of PET in TLE are discrepant results in EEG and MR and patients with dual disease or multiple lesions; whereas in ETLE; nonlesional epilepsy, cortical dysplasia (sensitivity around 70-90%; increases in fusion PET/MR), for the localization of invasive EEG, for evaluation of regional functional status and infantile epilepsy [53].

Recent research has all suggest evaluating patients with epilepsy by PET or SPECT especially in case of suspicion for localization of epileptic focus. Although the epilepsy surgery has great success considering its invasiveness it is extremely important to localize the epileptic focus correctly. Some previous studies discuss about whether to accept pathology or patient outcome for surgery success. In my opinion patient outcome has to be considered the target point and most of the studies show that Nuclear Medicine imaging methods provide a better outcome after surgery for the patients, have influence to change the treatment plan and show the resection zone more definitely.

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