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Structural adaptive smoothing increases sensitivity of DTI to detect microstructure grey matter alterations

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Introduction

Magnetic resonance (MR) diffusion tensor imaging (DTI) plays an increasing role in the identification of subtle brain alterations in patients with idiopathic and cryptogenic neurological syndromes. DTI-determined alterations in fractional anisotropy (FA) and/or mean diffusivity (MD) have been demonstrated in epilepsy patients with hippocampal sclerosis (Concha et al., 2009; Focke et al., 2008; Thivard et al., 2005) and focal cortical dysplasia in regions within and beyond the circumscribed abnormality (Lee et al., 2004; Widjaja et al., 2007). Such alterations also occur in juvenile myoclonic epilepsy in whom no structural abnormality on conventional MR is apparent (Deppe et al., 2008).

Recently, in a group of patients with temporal lobe epilepsy with unknown cause (TLEu) significant differences of the mean FA compared to normal controls in various ROIs have been observed (Keller et al., 2011). These results can be obtained only using appropriate eddy-current correction and image registrations and a suitable choice of data smoothing. As Gaussian filtering is known to lead to blurring at tissue borders, it is necessary to look for alternatives. Here, we demonstrate a higher sensitivity of structural adaptive smoothing compared to common Gaussian filtering. This may enable the possibility to detect smaller FA changes or to use smaller sample sizes

Methods

Ten patients (6 females, 4 men) with TLEu and 81 healthy age-matched volunteers as a control population (42 women, 39 men) were recruited into this study. All subjects gave their written informed consent to the examinations and the local ethics committee approved this study.

All participants underwent DTI at 3T (Philips Intera T30). We used echo planar imaging (EPI) with 20 diffusion directions (two b-factors, 0 s/mm2 and 1000 s/mm2, TR=9.8 s / TE=95 ms, acquisition matrix: 128 x 128, voxel size: 1.8 x 1.8 x 3.6 mm3 (reconstructed to 0.89 x 0.89 x 3.6 mm3), 2 averages, scanning time 7:46 min).

All DTI images were processed with the “Münster Neuroimaging Evaluation System (EVAL)” employing the recently created multi-contrast image registration toolbox that was developed for optimal image processing for FA images (Mohammadi et al., 2009) and a new, 3D eddy current correction approach (Mohammadi et al., 2010). *For noise reduction we employed a) Gaussian filtering with FWHM 2x2x4mm and b) Structural adaptive smoothing (Tabelow et al., 2008).*

Structural adaptive smoothing (see Poster #611-WTh)

- Algorithm for structural adaptive smoothing of DTI data using the general Propagation-Separation approach (PS), see Tabelow et al. (2008)
- Adaptation based on local comparison between the estimated diffusion tensor
- Iterative algorithm that performs smoothing directly on the diffusion weighted images and uses the re-estimated diffusion tensors for an improved adaptation in the next iteration step. Iteration is from small to large scale of local vicinities.
- The algorithm has been shown to improve estimates for diffusion tensor and fractional anisotropy (FA). Adaptive smoothing of diffusion weighted images enables reduction of Rician bias.
- Requires approximately 10-20 minutes on common hardware.
- Structural adaptive smoothing DTI data avoids blurring as inherent for the Gaussian filter, see Fig. 1.

Results

Structural adaptive smoothing automatically estimates the local noise level and adaptively reduces the noise in the data. It therefore leads to improved FA values not only overall in the brain, but also for very small structures like the putamen. Table 1 summarizes the mean FA values in several ROIs in the patient and in the control group and emphasizes the statistical differences via two-sample t-test. For all considered ROIs, the sensitivity of the difference is greatly increased.

- Increased sensitivity of the two-sample t-test for putamen FA differences with controls
- Possibility to detect smaller FA changes or to use smaller sample sizes.
- The intrinsic stopping criterion allows for larger maximum banwidths for structural adaptive smoothing (Tabelow et al., 2008) and therefore larger variance reduction.

Effect of Gaussian compared to structural adaptive smoothing on FA, e.g. in gCC

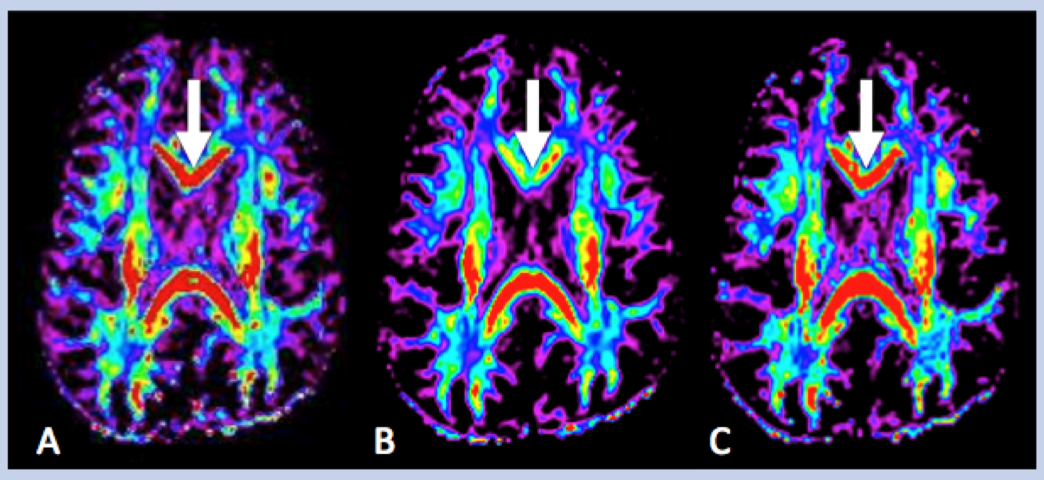

Figure 1: *Effect of (A) no smoothing (B) Gaussian smoothing (2x2x4mm) (C) structural adaptive smoothing (4mm) on the estimated FA value. While without smoothing the noise is known to lead to an intrinsic bias in the FA estimates and the diffusion direction is highly noisy, with Gaussian smoothing FA is systematically underestimated. Only structural adaptive smoothing reduces noise without blurring at structural borders.*

Results

	Control	Patient	t-value	df	p
Gauss Whole Brain	0.181	0.156	4.65458	87	0.000012
Gauss White Matter	0.351	0.319	5.11634	87	0.000002
Gauss Putamen	0.142	0.165	-2.62672	87	0.010187
Gauss Putamen left	0.142	0.162	-2.02725	87	0.045698
Gauss Putamen right	0.141	0.168	-3.01650	87	0.003352
STAD Whole Brain	0.217	0.172	6.06245	87	0.000000
STAD White Matter	0.392	0.355	5.65290	87	0.000000
STAD Putamen	0.131	0.159	-3.05426	87	0.002994
STAD Putamen left	0.132	0.157	-2.54891	87	0.012560
STAD Putamen right	0.131	0.160	-3.19691	87	0.001937

Table 1: *Mean FA values over control and patient group in different regions of interest. For the upper part of the table DTI data has been smoothed using Gaussian filter (Gauss), for the lower part structural adaptive smoothing (STAD) has been used. The t- and corresponding p-values for the FA differences between both groups are also given.*

Conclusions

Noise has a significant influence on the sensitivity of data analysis. Using structural adaptive smoothing in the analysis of FA alterations in TLEu compared to normal controls reduces the noise and thus increases the sensitivity. As a consequence smaller sample sizes are necessary to detect group differences.

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