Multivariate statistical comparison of diffusion tensor maps in normal aging

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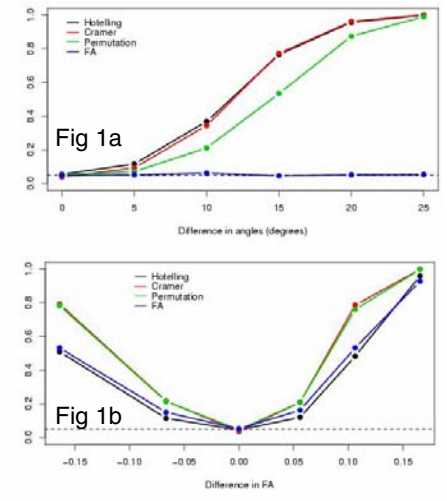
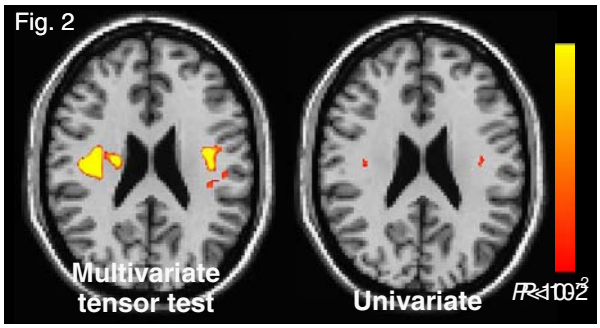
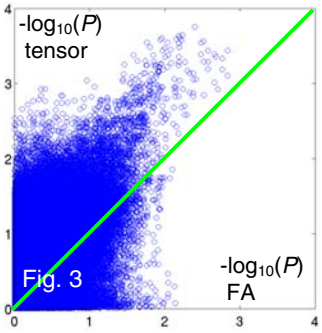
Introduction Diffusion tensor imaging (DTI) has emerged as a powerful tool for identifying white matter (WM) microstructural alterations in neurodegenerative pathology and neuropsychiatric disorders. The prevalent method for group analysis of DTI is a univariate statistical comparison of fractional anisotropy (FA). However, statistical tests based solely on FA cannot detect group differences in tensor orientation, for example, due to architectural differences or pathway-specific FA alterations in regions of fiber crossing. Recently there have been efforts to develop multivariate hypothesis tests suitable for group comparison of tensors [1, 2]; yet it is not clear whether such tests actually provide greater statistical sensitivity or additional anatomical information over standard univariate tests on FA. Here, we provide results from numerical simulations and DTI data from a normal aging study to show that statistical tests based on the full diffusion tensor provide substantially greater statistical sensitivity compared to univariate FA comparisons.

Methods *Simulation.* Group-level DTI data at a single voxel were simulated for two subject groups (n_1=n_2=20), first varying the angle of the dominant fiber direction while holding FA constant and then varying FA while holding the fiber direction constant. Inter-subject tensors were sampled from a Wishart distribution with 12 degrees of freedom. The MR signal was simulated using the non-central χ^2 (Rician) distribution. *Group study.* DTI data were acquired on a 1.5 T Siemens Sonata (7 directions, 6 averages, b=700 s mm^{-2}, 2mm isotropic resolution) from m=15 young participants (age: 25-39) and n=15 middle-aged participants (age: 40-59) [3]. The diffusion tensor maps were MNI-normalized using FLIRT [4] (12-dof, mutual info cost function), and the rotational portion of the affine transformation was then applied to the individual diffusion tensors. Voxel-wise statistical tests were performed on the FA maps using a standard t-test and on the diffusion tensor maps using the multivariate Cramér test [5].

Results *Simulation.* In simulation studies, the Cramér test was sensitive to both differences in PV and FA between groups. At typical SNR levels, the Cramér test could detect group PV differences as low as 20° and FA differences of ±0.12 with 80-90% power (Figure 1a,b). *Group study.* The FA t-test and the tensor Cramér test detected focal diffusion differences (nominal P<10^{-2}) in deep, bilateral corona radiata white matter (MNI peak 34/-16/24, -34/-14/24) (Figure 2). The tensor-based significance clusters had greater spatial extension and showed higher peak significance (Figure 3).







Discussion Multivariate statistical comparison of diffusion tensor maps in normal aging revealed more spatially extended effects than apparent of the FA statistical maps. The finding of early WM microstructural alterations in the coronate radiata is consistent with previous reports of FA decreases in the posterior limb of the internal capsule in middle-age [3]. Statistical comparison of diffusion tensors promises to significantly boost the statistical sensitivity of DTI group comparisons and to extend the methodology to conditions where FA is preserved yet the diffusion tensor orientation is altered.

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