## DTI reveals disease severity specific nerve fiber impairment in juvenile myoclonic epilepsy

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*Background:* Juvenile myoclonic epilepsy (JME) is a syndrome of idiopathic generalized epilepsy (IGE) without structural brain abnormalities detectable by magnetic resonance imaging (MRI) or computed tomography. *Objective*: In the present study, we addressed the question of whether diffusion tensor magnetic resonance imaging (DTI) can detect disease specific white matter (WM) abnormalities in JME patients.

*Methods:* We performed whole head DTI at 3T in 10 patients with JME, 8 age-matched patients with cryptogenic partial epilepsy (CPE), and 67 age-matched healthy volunteers. For DTI we employed echo planar imaging (EPI) at 3 Tesla with 20 diffusion directions (36 slices, thickness 3.6 mm, matrix 128 x 128, in-plane resolution 1.8 mm x 1.8 mm, eddy current correction). Nerve fiber integrity was compared between the groups on the basis of optimized voxel-by-voxel statistics of fractional anisotropy (FA) maps obtained by DTI (ANCOVA, categorical factor "group", covariate "age"). To assess the specificity of regional FA alterations on an individual basis, we defined a region of interest (ROI) outlining the most conspicuous and significant FA differences between JME patients and controls. Mean FA values of the ROI were calculated for all JME patients, CPE patients, and controls.

*Results:* FA was significantly reduced in a WM region associated with the anterior thalamus and prefrontal cortex in JME patients compared to both control subjects and patients with CPE ($p<0.001$). The patients with CPE showed completely normal values in this particular WM region. The FA reductions in the JME patients correlated with the frequency of generalized tonic-clonic seizures (Spearman's $R= 0.54$, $p= 0.05$). No significant correlations were found between FA reduction and the duration of antiepileptic medication, the duration of JME, or the age of the JME patients.

*Conclusions:* The results support the hypothesis that JME is associated with abnormalities of the thalamocortical network that can be detected by DTI. The alterations of the nerve fibers associated with the anterior thalamus seem to be (1) a marker for disease severity in JME and (2) no epiphenomenon of medication effects. From a clinical point of view, we may suggest DTI as a new sensitive tool to detect microstructural brain changes associated with epilepsy syndromes. It might be used to strengthen the diagnosis of JME.

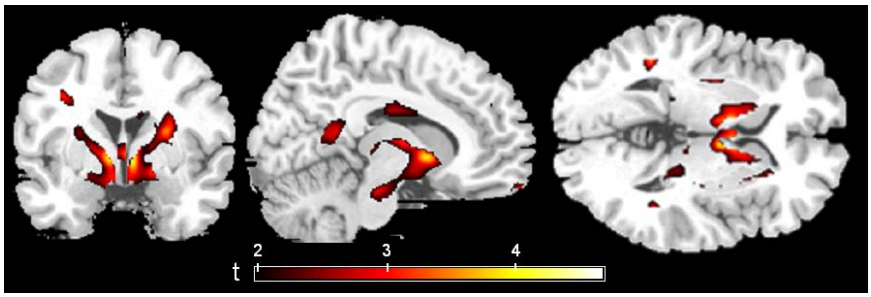


**Fig. 2** FA reductions ($p<0.001$, uncorrected, min cluster size 10 voxels) of the JME patients (N=10) compared to normal controls (N=67). A region of interest (ROI) in the anterior limb of the left and right internal capsule was defined for quantitative FA comparisons between JME patients, CPE patients, and healthy controls.

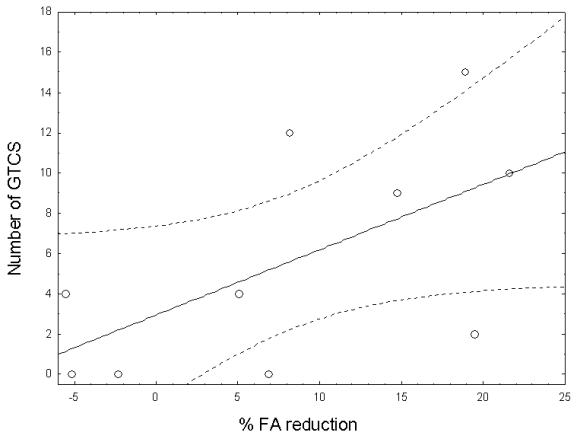


**Fig. 1** The number of generalized tonic-clonic seizures (GTCS) of JME patients in dependence of their thalamocortical FA reduction in the ROI compared to controls. The FA reduction is presented as percentage FA loss compared to the median FA value of the control group.