Improved Discriminant Analysis in Schizophrenia Using Fractional Anisotropy and Apparent Diffusion Coefficient Images of Water Diffusion in Brain

B. A. Ardekani[1,2], J. Nierenberg[1,2], D. D'Angelo[3], and M. J. Hoptman[2,3]

[1]Center for Advanced Brain Imaging, Nathan Kline Institute, Orangeburg, New York, United States, [2]Department of Psychiatry, New York University School of Medicine, New York, New York, United States, [3]Clinical Research Division, Nathan Kline Institute, Orangeburg, New York, United States

Introduction: Patterns of water diffusion in the brain, as measured by diffusion tensor imaging (DTI), differ between patients with schizophrenia and healthy control subjects (1,2). Thus, DTI can be used in pattern recognition algorithms for automatic discrimination between these groups. Caan et al. (3) applied a linear discriminant analysis (LDA) method to fractional anisotropy (FA) images from 34 patients with schizophrenia and 24 healthy control subjects. The accuracy of their classification method was estimated to be 75% using cross-validation.

In this paper, we applied LDA to DTI data from 42 patients with schizophrenia and 42 healthy controls. The main objective of the present study was to utilize *both* FA and apparent diffusion coefficient (ADC) images as bases for classification between patients and healthy controls. We hypothesized that using FA and ADC images concurrently would result in higher classification accuracy than using either FA or ADC alone.

Methods: Forty-two patients with schizophrenia and 42 matched healthy control subjects participated in this study, which was approved by the ethics committee of our institution, after providing written informed consent. DTI was performed on a 1.5 T Siemens Vision scanner. Diffusion sensitizing gradients were applied in 8 non-parallel directions with a b-value of 1000 $mm.s^{-2}$. FA and ADC images were estimated from these data. High-resolution MPRAGE structural images were also acquired from each subject to aid in spatial normalization of the DTI data. Images from all 84 subjects were corrected for spatial distortion and registered to a study-specific template based on the 'colin27' MNI template using the ART registration software as described elsewhere (4). Following image registration, ADC and FA data matrices were mean corrected and scaled by voxelwise estimates of within-class standard deviations. Feature extraction was performed using singular value decomposition (SVD) on ADC and FA images separately. The dimensions of the feature spaces for the ADC and FA were selected so as to retain at least 95% of the variance in the data matrices. A leave-one-out cross-validation procedure was performed to estimate classification accuracy. The minimum distance criterion was used to classify test subjects based on their FA and/or ADC projections onto the directions in the feature spaces determined by the training procedure.

Results: The specificity, sensitivity, and overall accuracy of the classification algorithms estimated using the leave-one-out cross-validation are summarized in Table 1.

Diffusion measure	Specificity	Sensitivity	Overall accuracy
ADC	85.7%	71.4%	78.6%
FA	88.1%	73.8%	81.0%
ADC and FA	90.0%	76.2%	83.3%

Discussion and Conclusions: We were able to independently confirm the results obtained in (3) that FA images could be used to discriminate between patients and controls. We obtained an overall accuracy of 81.0%. As noted above, Caan et al. (3) reported an accuracy of 75%. The increased accuracy indicated by our experiments could be attributed to factors such as the larger sample size in our study, differences in inter-subject registration methods used, differences in the implantation of the pattern recognition algorithms, DTI acquisition protocol, method of error estimation and variance in the estimated accuracies.

We also showed that ADC images discriminate between patients and controls, but with a lower specificity and sensitivity compared to using FA images. The results also suggest that using *both* ADC and FA concurrently results in more accurate classifications compared to using either ADC or FA alone. To the best of our knowledge, this is the first application of multiple DTI imaging measures in voxel-wise discriminant analysis in schizophrenia. The methodology can be extended to more than two imaging measures/modalities. For example, fMRI, magnetization transfer ratio (MTR), and morphometric structural MRI could also be used in the classification process, as well data from other imaging modalities such as PET. We predict that using multiple imaging measures would further increase the classification accuracy. Finally, the classification accuracy may be improved by applying other pattern recognition techniques such as *support vector machines*, and/or by using alternative feature extraction methods.

References:

1. Ardekani BA, Nierenberg J, Hoptman MJ, et al., Neuroreport. 2003, 14(16):2025-9.
2. Ardekani BA, Bappal A, D'Angelo D, et al., Neuroreport. 2005, 16(13):1455-9.
3. Caan MW, Vermeer KA, van Vliet LJ, et al., Med Image Anal. 2006, 10(6):841-9.
4. Szeszko PR, Ardekani BA, Ashtari M, et al., Arch Gen Psychiatry. 2005, 62(7):782-90.

Supported by NIMH Grant R01MH64783 (Hoptman)