Epilepsy & Behavior 80 (2018) 61–67

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

The relationship between structural MRI, FDG-PET, and memory in temporal lobe epilepsy: Preliminary results

Justus Berger [a,*], Michail Plotkin [b], Katharina Demin [a], Martin Holtkamp [a,c], Thomas Bengner [a]

[a] Epilepsy-Center Berlin-Brandenburg, Department of Epileptology, Evangelisches Krankenhaus Königin Elisabeth Herzberge, Berlin, Germany
[b] Vivantes Institute for Nuclear Medicine, Berlin, Germany
[c] Epilepsy-Center Berlin-Brandenburg, Department of Neurology, Charité - Universitätsmedizin, Berlin, Germany

ARTICLE INFO

Article history:
Received 11 August 2017
Revised 19 December 2017
Accepted 22 December 2017
Available online 3 February 2018

Keywords:
Nonlesional
Hypometabolism
Learning
Neuropsychology
Verbal
Nonverbal

ABSTRACT

Structural and metabolic abnormalities of the temporal lobe are frequently found in temporal lobe epilepsy (TLE). In the present retrospective study, we investigated whether structural abnormalities evident in magnetic resonance imaging (MRI) and hypometabolism evident in [^{18}F]fluorodeoxyglucose positron emission tomography (FDG-PET) independently influence verbal and nonverbal learning and delayed memory in patients with TLE. Sixty-eight patients with refractory unilateral TLE (35 left TLE, 33 right TLE) were divided into three groups: (1) no evidence of pathology in either MRI or FDG-PET studies (MRI−/PET−, $n = 15$), (2) temporal FDG-PET determined hypometabolism with normal MRI findings (MRI−/PET+, $n = 21$), and (3) evidence of temporal abnormalities in both MRI and FDG-PET studies (MRI+/PET+, $n = 32$). A fourth group (MRI+/PET−, $n = 4$) was too small for further statistical analysis and could not be included. Patients with MRI+/PET+ showed worse verbal memory than patients with MRI−/PET− ($p < 0.01$), regardless of side of seizure focus. Verbal memory performance of patients with MRI−/PET+ was located between patients with MRI+/PET+ and MRI−/PET−, although group differences did not achieve statistical significance ($ps > 0.1$). No group differences were found for nonverbal memory ($p = 0.27$). Our results may suggest an interactive negative effect of metabolic and structural temporal lobe abnormalities on verbal memory. Still, our results are preliminary and need further validation by studies involving larger patient groups and up-to date quantitative imaging analysis methods.

1. Introduction

Episodic memory relies on temporal lobe structures [1]. Accordingly, temporal lobe epilepsy (TLE) is related to impaired learning and memory [2,3]. Both structural and metabolic abnormalities of temporal lobe regions are frequently found in patients with TLE [4–6] and can disrupt memory function [7].

Magnetic resonance imaging (MRI) is routinely used to detect structural abnormalities associated with epilepsy [8]. Structural MRI determined abnormalities (short: MRI abnormalities) may be associated with neuropsychological dysfunction at epilepsy onset, already [9]. Structural MRI abnormalities of the left temporal lobe may be related to verbal memory deficits [10–14]. Similarly, MRI abnormalities of the right temporal lobe may be related to nonverbal memory impairment [15–17].

[^{18}F]fluorodeoxyglucose positron emission tomography (FDG-PET) reveals regional interictal hypometabolism. It can provide additional information to structural MRI regarding localization of epileptogenic foci and is especially important during preoperative epilepsy surgery evaluation when structural MRI and electroencephalogram (EEG) studies are inconclusive [18,19]. Hypometabolic areas evident in FDG-PET (short: FDG-PET hypometabolism or FDG-PET abnormality) may indicate dysfunctional neural networks independent of structural abnormalities [20]. An association between lateralized temporal lobe FDG-PET hypometabolism and material-specific memory deficits has been confirmed in some studies [21–24], but not in others [25,26].

Studies correlating FDG-PET hypometabolism with memory deficits in TLE, so far, have confounded patients with and without structural MRI abnormalities. Thus, the different possible influences of FDG-PET hypometabolism on memory in patients with MRI-negative and MRI-positive TLE are unknown. However, regional FDG-PET hypometabolism may have an effect on cognition even in focal MRI-negative epilepsy. For example, frontal lobe FDG-PET hypometabolism is related to executive dysfunction in MRI-negative frontal lobe epilepsy [27]. Further, FDG-PET hypometabolism of the temporal lobe can be found in patients with extratemporal epilepsy and is associated with memory deficits [28].

The extent of FDG-PET hypometabolism does not necessarily correlate with structural damage as determined by volumetric MRI,

* Corresponding author at: Epilepsy-Center Berlin-Brandenburg, Herzbergstrasse 79, 10365 Berlin, Germany.
E-mail addresses: j.berger@keh-berlin.de (J. Berger), michail.plotkin@vivantes.de (M. Plotkin), k.demin@keh-berlin.de (K. Demin), martin.holtkamp@charite.de (M. Holtkamp), t.bengner@keh-berlin.de (T. Bengner).

https://doi.org/10.1016/j.yebeh.2017.12.022
1525-5050/

or with the degree of histopathology as determined by neuropathological analysis of temporal lobe structures after epilepsy surgery [29,30]. That means, the extent of functional disturbance as depicted by FDG-PET does not invariably reflect the severity of structural damage. For instance, in some cases, patients with MRI and histopathologically negative TLE show pronounced temporal FDG-PET hypometabolism [31,32]. On the other hand, FDG-PET hypometabolism often extends the area of MRI abnormalities, e.g., due to diaschisis [33]. As a consequence, both MRI and FDG-PET abnormalities may be independently related to neuropsychological impairment in focal epilepsy. In line with this assumption, MRI and FDG-PET measures of the same mesial temporal structures have shown different correlations with memory performance [34].

The present study aimed to disentangle the confounding effects of MRI and FDG-PET findings and to study the allegedly independent influences of structural and metabolic changes of the temporal lobe on memory in TLE. To this aim, we wanted to compare both verbal and nonverbal learning and memory in patients with unilateral TLE with (1) no evidence of pathology in either MRI or FDG-PET studies (MRI −/PET −), (2) temporal FDG-PET hypometabolism with normal MRI findings (MRI −/PET +), (3) evidence of abnormalities in both MRI and FDG-PET studies (MRI +/PET +), and (4) pathological MRI but no hypometabolism (MRI +/PET −). We hypothesized that both MRI abnormalities and FDG-PET hypometabolism would have an additive negative effect on learning and memory. That is, both MRI and FDG-PET findings were expected to be associated with decreased memory performance individually. At the same time, we assumed that a combination of both MRI and FDG-PET abnormalities would be associated with the most dysfunctional memory performance.

2. Methods

2.1. Patients

We retrospectively selected patients who had undergone preoperative assessment for epilepsy surgery at the Epilepsy-Center Berlin-Brandenburg between 2005 and 2016. Patients were included into the present study if they participated in FDG-PET examination in addition to their routine diagnostic work-up, viz. long-term video EEG monitoring, MRI, and neuropsychological evaluation ($n = 315$). Seizure focus localization was determined by using extensive ictal and interictal EEG recordings in conjunction with seizure semiology, detection of structural abnormalities according to MRI, as well as detection of hypometabolic areas according to FDG-PET. Exclusion criteria were used in the following order: age < 16 ($n = 24$); vocabulary intelligence quotient (IQ)-score < 70 ($n = 17$); extratemporal seizure focus ($n = 87$); insufficient evidence of TLE (e.g., EEG seizure pattern ambiguous, $n = 34$); evidence or suspicion of bitemporal seizure origin ($n = 26$); evidence of seizures during FDG-PET scanning ($n = 0$); previous brain surgery ($n = 2$); significant MRI or FDG-PET abnormalities outside the affected temporal lobe ($n = 31$); insufficient comprehension of the German language (as documented by the examiner, $n = 12$); atypical language dominance as determined by functional MRI ($n = 3$; functional MRI was only conducted in a subgroup of patients undergoing TLE surgery with risk to vital language function); evidence of certain psychiatric diagnoses typically related to memory deficits (psychosis, dementia; $n = 0$); and missing memory test results ($n = 7$). According to these requirements, we could include 72 patients with unilateral TLE in our study. In the case of positive MRI or FDG-PET results, neuroimaging findings were concordant with EEG lateralization for all patients. Only four patients showed MRI +/PET − results. As this patient group was too small for further statistical group comparison, we excluded these four patients from further analyses. Epilepsy surgery for relief of refractory TLE was conducted in 39 patients after presurgical evaluation (66% of patients with MRI +/PET +, 67% of patients with MRI −/PET +, and 27% of patients with MRI −/PET − were operated). Two patients were not operated because of epileptogenic areas overlapping with eloquent cortex. In five cases, an operation was recommended, but had not been carried out at the time of data collection. In 22 cases, further presurgical assessment was recommended (e.g., implantation of subdural electrodes or depth electrodes to localize the epileptogenic focus more accurately within the temporal lobe), but had not been carried out yet. Thus, 68 patients (35 left TLE, 33 right TLE) were included in the final sample. The patient sample is described in Section 3.1. The study was approved by the Institutional Review Board of Charité - Universitätsmedizin Berlin.

2.2. MRI

In the first years of the study MRI images were obtained using a 1.5 T MRI scanner (Siemens SymphonyVision, Erlangen, Germany), while in the last 4 years of the study 3 T MRI was used (Siemens Skyra, Erlangen, Germany). The following sequences were performed in all cases: T2-weighted, fluid-attenuated inversion recovery (FLAIR)-weighted, and inversion recovery (IR)-weighted axial and coronal sections of the whole brain, perpendicular to the long axis of both hippocampi, and sagittal T1-weighted 3D MPRAGE.

For 1,5 T MRI, the following protocol was used: [1] T2-weighted: repetition time (TR) = 3100 ms, echo time (TE) = 118 ms, field of view (FOV) = 260 × 260 mm, slice plane = axial, slice thickness = 6 mm, number of excitations (NEX) = 1, flip angle = 150°, number of slices = 25, and gap = 0.6 mm; [2] FLAIR-weighted: TR = 8760 ms, TE = 116 ms, FOV = 202 × 240 mm, slice plane = coronal, slice thickness = 3 mm, NEX = 2, flip angle = 150°, number of slices = 38, and gap = 0.3 mm; [3] IR-weighted: TR = 6350 ms, TE = 62 ms, FOV = 172 × 230 mm (axial) & 192 × 220 mm (coronal), slice thickness = 3 mm, slice plane = axial & coronal, NEX = 1, flip angle = 180°, number of slices = 38, and gap = 0.3 mm; and [4] T1-weighted 3D MPRAGE: TR = 2200 ms, TE = 2.88 ms, FOV = 250 × 250 mm, slice plane = sagittal, NEX = 1, slice thickness = 1 mm, flip angle = 8°, number of slices = 176, and gap = 0 mm.

For 3 T MRI, the following protocol was used: [1] T2-weighted: TR = 5000 ms, TE = 94 ms, FOV = 185 × 220 mm, slice plane = axial, NEX = 1, slice thickness = 2 mm, flip angle = 150°, number of slices = 72, and gap = 0.1 mm; [2] FLAIR-weighted: TR = 9000 ms, TE = 138 ms, FOV = 185 × 220 mm, slice plane = coronal, NEX = 1, slice thickness = 3 mm, flip angle = 146°, number of slices = 45, and gap = 0.1 mm; [3] IR-weighted: TR = 2900 ms, TE = 9.8 ms, FOV = 185 × 220 mm, slice plane = axial & coronal, NEX = 1, slice thickness = 3 mm, flip angle = 150°, number of slices = 45, and gap = 0.2 mm; and [4] T1-weighted 3D MPRAGE: TR = 1900 ms, TE = 2.41 ms, FOV = 253 × 280 mm, slice plane = sagittal, NEX = 1, slice thickness = 1 mm, flip angle = 9°, number of slices = 192, and gap = 0 mm.

All images were evaluated by experienced epileptologists, neuroradiologists, and neurosurgeons in a multidisciplinary council. Images were classified as positive (evidence of MRI abnormalities) and negative (no evidence of MRI abnormalities) based on protocols of these meetings. In patients with MRI-positive TLE, MRI findings included suspicion of mesial temporal sclerosis (MTS; $n = 16$), cortical dysplasia ($n = 10$), MTS plus cortical dysplasia ($n = 2$), cavernoma ($n = 2$), DNET ($n = 1$), and tumor of unknown origin ($n = 1$).

2.3. FDG-PET

The PET/computed tomography (CT) studies were performed with standard static brain FDG-PET imaging protocol using a 3D acquisition mode, starting 60 min after intravenous administration of 250 MBq ^{18}F-FDG. A low-dose CT acquired immediately before the PET scan was used for attenuation correction. From 01/2005 to 05/2011, the PET/CT scans were acquired on the scanner Gemini TF 16 Astonish (Philips Medical Systems, transaxial field of view 18 cm, in-plane resolution at