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Perspectives in Clinical Imaging

Brain molecular imaging in pharmacoresistant focal epilepsy: Current practice and perspectives

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ABSTRACT

This review aims to synthesize all the available data on brain molecular imaging, such as single-photon emission computed tomography (SPECT) and interictal fluorodeoxyglucose positron emission tomography (FDG-PET), in focal epilepsies. SPECT imaging is able to measure regional cerebral blood flow and its major innovation remains its ictal imaging value. On the other hand, FDG-PET, which has higher spatial resolution and lower background activity than SPECT, enables glycolytic metabolism to be identified in interictal states. Therefore, interictal FDG-PET has greater sensitivity than interictal SPECT, especially in temporal lobe epilepsies (TLEs). Thus, ^{18}F-FDG-PET is a necessary step in the presurgical evaluation of TLEs, but also of extratemporal epilepsies (ETEs), contributing to > 30% of the decision to undertake surgery. In addition, FDG-PET has particular diagnostic value in focal epilepsies showing normal magnetic resonance imaging (MRI). PET also has good prognostic value for post-surgical outcomes as well as cognitive impairment, especially in cases where the hypometabolism extent is limited. Moreover, the notion of an epileptic network is well highlighted by functional PET imaging, allowing better understanding of the pathological substrates of these disorders. Future development of quantitative analysis software and of novel radiotracers and cameras will certainly enhance its clinical usefulness.

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1. Introduction

Seventy million people around the world suffer from epilepsy, with 34 to 76 new cases diagnosed per 100,000 population every year [1]. Focal epilepsies are the most common forms of the disorder and are characterized by seizure onset localized to a specific region (the epileptogenic zone; EZ) of the cerebral cortex. Focal seizures are generally characterized by the emergence of rapid discharges within networks that can be either discretely localized or more widely distributed [2,3]. Overall, > 30% of patients with epilepsy are thought to have drug-resistant seizures [1]. In this context, surgical resection of the EZ is a valid option if the potential benefit appears to outweigh the risks [4]. The EZ corresponds to the brain area necessary and sufficient for the generation of habitual seizures, and are generally less extensive than the entire irritative zone (the area generating interictal spikes) [5]. One medico-economic analysis showed that, in addition to being safe and effective, epilepsy surgery is cost-effective in the medium term and should therefore be considered earlier in the treatment of refractory epilepsy [6].

Preoperative evaluation aims to precisely define the EZ. To this end, surgical techniques have been refined for years with the help of non-invasive techniques such as high-resolution electroencephalography (EEG), magnetoencephalography (MEG) [7,8] and magnetic resonance imaging (MRI), as well as invasive techniques such as stereotactic electroencephalography (SEEG; precise guidance for positioning depth electrodes for intracerebral EEG monitoring). Such evaluations can also include brain molecular imaging with perfusion single-photon emission computed tomography (SPECT) and/or metabolic positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) labeling. This global approach has led to more precise EZ localization, thereby allowing removal of the least amount of tissue necessary to reduce postoperative neurological deficits [9]. It is noteworthy that the final decision to operate is taken after interpretation of all these data through multidisciplinary staff discussions.

The present review aims to synthesize all the available data on brain molecular imaging, including SPECT, but also interictal FDG-PET, of focal pharmacoresistant [temporal lobe (TLE) and extratemporal (ETE)] epilepsy. Future perspectives are also discussed for ^{18}F-FDG-PET analysis and novel PET radiopharmaceuticals.

2. SPECT in focal epilepsy

SPECT imaging is able to measure the regional cerebral blood flow (rCBF) associated with epileptic seizures [10], but its major innovation is its ictal imaging value. Radiopharmaceutical administration can be performed during an epileptic discharge, with irreversible brain uptake completed within 1–2 min [11]. During an ictal scan, brain regions involved in seizure generation and its early propagation demonstrate increased perfusion, whereas most epileptic networks are hypoperfused during interictal states [12]. Radiolabeled 99m-technetium (Tc) isotope tracers, such as hexamethylpropyleneamine oxime (HMPAO) and ethylene cystine dimer (ECD), are currently used, and SPECT imaging acquisition can start 30–90 min after their injection; acquisitions last for about 20 min and have a radiation dose of approximately 6 mSv [13].

Ictal SPECT has shown a sensitivity of 73% and specificity of 75%, while interictal SPECT has a much lower localization rate, with 50% sensitivity and 75% specificity [14]. However, SPECT has performed better in the detection of epileptic networks in temporal than in non-temporal epilepsies, but also in ictal as well as interictal states [15]. Subtraction ictal (and interictal) SPECT co-registered to MRI (SISCOM) is particularly useful (Fig. 1), as it has been shown to improve the sensitivity and specificity of seizure localization networks by only demonstrating hypoperfusion during interictal scans [16]. In fact, studies have found that SISCOM localization sensitivity is > 90% in TLE seizures, but much lower in ETEs [17,18]. Similarly, SISCOM provides useful information for seizure localization in patients with focal cortical dysplasia even in cases with normal MRI [19]. Notably, ictal SPECT also appears

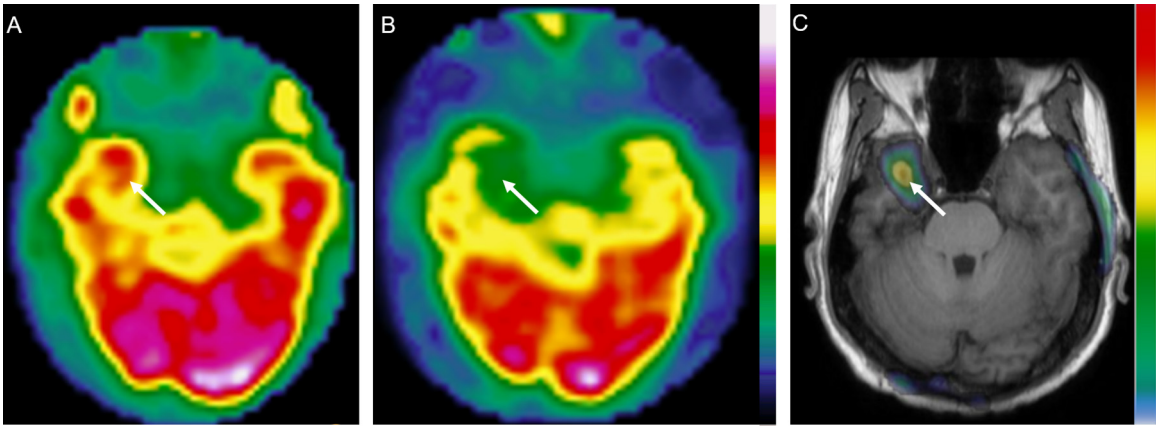

Fig. 1 – Axial views of perfusion SPECT imaging from a 40-year-old man with right temporal epilepsy in (A) ictal and (B) interictal phases, and (C) after subtraction of ictal and interictal SPECT images co-registered to MRI (SISCOM). Hyperperfusion is evident in the right mesial temporal area (A, white arrow), which is hypoperfused in the interictal state (B, white arrow). Subtraction of ictal and interictal states reveals a significant perfusion differential in the same area (C, white arrow), corresponding to the right mesial temporal lobe on SISCOM.

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