IS PRE-OPTIMIZATION OF DTI DATA NECESSARY FOR CORRECT INTERPRETATION OF GROUP DIFFERENCES OF REGIONAL FRACTIONAL ANISOTROPY?

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Introduction: Diffusion tensor magnetic resonance imaging (DTI) [1] is unique in providing information about organization and structural integrity of white matter (WM) tissue in vivo. The diffusion tensor (DT), a 3x3 matrix, is difficult to handle concerning non-linear transformation and statistical analysis. Thus, the degree of anisotropy incorporated in the diffusion tensor is often projected to a scalar, in our case to the fractional anisotropy (FA). Voxel based morphometry (VBM), a global search strategy, is chosen, when groups are compared without a priori-knowledge about spatial location and extent of differences. Usually, VBM is performed on T1-weighted images [2]. The T1 signal intensities, however, are not very well correlated to white matter (WM) integrity. Principally, the T1-weighted images provide a *qualitative* information about the tissue (0: "not WM" or 1: "WM" (hard segmentation)), whereas the FA-images provide more subtle *quantitative* ($0 \leq FA \leq 1$) information about WM-tissue architecture. Thus the number of brain conditions studied by voxel-based statistics of FA-images (FA-VBS) increases rapidly [3].
Objective: The FA-image is calculated from at least seven images (six diffusion weighted and one non-weighted image), which are susceptible to artefacts when measured with echo-planar imaging (EPI). We studied the effects of such artefacts to the FA-VBS results.
Methods: 23 healthy right-handed subjects participated in this study. For DTI we employed EPI at 3T with 20 diffusion weighted images and 3 acquisitions of non-diffusion weighted images. For each subject three different FA-images were calculated from EPI data: a) distortion corrected and smoothed, b) just distortion corrected, and c) just smoothed. For each FA-image VBM-preprocessing steps (segmentation, normalization, smoothing) were performed. Hemispheric differences in white matter composition were assessed by FA-difference maps (DFA) [$DFA = (FA_{left} - FA_{right})$] using SPM2 for statistical testing on group level (one-sample *t*-test, $P < 0.05$, corrected for multiple comparisons). Regions in the DFA-images with voxels, fulfilling statistical criteria for left-right differences, were in the following briefly denoted as blobs (cf. yellow areas in Fig. 1 and 2).
Results: Without correction for eddy current induced distortions (ECD) we found more false positive blobs close to the cortex (Fig. 1a) as with correction for ECD (Fig. 1b). For different VBM-parameters (smoothing kernel s= 6, 8 and 12 mm) remained the blobs at the arcuate fascicle only, if primary EPI data were sufficiently smoothed (Fig. 2a, marked green). With weaker, insufficient smoothing of primary EPI data (Fig. 2b), additional false positive blobs at the cortex appeared (marked red).
Discussion: Correction of ECD avoids false positive FA-VBS blobs at the cortex (Fig. 1). Where one intuitively expect that a higher noise level in the EPI data (small smoothing kernel) would only decrease sensitivity (green marked regions at the arcuate fascicle), we here showed that noise can also lead to additional false positive blobs (red marked regions).
Conclusion: The two examples in Fig. 1 and 2 show that insufficient preprocessing of EPI data falsify the FA-VBS results. In standard VBM of T1-weighted data the findings depend strongly on VBM-preprocessing. In FA-VBS it is additionally necessary to account for artefacts in the diffusion weighted images [4].

References:

[1] Basser *et al.*, JMR B **103**, 259-67 ('96)
[2] Ashburner *et al.*, NeuroImage **11**, 805-21 ('00)
[3] For a rev. cf. Jones *et al.*, NeuroImage **26**, 546-54 ('05)
[4] For a rev. cf. LeBihan *et al.*, JMRI **24**, 478-88 ('06)

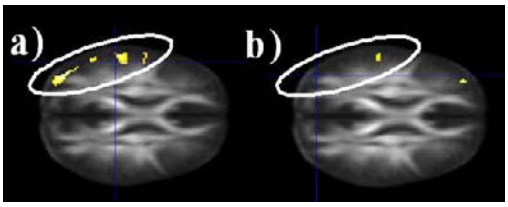

Fig. 1: Eddy current induced false positive blobs at the cortex (highlighted) projected onto an FA-image. a) EPI data *not* corrected for eddy current distortion, b) corrected.

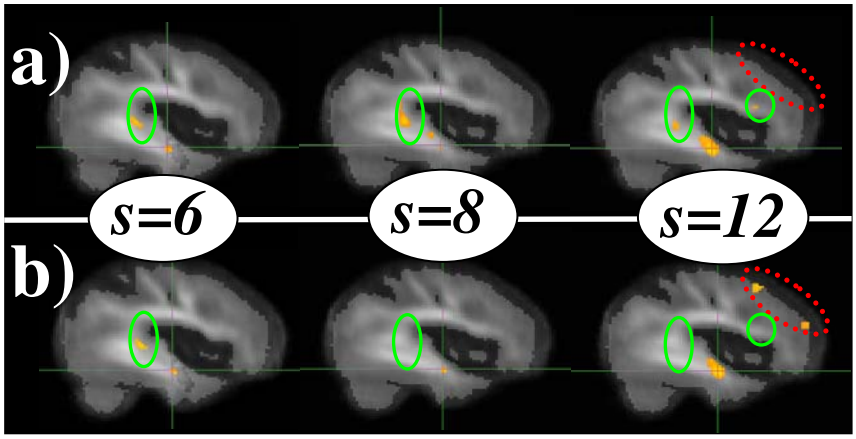

Fig. 2: Left-right differences revealed by FA-VBS (yellow) at three different VBM-parameters (s= 6, 8 and 12 mm), projected onto an FA-image. The FA was calculated from EPI data, smoothed with large (a) and small (b) Gaussian kernels. With a small smoothing kernel false positive blobs appeared (marked red), whereas with a large smoothing kernel physiologically meaningful blobs, i.e. asymmetries in the arcuate fascicle, were better detected (marked green).