CASE REPORT

Arterial spin-labeling MRI perfusion in tuberous sclerosis: Correlation with PET

Imagerie de perfusion par marquage des protons dans la sclérose tubéreuse : corrélation au PET

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Available online 3 July 2009

KEYWORDS
Arterial spin-labeling; MRI; Perfusion; Epilepsy; Tuberous sclerosis

Summary
Neuroimaging using magnetic resonance imaging (MRI) is required for the investigation of surgically intractable epilepsy. In addition to the standard MRI techniques, perfusion sequences can be added to improve visualization of the underlying pathological changes. Also, as arterial spin-labeling (ASL) MRI perfusion does not require contrast administration, it may even be advantageous in these patients. We report here on three patients with epilepsy and tuberous sclerosis who underwent brain MRI with ASL and positron emission tomography (PET), both of which were found to correlate with each other and with electrophysiological data.

Introduction
Imaging plays an important role in the management of patients with epilepsy [1]. Tuberous sclerosis is a genetic disease with abnormal neuronal migration, differentiation and proliferation that results in cortical tubers, subependymal nodules and subependymal giant cell astrocytomas. Seizures are a frequent symptom in these patients and, although pharmaceutical therapy remains the first-line therapeutic approach, some patients develop pharmacologically refractive seizures that may necessitate surgery. Thus, it is important to further improve the diagnostic armamentarium available for use in these patients. Perfusion techniques are usually employed as adjuncts to anatomical sequences in magnetic resonance imaging (MRI) [2]. Arterial spin-labeling (ASL) MRI requires no contrast medium and is therefore of considerable interest for patients in whom examinations...
must be repeated [3–6]. We report here on three epilepsy patients who underwent MRI with ASL.

**Patients and methods**

In this study, which was approved by our local ethics committee [study number: 08-097 R (NAC 08-031R)], we examined three patients, with known tuberous sclerosis and epilepsy, who were referred to our epilepsy presurgical work-up unit for evaluation of intractable seizures. In this unit, patients are seen by a multidisciplinary team comprising neurologists, neurosurgeons, neuroradiologists and pediatricians who specialize in the work-up of patients with epilepsy. In addition to a complete clinical examination, these patients also underwent non-invasive electroencephalography (EEG).

MRI was performed using a 3.0-T Magnetom Trio (Siemens; Erlangen, Germany) (Figs. 2 and 4). ASL was performed with a pulsed ASL sequence, using a QUIPSII perfusion mode and the following parameters: 16 slices; voxel size: \(3.4 \times 3.4 \times 6\) mm; \(T_A = 5:55\) min; \(\lambda = 0.9\) mL/g; \(\alpha = 95\%\); and \(TE/TR/T1/T2/T1\) (blood 3T) = 15/5000/700/1800/1496,19 ms. Relative cerebral blood flow (relCBF) maps for ASL were calculated online by the MRI scanner, and offline for contrast-enhanced perfusion-weighted imaging (cePWI) using Syngo Perfusion (MR) software.

An epilepsy protocol was used, comprising the following sequences: axial T2-weighted images (TE: 101 ms, TR 4000 ms, 26 slices, 4-mm thickness, \(372 \times 510\) matrix); sagittal T1-weighted multiplanar reconstructed (MPR) (TE: 2.32 ms, TR: 1900 ms, \(512 \times 512\) matrix); and sagittal threedimensional fluid-attenuated inversion recovery (3D FLAIR) (TE: 420 ms, TR: 6000 ms, \(256 \times 256\) matrix, 162 1-mm thick contiguous images).

Susceptibility-weighted imaging (SWI) was performed with 3D acquisition and an in-plane resolution of \(1 \times 1 \times \) mm. Diffusion-weighted imaging (DWI) with 30-direction scanning was acquired as well.

Interictal \([^{18}\text{F}]\)-2-fluoro-deoxy-\(\text{d}\)-glucose positron emission tomography with computed tomography (\([^{18}\text{F}]\)-FDG PET/CT) was used for comparison with ASL because of its known superior spatial resolution and greater sensitivity for correct localization of epileptogenic regions compared with interictal nuclear-medicine perfusion imaging techniques such as \(99\text{m}-\text{technetium ethylcysteinate dimer single-photon emission computed tomography (99m-Tc-ECD SPECT).}

Thirty minutes after intravenous injection of a mean dose of \(169 \pm 27\) MBq of \([^{18}\text{F}]\)-FDG, integrated PET/CT

![Figure 1](image1.png)

**Figure 1** From a girl aged two years and ten months: a: multiple hypoperfused areas are visible on the arterial spin-labeling (ASL) map, especially in the right frontal cortex (arrow); b: PET shows multiple hypometabolic areas in the cortex (arrow); and c: FLAIR shows multiple tubers as hyperintensities.

![Figure 2](image2.png)

**Figure 2** From a boy aged four years and nine months: a: ASL perfusion map shows hypoperfusion in the left lateral temporal region (arrow); b: PET shows hypometabolism also in the left lateral temporal lobe (arrow); and c: FLAIR shows bilateral hyperintensities (tubers) in the temporal lobes.
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Figure 3 From a 5-year-old girl: a: ASL perfusion map shows areas of hypoperfusion (arrow); b: PET shows hypometabolism in the same areas; and c: FLAIR reveals tubers in these regions.

was acquired, using a Siemens Biograph 16, following CT with no contrast enhancement (2-mm slices) for anatomical co-registration, attenuation and scatter correction. In addition to visual evaluation, the FDG PET scans were compared with a normal series collected from 12 healthy subjects to identify clusters of voxels with statistically significant \( P < 0.05 \) hypometabolism.

Cases

Case 1

This 2-year-and-10-month-old girl with tuberous sclerosis had an overall increase in seizure activity and a decrease in cognitive performance. She had up to 15 seizures per day, and combination therapy with oxcarbazepine, sodium valproate, topiramate, carbamazepine, clobazepam and vigabatrin failed to control her seizures. EEG showed a frontocentral focus on the right as well as a left-sided centrotemporal focus. PET showed right frontal hypometabolism. On MRI, multiple tubers were visible mainly on FLAIR sequences, as well as hypoperfusion on ASL in the same area as shown on the PET scans (Fig. 1).

Case 2

This 4-year-and-9-month-old boy had had tuberous sclerosis with partial epilepsy from the age of five months. At ten months of age, he began to show clonic movements in the right leg. Combination therapy with carbamazepine, valproic acid, lamotrigine and clobazepam had no beneficial effects. EEG showed centrotemporal spikes on the left that sometimes radiated into the temporal lobe. PET showed marked hypoactivity in the left hemisphere and in the temporal lobe. On MRI, multiple tubers were visible, mainly on FLAIR sequences, as well as hypoperfusion on ASL in the same area as shown on PET images (Fig. 2).

Case 3

This 5-year-old girl with partial complex seizures presented with two seizures per day, and treatment with lamotrigine, topiramate, carbamazepine, clobazepam and vigabatrin failed to control her seizures. EEG showed a frontocentral focus on the right as well as a left-sided centrotemporal focus. PET showed right frontal hypometabolism. On MRI, multiple tubers were visible mainly on FLAIR sequences, as well as hypoperfusion on ASL in the same area as shown on the PET scans (Fig. 3).

Results

On the ASL perfusion maps, multiple areas of hypoperfusion were found that corresponded well with the hypometabolic areas seen with PET imaging.

Discussion

The perfusion maps we obtained with ASL corresponded well with both the PET and EEG results. However, as PET with FDG represents metabolic activity and ASL perfusion provides maps of cerebral blood flow, this was not surprising. Patients with tuberous sclerosis experience epilepsy, and resection of the tuber and neighboring tissue has been shown to reduce ictal frequency [7]. Thus, imaging plays a crucial role [8], and adding ictal and interictal perfusion information has proved to be essential for evaluation of epilepsy in which the usual nuclear-medicine methods, especially the subtraction ictal SPECT co-registered to MRI (SISCOM) technique, are the standard imaging procedures. Also, with interictal perfusion imaging, the expected findings are well established: Sieg et al. found that interictal \(^{99m}\)Tc-HMPAO (hexamethylpropylene amine oxime) SPECT images—which reflect both perfusion and metabolism—demonstrated reduced uptake in cortical tubers [9]; and Widjaja et al. found reduced cerebral blood volume in cortical tubers [10].

Given that ASL offers visualization of flow values and not metabolism, it is better able to reveal the hypoperfusion present interictally in such patients. Also, ASL has the advantage of not requiring the use of intravenous contrast agents in such young patients and/or in those with possible renal impairment. In addition, this is an advantage for patients in whom standard ictal perfusion imaging cannot be performed, and where interictal examinations may have to be...
repeated often—given these current times of concern over the potential occurrence of systemic nephrogenic fibrosis with exposures to contrast media. For these reasons, we believe that adding brain perfusion to the MRI protocols in patients with intractable epilepsy may have advantages.

References