DIFFUSION TENSOR IMAGING (DTI) IN PATIENTS WITH PARTIAL EPILEPSY DUE TO KNOWN OR PRESUMED MALFORMATIONS OF CORTICAL DEVELOPMENT (MCD) – PRELIMINARY RESULTS OF AN ONGOING STUDY

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Introduction:

•Malformations of cortical development (MCD) are an important cause of partial epilepsy and have been described in 8-12% of adults with this form of epilepsy[1,2], however, the lesions may be difficult to detect on routine imaging.
•epilepsy surgery on patients without any visible pathology on MRI is known to be associated with a less favorable outcome.
•MCD are a result of abnormal proliferation, migration or organization during brain development and therefore involve both the gray and the white matter.[3, 4]
•diffusion tensor imaging (DTI) is an MRI technique, which incorporates pulsed magnetic field gradients into a standard MRI sequence, thus eliciting the differences in the diffusion of water molecules among various biologic tissues.
•the anisotropy of white matter and nerves is caused by tightly packed axonal membranes and, if present, the myelin in these tissues, which allow diffusion only in a direction parallel to the fibers.[5]
•DTI is able to provide structural data about brain tissue and information about white matter in particular, which cannot be obtained by other imaging techniques.

Methods:

SUBJECTS:
- •3 patients:
  - •aged 21,23,39
  - •2 female, 1 male
  - •2 with seizures of frontal lobe origin, 1 with seizures of temporal lobe origin
  - •1 with a cortical dysplasia visible on MRI, 2 with normal structural MRIs
- •11 normal controls:
  - •aged 19-46, median 29
  - •no history of neurological illness, seizures or structural MRI abnormalities

IMAGING:
- •1.5 T Phillips Gyroscan ACS NT
  - •DTI acquisition:
    - •50-60 axial slices with a slice thickness of 2.5 mm
    - •diffusion weighting was applied along 30 independent axes
    - •other imaging parameters: TR=6543, TE=80, acquisition matrix 96x96, reconstruction matrix 256x256, FOV 240, 3 acquisitions
  - •MPRAGE acquisition:
    - •TR / TE of 8.1 / 3.7, flip angle of 8, acquisition matrix was 256 x 256, reconstruction matrix was 256 x 256 and the FOV 25.6 cm

ANALYSIS:
- •fractional anisotropy (FA) maps were calculated using software developed in-house
- •statistical parametric mapping (SPM2)
  - •grey-white matter segmentation
  - •normalization of study subject and normal control data onto a template
  - •voxel-wise t-test of higher or lower anisotropy of each subject against the normal group
  - •reported results are significant at $p_u < 0.001$ (uncorrected for multiple comparisons)

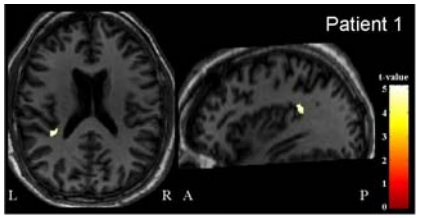

Fig. 1:
Area showing significant decrease of FA in the white matter of patient 1 in comparison to the collection of normals ($p_u < 0.001$) superimposed on the normalized T1-weighted anatomical image of patient 1 (Talairach-coordinates: -36, -41, 19). L = left; R = right; A = anterior; P = posterior.

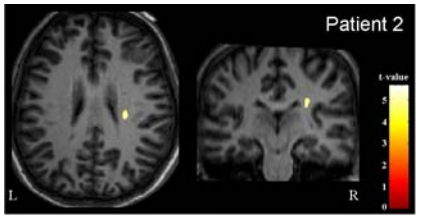

Fig. 3:
Area showing significant decrease of FA in the white matter of patient 2 in comparison to the collection of normals ($p_u < 0.001$) superimposed on the normalized T1-weighted anatomical image of patient 2 (Talairach-coordinates: 28, -24, 24). L = left; R = right.

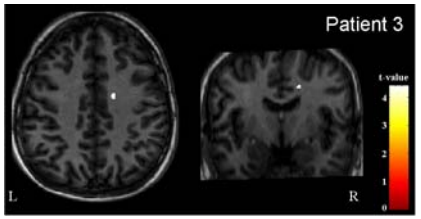

Fig. 5:
Area showing significant decrease of FA in the white matter of patient 3 in comparison to the collection of normals ($p_u < 0.001$) superimposed on the normalized T1-weighted anatomical image of patient 3 (Talairach-coordinates: 16, -5, 39). L = left; R = right.

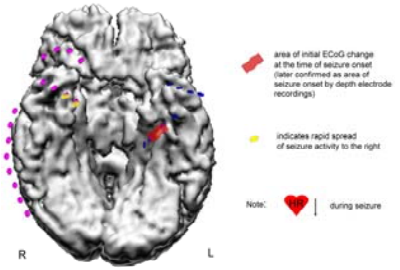

Fig. 2
Results of grid recordings confirming a left temporal seizure onset in patient 1

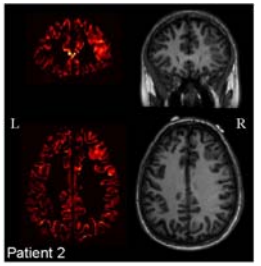

Fig. 4:
Corresponding coronal (top) and axial (bottom) slices of gray matter FA-maps and T1-weighted anatomical image of patient 2 showing an area of increased FA in the known dysplastic lesion. L = left, R = right.

Results:

PATIENT 1:
- •39 y old male
- •temporal lobe seizure semiology (confusion, automatisms)
- •marked bradycardia / syncope during seizures
- •normal MRI, normal 18-FDG PET
- •anisotropy map identified cluster of decreased anisotropy in the white matter of the left insula
- •subdural strip recordings and depth recordings localized seizure onset to left temporal lobe
- •patient did not have a resection, continues to have seizures on AEDs

PATIENT 2:
- •23 y old female
- •frontal lobe seizure semiology (head turn to left)
- •MRI showed large right frontal dysplasia
- •anisotropy map identified cluster of decreased anisotropy in the white matter of the right hemisphere, fronto-parietal area
- •anisotropy map also identified increased anisotropy all throughout the right frontal dysplasia
- •subdural grid recordings identified right frontal dysplasia as seizure focus
- •pathology: large neurons, large bizarre astrocytes, abnormal lamination (cortical dysplasia)
- •patient is seizure free post resection on AEDs

PATIENT 3:
- •21y old female
- •frontal lobe seizure semiology (head turn to right)
- •normal MRI, 18-FDG PET showed minimal hypometabolism in right temporal lobe, ictal SPECT showed increased tracer uptake in right frontal and right insular region
- •anisotropy map identified a cluster of decreased anisotropy in the white matter of the right frontal lobe
- •seizure monitoring with bilateral strip electrodes showed seizure discharges in several left frontal strips. Seizure monitoring with subdural grid electrodes over left hemisphere showed seizure discharges in the left mesial frontal and the left lateral frontal cortex
- •pathology: no cortical dysplasia identified
- •patient continues to have seizures

NORMAL CONTROLS:
- •3 normal controls had small areas of statistically significant anisotropy decrease in areas of their white matter
- •the identified areas of decreased anisotropy in normal controls were generally smaller than those identified in the 3 patients

Discussion:

- •DTI identified areas of decreased anisotropy in the white matter of 3 patients with partial seizures
  - •correlation of area of decreased fractional anisotropy (FA) in white matter with area of seizure onset:
    - •Patient 1: seizure onset left temporal, decreased FA left insula (Fig. 1, Fig. 2)
    - •Patient 2: seizure onset right frontal, decreased FA right hemisphere (fronto-parietal); possibly indicating a larger than suspected area of microdysgenesis in this patient with proven cortical dysplasia (Fig. 3)
    - •Patient 3: seizure onset unknown (conflicting results from various tests and unsuccessful seizure surgery); decreased FA right frontal; possibly indicating that this patient's seizures actually do originate from the right frontal lobe with fast spread to the left (Fig. 5)
- •DTI identified increased anisotropy in the gray matter of the known cortical dysplasia therefore depicting structural change within the cortex not visible with other imaging methods (Fig. 4)
- •3 normal control subjects had small areas of decreased anisotropy in the white matter of unclear significance

Conclusions:

- •DTI is a promising, non-invasive technique for the localization of abnormalities associated with malformations of cortical development that give rise to partial epilepsy
- •further studies are needed to evaluate the potential of DTI in this area further
- •further studies are needed to define the normal range of white matter anisotropy

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