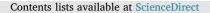
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Unusual diagnostic findings in temporal lobe epilepsy: A combined MRI and ¹⁸F-dopa case study

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ABSTRACT

Temporal lobe epilepsy is the most common focal epilepsy in adults and often causes pharmacoresistant seizures. Magnetic resonance imaging (MRI) and PET studies have widely demonstrated a number of morphological and molecular abnormalities in epilepsy. However, considering the dopaminergic system, only a bilateral ¹⁸F-DOPA uptake reduction within the basal ganglia has been described. We report the unusual finding of increased ¹⁸F-DOPA uptake in a patient with focal recurrent seizures and "deja vu" experiences in the setting of cortical swelling detected at MRI exam. The final diagnosis was in in keeping with hippocampal sclerosis, confirmed during follow-up MR exams. In this case ¹⁸F-DOPA uptake may represent increased dopamine transport induced by seizures. Nuclear medicine physicians and radiologists should be aware of clinical and electroencephalographic findings when interpreting brain areas of tracer uptake, which are not always related to malignancy.

1. Introduction

ARTICLE INFO

Temporal lobe epilepsy is the most common focal epilepsy in adults and often causes pharmacoresistant seizures [1]. Multimodal neuroimaging usually includes high-resolution MRI, 18 F-fluorodeoxyglucose positron emission tomography (¹⁸FDG-PET) and SPECT. PET is a wellknown neuroimaging method that offers comprehensions into the molecular functioning of the human brain. It has been widely used to study metabolic and neurotransmitter abnormalities in people with epilepsy playing an important role as a biomarker by revealing the molecular processes involved in the development of epileptogenesis. Considering the dopaminergic system, and the use of 18 F-radiolabeled non proteinogenic dihydroxy-6-[18 F]fluorol-phenylalanina (¹⁸F-DOPA), a bilateral reduction within the basal ganglia has been described as a nonspecific reaction to different type of seizures [2].

We report an unusual ¹⁸F-DOPA uptake in a patient with mesial temporal lobe epilepsy (MTLE) with corresponding MRI abnormalities.

2. Clinical and imaging findings

A 37-year-old man, come to our observation with focal recurrent seizures and sensation of "deja vu". He had a history of febrile convulsions in early childhood and presented a feverish episode a week before admission. At the hospitalization for generalized tonic-clonic seizures, an EEG was performed showing an spike focal focus in the left temporal lobe. Antiepileptic therapy was started (Valproate). The MR exam showed moderate swelling and increased of T2w/FLAIR signal on the left hippocampus without contrast enhancement, DWI restriction or microbleeds in T2*w images (Fig. 1a,c). Advanced MRI, performed the next day, including spectroscopy and arterial spin labelling (ASL) sequences, showed only a mild decrease of NAA, but an hyperperfusion (rCBF = 2) at the level of the left hippocampus at ASL study (Fig. 2a).

Cerebral ¹⁸FDG-PET done few days later to exclude limbic encephalitis, detected bilateral hypometabolism of the hippocampus more evident on the left side (Fig. 2b). During this period, due to a platelet dysfunction related to the use of Valproate, the patient changed therapy (Levetiracetam). Although the partial seizures were controlled, the episodes of "deja vu" continued. Thus, an¹⁸F-DOPA PET was performed to exclude a low grade tumor. The exam demonstrated an unexpected diffuse, mild increased tracer uptake of the left mesiotemporal region matching the MRI-FLAIR abnormalities (Fig. 2c). Afterwards, the patient's clinical condition stabilized, with complete response to the therapies, and a series of follow-up MR exams were planned (Fig. 1b,d).

During these, the volume of the left hippocampus progressively decreased and the diagnosis was in keeping with MTLE due to hippocampal sclerosis.

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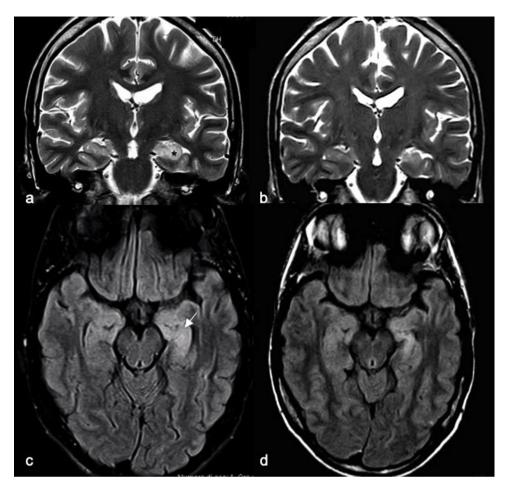


Fig. 1. Conventional MRI. Coronal T2w and axial FLAIR in a patients with MTLE: (a,c) at the onset, the MR shows hyperintense changes involving the hippocampal structures of the left side (asterisk and arrow) with associated cortical swelling. In the follow-up exam (b,d) the same features are less evident with hippocampal atrophic evolution.

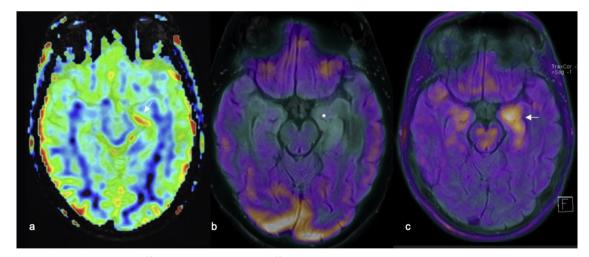


Fig. 2. Axial, Arterial spin labelling (a), fused ¹⁸FDG-PET/MRI (b) and fused ¹⁸F-DOPA-PET/MRI (c). Hyperperfusion (rCBF = 2) at the level of the left hippocampus (arrow); (b) Bilateral hypometabolism of the hippocampus more evident on the left side (asterisk). (c) Diffuse, mild tracer uptake of the left mesiotemporal region matching the MRI-FLAIR abnormalities (arrow).

3. Discussion

In our case at conventional MRI the patient showed swelling on the left hippocampus, probably caused by local vasogenic edema secondary to seizure activity [3], but it brought the suspect of an inflammatory/ neoplastic process.

The ¹⁸FDG-PET, performed to rule out limbic encephalitis, excluded it and revealed hypometabolism of the epileptogenic focus in the interictal phase. Actually, in the clinical context of an estabilished MTLE, ¹⁸FDG-PET is a well proved modality with high sensitivity of 85–90 % for detecting the typical focal hypometabolism of the affected side [4]. However, at clinical onset it has a low specificity because the tracer is uptaken not only by malignant tissues but also by inflamed and healthy tissues that exhibit a high glucose metabolism, resulting in low tumorto-background ratios in CNS malignancies. In contrast, brain tumors exhibit high uptake of amino acid tracers relative to the normal surrounding brain. Amino acid PET, and in particular ¹⁸F-DOPA PET, is a metabolic imaging modality that has been reported to better visualize gliomas than MRI alone. ¹⁸F-DOPA is the precursor of the neurotransmitter dopamine, it accumulation in the brain reflects the functional integrity of the presynaptic dopaminergic synthesis [5] and visualizes the activity of aromatic amino acid decarboxylase, which converts ¹⁸F -DOPA to 18 F-dopamine. Many studies were conducted establishing ¹⁸F-DOPA as the main diagnostic tool for brain tumor imaging giving more favourable diagnostic results than ¹⁸F-FDG [6].

In our case ¹⁸F-DOPA exam, performed to rule out a low grade tumor, interesting showed a diffuse, mild increased of the tracer uptake at the left mesiotemporal region. This finding at first suspected to be a low grade tumor, was finally related to a MTLE with hippocampal sclerosis, due to the atrophic evolution at the follow-up MR exams and to the therapies response. Moreover, the hyperperfusion found at ASL sequence supported this diagnosis. Indeed, ASL likely detect the epileptogenic focus even beyond 24 h after seizures [7].

Temporal lobe epilepsy is the most common focal epilepsy in adults and often causes pharmacoresistant seizures [1].

PET studies have successfully demonstrated a number of molecular functional abnormalities in epilepsy. Considering the dopaminergic system, a bilateral ¹⁸F-DOPA uptake reduction within the basal ganglia has been described. This finding appears independent of the underlying type or pathology of epilepsy suggesting that these alterations are a nonspecific reaction to seizures [2]. Dopamine is known to regulate seizure activity together with acetylcholine, serotonin and noradrena-line. Dopaminergic pathway arising from the ventral mesencephalon innervate the basal ganglia, the limbic system, and the cerebral cortex. Seizures involving the limbic system appear to be the most critically affected by modulation of DA signalling [8]. However, it is interesting to note that increased levels of DA were detected in rodent models of TLE [9].

Although it is difficult to assess dopaminergic binding outside the basal ganglia, two studies described decreased uptake of the epileptogenic zone of patients with temporal lobe epilepsy [10,11]. Only a case of increased ¹⁸F-DOPA uptake corresponding to transient seizure-induced MRI abnormalities, was previously reported, but associated to a temporoparietal low-grade diffuse astrocytoma [12].

To the best of our knowledge, we report the first "incidental" case of positive ¹⁸F-DOPA PET in MTLE. This finding may represent increased dopamine transport induced by seizures and probably related to their persistence secondary to incomplete response to antiepileptic therapy.

Finally,¹⁸F-DOPA uptake should be carefully interpreted in light of clinical and electroencephalographic findings related to seizure activity. Attention must be focused in case of persistent seizures due to poor response to antiepileptic therapy. Moreover, with the increasing contribution of ¹⁸F-DOPA PET in the brain diagnostic routine imaging, this kind of behaviour should be known by nuclear medicine physicians and neuroradiologists, who should be aware of clinical and

electroencephalographic findings, when interpreting brain areas of increased tracer uptake, which are not always related to malignancy.

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CRediT authorship contribution statement

Paola Feraco: Conceptualization, Supervision, Writing - original draft, Writing - review & editing. **Davide Donner:** Supervision, Writing - review & editing. **Lorena Picori:** Visualization, Writing - review & editing. **Umberto Rozzanigo:** Data curation, Conceptualization, Validation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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