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Continuing Education

PET and SPECT in epilepsy☆

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ABSTRACT

Epilepsy is one of the most frequent chronic neurological disorders, affecting 1–2% of the population. Patients with complex partial drug resistant episodes may benefit from a surgical treatment consisting in the excision of the epileptogenic area. Localization of the epileptogenic area was classically performed with video-EEG and magnetic resonance (MR). Recently, functional neuroimaging studies of nuclear medicine, positron emission tomography (PET) and single photon emission tomography (SPECT) have demonstrated their utility in the localization of the epileptogenic area prior to surgery. Ictal SPECT with brain perfusion tracers show an increase in blood flow in the initial ictal focus, while PET with ^{18}FDG demonstrates a decrease of glucose metabolism in the interictal functional deficit zone.

In this review, the basic principles and methodological characteristics of the SPECT and PET in epilepsy are described. The ictal SPECT injection mechanism, different patterns of perfusion based on the time of ictal, postictal or interictal injection are detailed and the different diagnostic sensitivities of each one of these SPECT are reviewed. Different methods of analysis of the images by subtraction and fusion systems with the MR are described. Similarly, the injection methodology, quantification and evaluation of the images of the PET in epilepsy are described. Finally, the main clinical indications of SPECT and PET in temporal and extratemporal epilepsy are detailed.

PET y SPECT en la epilepsia

Palabras clave:
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SPECT ictal
SPECT interictal
Tomografía por emisión de positrones

RESUMEN

La epilepsia es uno de los trastornos neurológicos crónicos más frecuentes, afectando al 1–2% de la población. Los pacientes con crisis parciales complejas resistentes al tratamiento farmacológico pueden beneficiarse de un tratamiento quirúrgico que consiste en la extirpación de la zona epileptógena. Clásicamente la localización de la zona epilpetógena se realiza con vídeo-EEG y resonancia magnética (RM). Recientemente las exploraciones de neuroimagen funcional de medicina nuclear, la tomografía por emisión de positrones (PET) y la tomografía por emisión de fotón único (SPECT) han demostrado utilidad en la localización de la zona epileptógena antes de la cirugía. La SPECT ictal con trazadores de perfusión cerebral demuestra un aumento del flujo sanguíneo en la zona de inicio ictal, mientras que la PET con ^{18}FDG muestra una disminución del metabolismo de la glucosa en la zona de déficit funcional interictal.

En esta revisión se describen los principios básicos y las particularidades metodológicas de la SPECT y la PET en la epilepsia. Se detalla el mecanismo de inyección de la SPECT ictal, los diferentes patrones de perfusión en función del momento de inyección ictal, postictal o interictal y se revisan las diferentes sensibilidades diagnósticas de cada uno de estos SPECT. Se describen diferentes métodos de análisis de las imágenes con sistemas de substracción y fusión con la RM. Del mismo modo, se describe la metodología de inyección, cuantificación y evaluación de las imágenes de la PET en la epilepsia. Finalmente se detallan las principales indicaciones clínicas de la SPECT y de la PET en la epilepsia temporal y extratemporal.

Introduction

Epilepsy is one of the most frequent chronic neurological disorders, affecting 1.2% of the world population and its prevalence is 410 cases per 1000 inhabitants. In the United States the prevalence is 5 per 1000 inhabitants, affecting around 2 million people.[1] The pharmacological treatment of epilepsy with one or several drugs achieves the seizure control in 60–70% of the cases.[2] The remaining cases in which medication is not able to control the seizures constitute the group of patients with pharmacoresistant epilepsy. In these patients the seizures have a focal or partial origin in a limited, specific area of the cerebral cortex. These patients with partial pharmacoresistant seizures may benefit from surgical treatment which consists of surgical resection of the epileptogenic zone (EZ) defined as the cerebral tissue necessary and sufficient to generate an epileptic seizure. The success of surgery in epilepsy fundamentally depends on the correct presurgical

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Table 1
Description of the epileptogenic zone and the cortical zones involved in the epileptic seizures.[3]

Zone	Cortex which:...	Detection method
Epileptogenic zone	Cerebral cortical region responsible for generating the epileptic seizure. By definition, its surgical resection or complete disconnection is sufficient to eliminate the seizures	Its location is obtained by consensus or concordance of all the complementary studies
Irritative	Generates the interictal epileptic discharge	Non-invasive EEG Invasive EEG MEG Interictal fMR
Ictal onset	Initiates the clinical seizure	Non-invasive EEG Invasive EEG Ictal SPECT MEG Ictal fMR
Symptomatogenic	Is responsible for the clinical signs and symptoms	v-EEG
Lesional or epileptogenic lesion	Structural lesion with the capacity to generate epileptic seizures: lesion itself, MTS, cortical dysplasias, gangliomas, DNET ... By secondary hyperexcitabiilty of the adjacent cortex: angioma, gliomas ...	MR (CT)
Of functional deficit	Is not functionally normal during the interictal period	Neurological study Neuropsychological tests Interictal PET Interictal SPECT

DNET, dysembryoplastic tumors; MTS, mesial temporal sclerosis; MEG, magnetoencephalography; fMR, functional magnetic resonance; CT, computed tomography.

localization of the EZ and the prediction of possible sequelae from the intervention.

Presurgical localization of pharmacoresistant epilepsy

For presurgical localization of the EZ, patients with pharmacoresistant epilepsy are admitted to the Epilepsy Unit where the presurgical assessment of the epilepsy is performed including the following diagnostic tests: clinical symptomatology, video-electroencephalogram (v-EEG), neuropsychological tests, psychiatric evaluation and neuroimaging studies. These tests help to define 6 cortical zones involved in the localization and extension of the EZ which are described in Table 1.[3] During admission the antiepileptic medication is reduced or withdrawn to allow the appearance of a seizure which is registered with v-EEG. Analysis of the v-EEG during the interictal and ictal periods as well as the symptomatology of the seizure are essential to know the right or left hemispheric lateralization and lobar-frontal, temporal, parietal or occipital localization of the EZ. With surface electrodes the v-EEG is often not able to identify the EZ with sufficient precision. This occurs when the seizure originates in deep cerebral structures or when the seizure spreads rapidly. In this situation multiple electrodes are affected by the discharges making it difficult to decide where they initiate. In these patients it may be necessary to perform electroencephalogram (EEG) monitoring by the surgical placement of subdural or deep electrodes. This invasive procedure significantly increases the possibility of detecting the zone of ictal onset, the region in which the electric seizures of the patient originate. However, invasive monitoring represents a series of risks among which the appearance of infection, epidural hematoma, headache and an increase in intracranial pressure are of note. In addition, for invasive monitoring to be useful it is essential to have a previously correct hypothesis as to the possible zones involved in the generation of the seizures. This hypothesis is what should guide the placement of the electrodes.

Morphological imaging in the presurgical localization of pharmacoresistant epilepsy

Morphologic neuroimaging with magnetic resonance (MR) has considerably reduced the need to implant intracranial electrodes due to its capacity to detect lesions acting as the EZ. However, conventional MR is inadequate for detecting subtle epileptogenic lesions which usually remain undetected in the usual T1-weighted and T2-weighted sequences. The MR should be acquired in high field equipment (1.5 T or 3.0 T), following a standard protocol for epilepsy including the 3D, T1-weighted, T2-weighted, FLAIR sequences and the ECHO gradient.

The cerebral lesion with the greatest epileptogenic capacity is mesial temporal sclerosis (MTS) which is the main cause of pharmacoresistant epilepsy in adult patients. This lesion consists in atrophy and gliosis of the hippocampus, and on MR it is manifested as a reduction in size and hyperintensity of the signal of the hippocampus in T2-weighted and FLAIR sequences (Fig. 1A). From a surgical point of view MTS is considered as a surgically treatable epileptic syndrome different from partial neocortical or extratemporal epilepsies. The natural evolution is known and does not require studies with invasive electrodes and may be surgically treated by temporal anteromesial resection or selective amygdalohippocampectomy, achieving remission of the seizures in up to 80% of the cases.[4]

Focal cortical dysplasia and heterotopy are included among the malformations of cortical development (MCD) and are the first cause of pharmacoresistant epilepsy in infancy and the second/third cause in adults.[5,6] These malformations are due to a disorder in the migration of the neuron levels in the embryonary stage and are shown as a subtle thickening of the gray matter and blurring of the margins between the gray and white matter. It is of note that the MR is normal in 40% of the cases of type 1 cortical dysplasia, and that the dysplastic region may be larger than the lesion detected on MR.[7] Cortical dysplasias usually require complementary studies for diagnostic confirmation since the EEG and MR are usually not successful in locating these lesions.

Some cerebral tumors of slow growth may generate epileptic seizures by themselves or by infiltration or irritation of the surrounding tissue.[8] The most epileptogenic tumors are low grade astrocytomas, oligodendrogliomas, ganglyogliomas, meningiomas in adults and dysembryoplastic neuroepithelial tumors (DNET) in children.

The last notable group of epileptogenic lesions is constituted by cavernoma-type vascular and arteriovenous malformations.

When MR localizes a structural lesion and the v-EEG coincides in locating the zone of seizure origin in the same region, the patients do not usually require other complementary neuroimaging studies to undergo surgery for the epilepsy. In addition, the presence of a lesion in the MR increases the success of the epilepsy surgery compared with patients with no lesion in the structural images.[9] However, the percentage of surgical failure for epilepsy increases in the cases with suspicion of multiple foci, non-lesional MR, poorly defined cortical dysplasias or in those cases in which the lesion of the MR does not coincide with the