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Comparison between simultaneously acquired arterial spin labeling and ^{18}F-FDG PET in mesial temporal lobe epilepsy assisted by a PET/MR system and SEEG

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ABSTRACT

Objective: In the detection of seizure onset zones, arterial spin labeling (ASL) can overcome the limitations of positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (^{18}F-FDG), which is invasive, expensive, and radioactive. PET/magnetic resonance (MR) systems have been introduced that allow simultaneous performance of ASL and PET, but comparisons of these techniques with stereoelectroencephalography (SEEG) and comparisons among the treatment outcomes of these techniques are still lacking. Here, we investigate the effectiveness of ASL compared with that of SEEG and their outcomes in localizing mesial temporal lobe epilepsy (MTLE) and assess the correlation between simultaneously acquired PET and ASL.

Methods: Between October 2016 and August 2017, we retrospectively studied 12 patients diagnosed with pure unilateral MTLE. We extracted and quantitatively computed values for ASL and PET in the bilateral hippocampus. SEEG findings and outcome were considered the gold standard of lateralization. Finally, the bilateral asymmetry index (AI) was calculated to assess the correlation between PET and ASL.

Results: Our results showed that hypoperfusion in the hippocampus detected using ASL matched the SEEG-defined epileptogenic zone in this series of patients. The mean normalized voxel value of ASL in the contralateral hippocampus was 0.97 ± 0.19, while in the ipsilateral hippocampus, it was 0.84 ± 0.14. Meanwhile, significantly decreased perfusion and metabolism were observed in these patients (Wilcoxon, $p < 0.05$), with a significant positive correlation between the AI values derived from PET and ASL (Pearson's correlation, $r = 0.74$, $p < 0.05$).

Significance: In our SEEG- and outcome-defined patients with MTLE, ASL could provide significant information during presurgical evaluation, with the hypoperfusion detected with ASL reliably lateralizing MTLE. This non-invasive technique may be used as an alternative diagnostic tool for MTLE lateralization.

1. Introduction

During presurgical evaluation of mesial temporal lobe epilepsy (MTLE), a significant relationship between treatment outcome and accuracy in identifying the epileptogenic zone has been recognized (Hardy et al., 2003). Conventional non-invasive presurgical evaluation includes semiology, electroencephalography (EEG), structural imaging, and functional imaging (Chavakula and Cosgrove, 2017; Duncan, 2010; Fisher et al., 1997; Rosenow and Luders, 2001). In recent years, ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) has been considered as the leading functional imaging option for presurgical evaluation during the interictal phase, particularly in patients with structural imaging-negative refractory epilepsy. This is because high consistency has been observed between regional hypometabolism and the epileptogenic zone (Rathore et al., 2014). However, there remain some limitations in the use of ^{18}F-FDG PET in clinical practice: 1) it is invasive and expensive, 2) it involves exposure to radiation, 3) it is unavailable in many epilepsy centers.

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Notably, arterial spin labeling (ASL), a magnetic resonance (MR) imaging technique that measures perfusion, has been increasingly used to evaluate brain function in multiple neurological disorders in recent years (Blauwblomme et al., 2014; Boscolo Galazzo et al., 2015). It provides information on regional cerebral blood flow (CBF) by using magnetically-labeled arterial blood water as an endogenous contrast agent (Detre et al., 1992; Williams et al., 1992).

Previous studies have compared ^{18}F-FDG PET and ASL (Boscolo Galazzo et al., 2016; Kim et al., 2016; Storti et al., 2014; Wolf et al., 2001); however, many of them have failed to conduct further investigations involving simultaneous comparisons of the two modalities. PET and MRI co-registration images may exhibit limitations with respect to detection of seizure foci, since the two images are acquired at different times using different machines (Ding et al., 2014). Misregistration or various motion artifacts may introduce errors (Rakheja et al., 2013). A combined PET/MR scanner with simultaneous acquisition permits simultaneous imaging of physiological and pathophysiological processes and provides both anatomical and functional information on the same subject (Ding et al., 2014; Fraioli and Punwani, 2014; Tudisca et al., 2015). Thus, a better comparison of different modalities under identical conditions can be achieved with this system. One previous report has compared simultaneous ^{18}F-FDG PET and ASL with a PET/MR system, but it lacked a gold standard diagnosis for most of the included cases, with no invasive treatment and with unavailable outcome data (Boscolo Galazzo et al., 2016). To the best of our knowledge, few studies have investigated the correlations between PET and ASL, simultaneously acquired with PET/MR, and no previous study has systematically compared these with invasive techniques (stereoelectroencephalography, SEEG) and outcome in MTLE. Based on previous studies, we have conducted further investigations using SEEG and treatment outcome as gold standards to assess the usefulness of ASL, with data collected using combined PET-MRI, in patients with MTLE.

Therefore, in this study we aimed to: 1) clarify the effectiveness of ASL in lateralizing the seizure onset zone (SOZ) in MTLE by comparing the results from ASL with those from SEEG and its outcome results and 2) assess the correlation between perfusion data from ASL and metabolism data from ^{18}F-FDG PET, which were simultaneously acquired with a PET/MR scanner.

2. Methods

2.1. Patients

Between October 2016 and August 2017, we retrospectively studied 12 patients (mean age: 25 years, range: 17–35 years; male: $N = 6$, female: $N = 6$) who had confirmed pure MTLE diagnosed with semiology, EEG, structural MRI, and SEEG. The patients had a mean seizure duration of 14.00 ± 4.63 years. Table 1 shows the demographics and clinical features of the included patients.

The inclusion criteria were as follows: 1) pure unilateral MTLE, 2) an invasive SEEG evaluation, and 3) ASL and ^{18}F-FDG PET simultaneously acquired with PET/MR. The exclusion criteria were bilateral MTLE or other types of epilepsy and lack of ASL, ^{18}F-FDG PET, or SEEG evaluation.

The 12 patients underwent the same protocol. First, ^{18}F-FDG PET, ASL, and 3D MRI were simultaneously acquired with a PET/MR scanner after long-term video scalp EEG examination. Second, SEEG electrode implantation and electro-clinical evaluation were conducted by a multidisciplinary team (MDT) to precisely localize the SOZ. Subsequently, radiofrequency thermocoagulation (RFTC) was also performed in these patients (unpublished data).

This study was approved by the ethics committee at Xuanwu Hospital and conducted in accordance with the Declaration of Helsinki. All patients provided informed consent prior to their inclusion in the study.

2.2. ^{18}F-FDG PET, ASL, and 3D MRI data acquisition

All patients underwent a static PET scan and the clinical scan protocol was as follows. Each patient was instructed to fast for at least 6 h and had a confirmed serum glucose level below 8 mmol/L; brain images were acquired with the patient in the supine position 60 min after an intravenous injection of 3.7 MBq/kg of 18F-FDG. PET/MR allowed for the simultaneous comparison of PET with ASL under the same conditions. The images were acquired using a GE SIGNA TOF PET/MR system (GE Healthcare, Milwaukee, WI, USA). Simultaneous PET and 3 T MR imaging data were acquired. 3-Tesla MR were conducted with a 19-channel head-neck coil. PET reconstruction was performed with a TOF-OSEM algorithm (time-of-flight ordered subset expectation maximization; 8 iterations and 32 subsets) on a 192 × 192 matrix, 35-cm field-of view, 2.78-mm slice thickness, and included correction for scatter, random counts, dead time, and point spread function (full width at half maximum of a 3.0-mm Gaussian filter). For this integrated PET/MR, attenuation correction was performed with T1WI. The PET acquisition was performed before and after contrast injection. The duration was approximately 10 min for each task.

ASL perfusion imaging was performed simultaneously with the ^{18}F-FDG PET/MR scanning. All ASL scanning independently used the 3D pseudo-continuous arterial spin labeling technique in a region of interest (ROI) and voxel-wise manner. The parameters were as follows: repetition time (TR) = 4809 ms; echo time (TE) = 10.7 ms; post-labeling delay = 2025 ms; field of view (FOV) = 240 × 40 mm; number of excitations (NEX) = 3; spiral readout of 8 arms × 512 samples; 32 × 4.0 mm axial sections with whole brain coverage; and duration = 4 min 39 s.

All patients underwent 3D T1-weighted scans with a sagittal 3D brain volume sequence (FOV = 256 × 256 mm; NEX = 1; TR/TE = 8.5/3.2 ms; flip angle = 15; slice thickness = 1 mm; and duration = 5 min 8 s). Fat saturation was applied.

2.3. SEEG implantation and outcome data

All 12 patients underwent implantation of frameless SEEG electrodes (Alcis, Besancon, France) with the guidance of Robotic Stereotactic Assistance (Medtech, Montpellier, France). The contacts mainly covered the area of the mesial temporal lobe of the ipsilateral side. The others were mainly distributed across the frontal and insular lobes in cases of temporal plus epilepsy. In most patients, there was further implantation in the contralateral hippocampus in cases of bitemporal lobe epilepsy.

After implantation, all patients underwent long-term intracranial SEEG recording until at least one ictal onset EEG was captured. The invasive EEG recordings of both the interictal and ictal periods were analyzed by the MDT. The SOZ was defined from the SEEG recordings using the standard as: 1) low-voltage fast activity over 20 Hz, 2) recruiting fast discharge (around 10 Hz or more) of spikes or polyspikes, and 3) rhythmic activity (around 10 Hz) of low amplitude (David et al., 2011). Brain mapping and electro-stimulation were conducted before RFTC. The outcome was categorized following Engel's classification (Engel Jr., 1993).

2.4. Quantitative hippocampus volume analysis

Given that our patients had pure unilateral MTLE, we chose the ipsilateral hippocampus, which was individually segmented, as the object of our analysis. For individual patients, the 3D-T1 image was processed for cortical reconstruction and volumetric segmentation with the standard FreeSurfer image analysis v5.3.0 package, according to the developer's online guidelines (http://www.freesurfer.net/fswiki/DownloadAndInstall). Bilateral hippocampal volumes were quantitatively assessed, with the bilateral hippocampus extracted as a ROI for further analysis. Furthermore, the T1 image in the right-anterior-