**Diffusion tensor imaging of PET glucose hypometabolic cortex in children with intractable partial epilepsy.**

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**Synopsis**
Four children with intractable epilepsy and normal structural MRI underwent diffusion tensor (DT) MRI and 2-deoxy-2[$^{18}$F]fluoro-D-glucose positron emission tomography (FDG-PET) scans as part of their pre-surgical evaluation. The purpose of this investigation was to examine changes of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) in cortical areas identified as structurally normal but showing glucose hypometabolism on FDG-PET. We found decreased FA in 12/16 hypometabolic regions, and increased ADC values in 11/16 hypometabolic regions identified on the PET scans. This preliminary study suggests that DTI may be a useful complementary method to identify functionally abnormal regions in patients with non-lesional intractable partial epilepsy, but the electrophysiological significance of these DTI abnormalities remains to be determined.

**Introduction:** Structural and functional neuroimaging studies, including MRI and PET, are often used to assist in the localization of epileptic foci during presurgical evaluation in patients with intractable partial epilepsy. Cortical hypometabolism on FDG PET commonly coincides with the general region of the epileptic focus. Recent studies suggest that diffusion tensor imaging (DTI) may be a useful additional method to identify potential epileptogenic regions, as well as dysfunctional areas outside the epileptic lobe [1,2]. However, the relationship between DTI abnormalities and metabolic abnormalities seen on PET is unclear. The purpose of this study is to explore whether non-lesional areas with cortical hypometabolism show changes of FA and/or ADC values measured on DTI.

**Methods:** Four children (mean age: 10 years; age range: 7 to 14 years) with intractable partial epilepsy underwent MRI, including DTI, and FDG PET scanning as part of their presurgical evaluation. All of them had a left hemispheric focus defined by EEG and seizure semiology. All DT images were acquired on a 1.5T GE Signa whole body using spin-echo EPI based sequence with twice refocusing pulse [3] to reduce eddy-current effects. DTI uses six sampling orientations optimally arranged and 34 axial slices to cover the entire brain. Image parameters are as follows: TR/TE = 11000/89 ms, 6 averages, FOV=24*24 cm$^2$, Matrix (128*128) reconstructed in (256*256), b= 0 and 1000 s/mm$^2$, slice thickness=3mm and no gap, resulting in 8 min scan time. All patients underwent structural MRI before DTI, but none showed a structural abnormality.

Cortical areas showing glucose hypometabolism were marked as regions with abnormal (>10%) asymmetry using an objective semi-automated software package [4]. These marked PET images were co-registered to the MR and DT images. To remove partial volume effects, gray matter in the hypometabolic areas as well as in contralateral homotopic regions was segmented using a threshold-based program. Subsequently, glucose metabolic activity, FA and ADC values were measured in the segmented hypometabolic cortex, and asymmetry indices (AI: (left-right)/[(left+right)/2] * 100) were created to characterize decreases and increases on the side of hypometabolism.

**Results:** On FDG PET, a total of 16 noncontiguous regions could be marked as hypometabolic in the 4 patients. Twelve of these 16 regions showed *decreased FA* (mean AI: -16.0%; range: -1 - -30%), and 4 regions showed increases (AI≤1% in 3, and 15% in one region). In contrast, ADC values were moderately *higher* in 11/16 regions (mean AI: 8.5%; range: 4 – 16%) and showed mild decreases (mean AI: -3.9%, range: -1- -6%) in the remaining 5 regions. FA and ADC abnormalities were not necessarily in the same regions, although there was significant overlap. No correlation was found between ADC, FA, and FDG AIs (p>0.3 in all correlations).

**Table.** FA and ADC decreases (negative AI) and increases (positive AI) in 16 hypometabolic (>10% AI on FDG) regions

| | Decreased (n) | AI Mean/SD | Increased (n) | AI Mean/SD |
|---|---|---|---|---|
| **FDG** | 16 | -19.7 ± 3.5% | -- | -- |
| **FA** | 12 | -16.0 ± 10.5% | 4 | 4.4 ± 7.3% |
| **ADC** | 5 | -3.9 ± 1.7% | 11 | 8.5 ± 4.1% |

**Conclusion:** These preliminary findings suggest that hypometabolic cortex commonly shows decreased FA and/or increased ADC values on DTI, even if MRI does not reveal any obvious structural abnormalities. FA decreases appear to be more robust in magnitude than changes in ADC values. Thus, DTI may be a useful complementary method to identify functionally abnormal cortical regions in patients with intractable non-lesional partial epilepsy. These findings warrant further studies comparing the localization value of DTI vs. the scalp and intracranial electroencephalogram in order to determine whether DTI is accurate in delineating epileptic foci and dysfunctional regions outside the primary seizure focus.

**References:**
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