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Review

Neuroimaging for patient selection for medial temporal lobe epilepsy surgery: Part 2 functional neuroimaging

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ABSTRACT

We evaluate and discuss the various functional imaging techniques that are currently in use to assess the eligibility of a refractory temporal lobe epilepsy (TLE) patient for treatment with medial temporal lobe surgery. The assessment of eligibility for treatment is challenging and relies heavily on functional imaging modalities that provide physiological information, in addition to structural data acquired by different imaging techniques. This review is the final segment of a two part study, the first of which focused on the structural and anatomical imaging modalities that are in use for the surgical treatment of TLE. The authors performed a comprehensive query of PubMed, Embase and Medline databases in search of all relevant English language studies that were published between 1990 and 2013. Overall, 56 papers were reviewed (50% of them covering primarily functional neuroimaging), including a total of 1517 patients. The extracted data included the general study identification, demographics, population, study design, neuroimaging methods, reference standard imaging method used (gold standard), outcomes, and conclusions. As the majority of the studies investigated functional MRI, single photon emission computed tomography and positron emission tomography, the authors focus the review on these specific modalities.

1. Introduction

Temporal lobe epilepsy (TLE) is the most common cause of refractory epilepsy [1]. Approximately 20% of patients with TLE will continue to have seizures after treatment with antiepileptic drugs [2]. Patients with medically refractory TLE are surgical candidates for seizure control [3]. Temporal lobe resection (TLR), including anterior temporal lobectomy or selective amygdalohippocampectomy, is a well-established and effective method of treatment [4]. Patients who meet the criteria for surgery and are seizure-free after TLR have a lower mortality rate than those with persistent postoperative seizures [5]. Postoperatively, 80% of patients may be rendered seizure-free, but up to 40% are at risk of a deterioration in memory and language [3].

The accurate identification of the epileptogenic region is essential for successful surgery and is highly dependent on presurgical evaluation. Several functional neuroimaging techniques are used for the presurgical evaluation of TLE patients to determine ideal candidates for TLR, identify the epileptogenic region, and predict and prevent postoperative complications. Particularly, the localization of cortical functions in patients undergoing TLR enables risk assessment, definition of surgical boundaries, and preoperative localization of epileptogenic brain regions. The intracarotid amobarbital (or Wada) test was first used to localize the lateralization of language and memory functions across the left and right hemispheres [6,7]. However, the Wada test does not provide specific information for surgical guidance, is highly dependent on the symmetric arterial supply of the two hemispheres, is invasive, and has a complication rate of up to 3% [8]. As such, less invasive and more accurate functional methods have been developed for the presurgical evaluation of TLE patients, which are described in the current review.

Several modern functional neuroimaging studies have attempted to illuminate the structural and functional consequences of epilepsy surgery and to study functional reorganization after TLR [8–14]. We surveyed the literature and found that functional MRI (fMRI), magnetic resonance spectroscopy, single photon

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emission computed tomography (SPECT) and positron emission tomography (PET) scans are common functional neuroimaging methods that are used to evaluate TLE patients, either through routine application or investigational use. In this review, we discuss the role of these methods in identifying surgical candidates, enhancing the reliability of preoperative assessment and selection of epilepsy patients, and improving the postoperative prognosis.

2. Methods

2.1. Identification and selection of studies

A predefined search strategy was used to select suitable papers to be reviewed in this article, published between 1990 and 2013. PubMed was the primary search engine for identifying relevant data. The key words used were: temporal lobe epilepsy, surgery, neuroimaging, medial temporal lobe surgery, fMRI, SPECT, and PET. The search was performed in two stages. First, a search to locate general information on TLE, prediction, prognosis, treatment, diagnosis and current indications for surgery was performed. Second, a search for all primary studies reporting the accuracy of diagnostic tests for preoperative evaluation of medial TLE patients was performed. For the selection of the papers that were included in this review, we applied specific inclusion and exclusion criteria (Table 1).

2.2. Assessment of validity and quality

The standards for the reporting of diagnostic accuracy studies checklist was used to assess and select the papers. The extracted data included: study identification (country of investigation, language, author, year of publication), study population, study design (participant recruitment and sampling, data collection), reference standard imaging method used, results (reproducibility, mode of presentation, amenability to formatting as 2×2 tables), and conclusions. A specific data extraction form was used for each review.

3. Results

Based on the search strategy described above, 114 papers were identified in the literature. From these, 56 papers met the inclusion criteria and were included in the study, whereas 58 papers were excluded (Table 1). In the functional imaging group, 28 papers were included, and 28 were included in the structural imaging group. The grouping of the papers was performed according to the functional neuroimaging method to which they refer: fMRI, PET, or SPECT scans. This grouping facilitated the evaluation of each neuroimaging test and the extraction of the results. The most frequent criteria for excluding a paper were: publication before 1990, patients with focal epilepsies other than TLE, patients with temporal and extratemporal epilepsy, a patient cohort less than 10, or publication in a language other than English (Table 1). This is the second part of a two part review, in which we discuss the role of frequently used functional neuroimaging (fMRI, SPECT and PET scans) for the evaluation of medial TLE patients. In Part 1, the structural neuroimaging techniques (MRI, diffusion-weighted imaging, tractography and magnetoencephalography) were discussed.

Table 1
Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients with temporal lobe epilepsy intractable to medical treatment	Use of neuroimaging techniques in patients with partial epilepsy, including temporal lobe epilepsy
Published after 1990	Published prior to 1990
Prospective and retrospective studies	No restrictions on countries where the study was performed
Blinded and non-blinded studies	Published in a language other than English
Valid statistical methods for the extraction of the results and explanation of the methods used to quantify sensitivity, specificity and uncertainty	
Homogeneity with regards to sex and age of the subjects	
Use of any of the following imaging methods or combination thereof: MRI, DWI, MRS, tractography, MEG, SPECT, PET	
English language publication	
Reproducibility of the results	

DWI = diffusion-weighted imaging, MEG = magnetoencephalography, MRS = magnetic resonance spectroscopy, PET = positron emission tomography, SPECT = single photon emission computed tomography.

3.1. fMRI

We identified 23 papers that described investigations of TLE patients with fMRI. These were further separated into two groups: those that applied fMRI to investigate language function and those that investigated memory function. These papers are listed in Table 2 and 3, respectively.

fMRI is based on the increased blood flow in neurally activated brain regions. The increased blood flow results in reduced deoxy-hemoglobin, which is paramagnetic, and increases the signal in T2-weighted MRI (blood oxygen level dependent imaging). fMRI enables the mapping of brain functions and networks based on changes in the brain hemodynamics that correspond to cerebral operations. During the last decade, fMRI has developed as a leading technique for the pre- and postoperative evaluation of patients with refractory TLE, and who are candidates for temporal lobe surgery. It is also widely used for preoperative planning to balance the risks and benefits of surgery.

fMRI assessments of epilepsy patients have led to the discovery that a network of brain areas, rather than a single zone, are responsible for the onset and maintenance of seizures. Functional connectivity analyses of fMRI data have been used to correlate the networks of brain activity with functional connectivity [15–17]. Others have studied functional connectivity in epilepsy patients by acquiring fMRI data during rest [18–22] and during language and memory tasks [23,24]. Negishi et al. used simultaneous preoperative resting state electroencephalography (EEG) and fMRI in patients with refractory epilepsy, and compared the results to healthy controls. They observed that patients who were seizure-free postoperatively had more lateralized functional connectivity than patients with recurrent seizures, which is an important positive functional predictor of good surgical outcomes [25].

Structural and functional changes have been observed in TLE patients, both in the seizure focal region and in distal areas. Among these are mossy fiber sprouting [26], neuronal loss [27], inflammation [28] and loss of functional inhibition [29] in both the ipsilateral and contralateral structures. It is believed that these changes provoke brain atrophy, decrease glucose metabolism in the ipsilateral temporal lobe, and lead to the development of neural networks that promote seizure propagation, such as connections between the left and right hippocampus. Resting state fMRI [30] has been used to investigate resting state interictal hippocampal network alterations and their relationship to epilepsy duration in mesial TLE patients [31]. Interhemispheric hippocampal connectivity is initially disrupted, then increases linearly, with the hippocampus contralateral to the epileptogenic focus influencing the ipsilateral hippocampus [31].