Multivariate Linear Discriminant Analysis of DTI Data Improves the Detection of Microstructural Damage in Young Professional Boxers

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Introduction

Different diffusion metrics, such as mean diffusivity (MD), fractional anisotropy (FA) and mode, are sensitive to different changes in the microstructure of the brain. Using a single metric to identify differences between a patient group and a control group ignores much of the information contained in the diffusion tensor in terms of the other unused metrics. We therefore investigated whether Linear Discriminant Analysis (LDA) provides a robust multivariate method to identify microstructural damage in a group of young professional boxers. In general, LDA writes the data as a linear discriminant function of the form:

$$y = a_0 + a_1x_1 + a_2x_2 + \ldots + a_nx_n$$

where a_i are the linear discriminant coefficients, and x_i are the metrics being used. LDA determines the a_i in such a way as to obtain maximum discrimination between the two groups of interest. As LDA maximizes group difference, the y-value for each subject at each voxel provides an optimal variable for statistical analysis. LDA has been used by other researchers: with combined MRI and MRS data to identify brain tumors[1]; and using two-dimensional histograms of apparent diffusion coefficient and FA to classify different neurological conditions[2]. This study takes this approach a step further by applying it to voxel based DTI analysis.

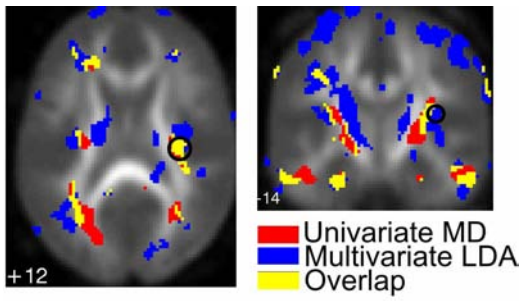

Fig. 1. Axial and coronal views of regions where the boxers' brain maps are statistically different from the controls' (FDR correction, α=0.05, k=8), for either MD only, LDA only or both measures.

LDA has two other features. First, when statistically normalised data are used as input, the a_i coefficients give the relative contribution of each metric to any differences between the two subject groups. Second, LDA has the possible clinical application of identifying whether a given individual belongs to the patient group (i.e. has similar brain damage) or not. This is done firstly by finding the coefficients of the linear discriminant function, a_i, and then evaluating that function for a given individual. If $y < 0$ the subject is classified as a control; if $y \geq 0$ the subject is classified as belonging to the patient group. When group membership is already known, as in the current study, cross-validation of the LDA classification can be made, and its predictive ability determined from the proportion of subjects successfully classified at a particular voxel.

Methods

In vivo data were acquired from 59 professional male boxers aged 22-31years, and 12 age-matched male control subjects. Scans were performed on two GE 1.5T MRI scanners with 22mT/m gradient strength. A quadrature head coil was used, and in all cases the slice thickness was 5 mm, with no intersection gaps. A 2D spin echo EPI acquisition was used with TE/TR = 100ms/ 12s. An acquisition matrix of 128×128×30 and 1.7×1.7×5 mm^3 voxels in 26 gradient directions with b-values between 815 and 1152 $s.mm^{-2}$, and 6 acquisitions with no diffusion weighting, was used. Conventional univariate analyses were compared with the multivariate LDA analysis of the same dataset, using SPM2 with False Discovery Rate (FDR) correction for multiple comparisons, at a level of significance of 0.05, and a minimum cluster size of 8 voxels.

Results and Discussion

Overall, MD was found to be the most sensitive of the three univariate metrics, so it was used as the comparison with the LDA analysis. Fig. 1 shows that LDA is more sensitive for both cortical and subcortical damage than MD alone. A voxel where LDA found a highly significant difference between boxer and control groups was selected as an example. It is circled in Fig. 1, with MNI coordinates [36 -14 12]. The linear discriminant function for that voxel was:

$$y = 0.0251 + 0.0087 \times MD_z - 0.0081 \times FA_z - 0.0369 \times Mode_z$$

where the z subscript refers to normalised values (to a mean of 0 and standard deviation of 1). The coefficients show that at this voxel, mode was the strongest metric, with MD and FA making similar, weaker contributions. This is an important feature of LDA: the best predictor is automatically more heavily weighted than metrics with weaker correlations. The predictive ability of LDA at voxel [36 -14 12] was 90% using all three metrics. To provide a 2-D illustration of LDA, we used MD and FA as they are the more commonly used metrics. Fig. 2 shows the expected result that head injury causes MD to increase and FA to decrease[3], and also the separation between the two groups achieved by LDA. The effect of removing mode, the strongest metric at this voxel, from the analysis was to reduce the predictive ability in the bi-metric LDA to only 73%.

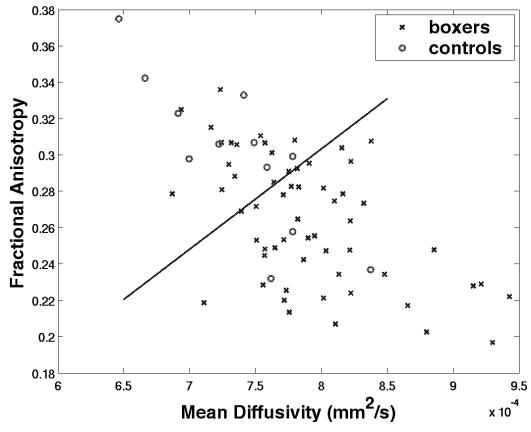

Fig. 2. Scatterplot for voxel [36 -14 12] with the linear discriminant function overlaid.

Conclusions

Using DTI data, LDA multivariate analysis was more sensitive than univariate MD analysis in detecting the diffuse nature of cortical and subcortical damage of repetitive mild closed head injury. This study also illustrates two other features of LDA: being able to determine which metric is making the greatest contribution to any identifiable difference between the two groups; and possibly being able to make an important contribution in the clinical setting, especially for future study when used at the ROI scale. When support for a positive or negative diagnosis is required, LDA may be able to provide such a binary decision, based on multiple components. As well as having the flexibility to be multimodal[1], LDA could also accommodate non-imaging parameters related to the study, which would further increase its sensitivity.

References

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