Co-Analysis of Structural Imaging and DTI in Alzheimer's Disease

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Introduction

In voxel-wise analysis, images are first aligned to a standard coordinate system using nonlinear registration techniques, and then statistics are performed at every voxel individually to relate diagnosis and/or other clinical measures to the imaging metric. Our current implementation of nonlinear registration of structural images uses T1-weighted images with uniform contrast white matter, and therefore voxel-wise analyses of structural changes may be insensitive to disease-effects within the white matter. To address this limitation, we proposed a deformation morphometry co-analysis with diffusion tensor imaging (DTI). DTI provides good imaging of white matter, potentially allowing delineation of individual fiber tracts. A co-analysis of structural and DTI may reveal more disease-related brain abnormalities than a voxel-wise analysis of either modality alone.

Methods

Twenty-two patients with Alzheimer's Disease (AD; 65 ± 10 yrs, range 51-84 yrs, 8 women, MMSE 21 ± 8) and 27 cognitively normal healthy elderly controls (CN; 66 ± 8 yrs, range 51-82 yrs, 19 women, MMSE 29 ± 1) were studied. T1-weighted imaging and DTI was collected on a 4T MRI system (Bruker/Siemens) [1]. Images were registered to standard space, which was an average atlas created from 10 healthy elderly normal controls, using a fluid-flow registration technique [2]. The determinant of the Jacobian from registration of each T1 image to the atlas was computed at each voxel to yield maps of deformation (JAC). Fractional anisotropy (FA) at each voxel was computed in subject space, then each subject's T1-> atlas registration was applied to each subject's FA map to yield FA maps in standard space. Several linear models were fit: 1) FA maps as dependent variables (DV) with group and age as independent variables (IV), 2) JAC maps as DVs with group and age as IVs, 3) multivariate analysis with JAC and FA maps as DVs with group and age as IVs, and 4) JAC maps as DVs with group, age, and FA maps as IVs.

Results

Fig. 1 shows t-statistic maps overlaid on the atlas image, thresholded at |T|>2. The top panel shows several small regions where reduced FA is associated with AD (shown in blue/green), particularly in the posterior parietal and temporal lobes. The bottom panel shows that AD is associated with large regions of atrophy (shown in blue/green) throughout the brain, particularly in the posterior parietal and temporal lobes, extending into frontal regions. In addition, AD is associated with increased ventricular and sulcal CSF (shown in red/yellow). The top panel of Figure 2 overlays the group t-statistic maps from the multivariate analysis with the univariate FA analysis, and the bottom panel shows overlays with the univariate JAC analysis, to demonstrate where multivariate analysis leads to improved detection of disease effects. Red shows regions where the effect of AD was only detected when both FA and JAC were used as DV. Yellow shows regions where an AD effect was detected using either the multivariate or the univariate model. Green shows regions where the AD effect was only detected using the univariate analysis. As shown, the multivariate analysis is far superior than the univariate FA analysis (note large regions of red, few regions of yellow or green in Figure 2, top), while the univariate analysis of JAC is nearly as sensitive as the multivariate analysis (note large regions of yellow, few regions of red or green in Figure 2, bottom). Lastly, co-analysis using JAC as DV covarying for FA did not result in greater detection of the effect of AD.

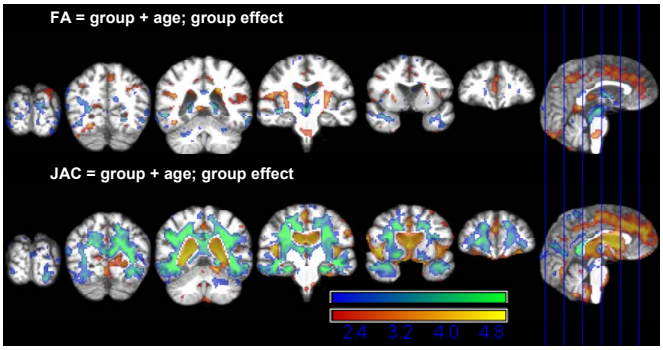

Figure 1: Group effects on FA and JAC.

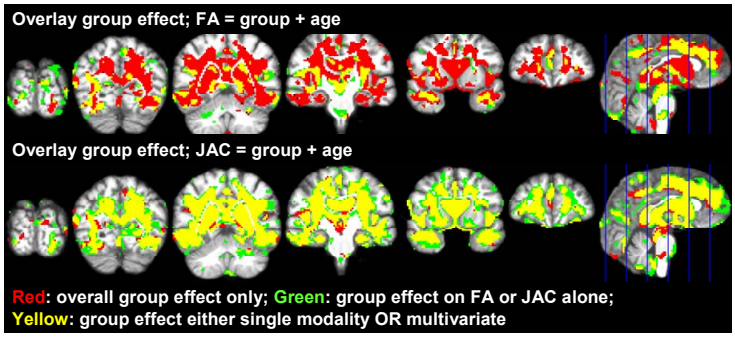

Figure 2: Overlay group t-statistic maps.

Discussion

We found that co-analysis of structural images and DTI did not reveal significantly more AD-related brain abnormalities than a voxel-wise analysis of structural images alone. However, the value of co-analysis may vary across different stages of the disease, especially in early AD. Univariate analysis of FA images did not reveal many AD-related abnormalities. We did not use optimal registration of FA maps to standard space, and this may limit our sensitivity to detect AD-related effects. Furthermore, other metrics of diffusion, such as full diffusion tensor or kurtosis, could be more sensitive measures than FA. In future work, we will determine the feasibility of fused T1-FA coregistration to improve detection of disease-related white matter changes, and explore alternatives to voxel-wise analysis to identify regions in different modalities jointly associated with disease.

References [1] Zhang et al., Brain 2009 Sep; 132(Pt 9):2579-92. [2] Lorenzen et al., MICCAI, 2005; 8(pt 2):411-8.

Acknowledgments This work was supported in part by NCRR P41RR023953.