

# Classification of 3-D MRI Brain Data Using Modified Maximum Uncertainty Linear Discriminant Analysis

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## Abstract

Recent studies have demonstrated that diagnostics of schizophrenia based on image data is a difficult task because of extensive overlaps of brain regions distinguishing patients with schizophrenia from healthy controls and also because of the small sample size problem. An algorithm for the automatic classification of first-episode schizophrenia patients and healthy controls based on deformations and gray matter (GM) density images extracted from their MRI intensity data is introduced here. The deformations and GM density images are reduced by principal component analysis, which is here based on the covariance matrix of persons (pPCA). The reduced image data is then classified with the use of modified maximum uncertainty linear discriminant analysis (MLDA), which gives better sensitivity than original MLDA. The classification efficiency of the proposed algorithm is comparable with other state-of-art studies in the schizophrenia research.

## 1 Introduction

Development of medical imaging methods, such as magnetic resonance imaging (MRI), functional MRI or positron emission tomography, has enabled searching for morphological areas in the brain where patients with schizophrenia differ from healthy people [9]. Recently, there is also an effort to use medical imaging methods for diagnostics of schizophrenia [3, 6, 7]. Diagnostics is a very demanding task because there are usually broad overlaps of regions which differentiate schizophrenia patients from healthy control subjects. Another common problem in classification of 3-D medical image data is the so-called small sample size: the number of subjects is considerably smaller than the number of features, what often leads to instable classification results.

Thomaz *et al.* [10] proposed maximum uncertainty linear discriminant analysis (MLDA) to overcome the mentioned problems in the classification based on brain images of patients with Alzheimer disease. Here, the concept of MLDA is followed and further modified to solve classification of 3-D MRI brain data sets in the schizophrenia research.

## 2 Methods

### 2.1 Data Sets

Unlike in [10], gray matter density images and deformations of images are used here instead of original MRI intensity data.

The gray matter density images are by-products of voxel-based morphometry [1], where original intensity images are spatially normalized and segmented into the gray matter (GM), the white matter and the cerebrospinal fluid. The GM density images are appropriate for classification of schizophrenia patients because many anatomical areas which differentiate patients from healthy controls lie in GM [9].

The deformations are results of deformation-based morphometry in which high-dimensional nonlinear registration of MR images with a digital brain atlas is performed [8]. The deformations represented by displacement fields or their Jacobians clearly show how the brain anatomy of a diagnosed subject differs from the normal template anatomy in the terms of local volume expansions and contractions.

### 2.2 Data Reduction

Both the GM density images and the deformations are 3-D data which contain more than one million voxels even after removing extracerebral voxels. Such large image data leads to the small sample size problem. Therefore, principal component analysis (PCA) is used here for reducing the huge data. However, the GM density images and the deformations are too large even for computation of covariance matrix of voxels which is one of the steps in PCA [5].

Thomaz *et al.* [10] and Demirci *et al.* [3] used PCA based on covariance matrix of persons (pPCA) to overcome the small sample size problem in an analysis of brain images of patients with Alzheimer disease and an analysis of functional magnetic resonance images of patients with schizophrenia respectively. Let  $\mathbf{X}$  be  $N \times n$  matrix composed of  $N$  input images with  $n$  voxels. According to linear algebra rules, nonzero eigenvalues of the covariance matrix of voxels  $\mathbf{X}^T \mathbf{X}$  and the covariance matrix of persons  $\mathbf{X} \mathbf{X}^T$  are the same and eigenvectors corresponding to the higher dimensional covariance matrix can be derived from the eigenvectors of the smaller one by:

$$\mathbf{V}_j = \frac{\mathbf{X}^T \phi_j}{\sqrt{\lambda_j}}, \quad (1)$$

where  $\mathbf{V}_j$  is the  $j^{\text{th}}$  eigenvector of the covariance matrix of voxels,  $\mathbf{X}^T$  is the transposed image data matrix,  $\phi_j$  and  $\lambda_j$  are the  $j^{\text{th}}$  eigenvector and the  $j^{\text{th}}$  eigenvalue of the covariance matrix of persons respectively.

The original data matrix  $\mathbf{X}$  is then multiplied by a matrix with column-wise computed eigenvectors  $\mathbf{V}_j$ ,  $j = 1, \dots, N - 1$  to obtain the reduced data matrix  $\mathbf{X}_r$ . Unlike in commonly used PCA, which leads to decrease of the data variance, pPCA allows using all  $m = N - 1$  eigenvectors with non-zero eigenvalues for data reduction which enables preservation of all sample variance and thus maintenance of the whole information important for classification.

### 2.3 Data Classification

The reduced data matrix  $\mathbf{X}_r$  is the input into the classification. MLDA, first described by Thomaz *et al.* [10], is used here for its good performance even in data with small sample

sizes and this method is further modified here to improve its classification results. MLDA enables reduction of the matrix  $\mathbf{X}_r$  with the size  $N \times m$  into a classification vector with the size  $N \times 1$  in the two-class classification. It means that every input image is reduced into one number with the use of pPCA and MLDA. Steps of data reduction by MLDA are fully described in [4] or [10] and can be shortly summarized in this way:

1. Let a within-class scatter matrix  $\mathbf{S}_w$  be defined as  $\mathbf{S}_w = \sum_{i=1}^g \sum_{j=1}^{N_i} (x_{i,j} - \bar{x}_i)(x_{i,j} - \bar{x}_i)^T$  and a between-class scatter matrix  $\mathbf{S}_b$  be defined as  $\mathbf{S}_b = \sum_{i=1}^g N_i (\bar{x}_i - \bar{x})(\bar{x}_i - \bar{x})^T$ , where  $g$  is the total number of groups (here  $g = 2$ ), the vector  $x_{i,j}$  is the  $m$ -dimensional pattern  $j$  from group  $\pi_i$  (here  $\pi_1$  is the class of schizophrenia patients and  $\pi_2$  is the class of healthy control subjects),  $N_i$  is the number of training patterns from group  $\pi_i$ , the vector  $\bar{x}_i$  is the unbiased sample mean of group  $\pi_i$  and  $\bar{x}$  is overall mean vector.
2. Find the eigenvectors  $\phi$  and the eigenvalues  $\lambda$  of  $\mathbf{S}_p$ , where  $\mathbf{S}_p = \mathbf{S}_w / [N - g]$ .
3. Calculate average eigenvalue  $\bar{\lambda}$  of matrix  $\mathbf{S}_p$  by  $\bar{\lambda} = \frac{\text{trace}(\mathbf{S}_p)}{m}$ .
4. Construct a new matrix of eigenvalues based on the following largest dispersion criterion  $\Lambda^* = \text{diag}[\max(\lambda_i, \bar{\lambda}), \dots, \max(\lambda_m, \bar{\lambda})]$ .
5. Form the modified within-class scatter matrix  $\mathbf{S}_w^*$  by  $\mathbf{S}_w^* = (\phi \Lambda^* \phi^T)(N - g)$ .
6. Finally, calculate the projection matrix  $\phi_{MLDA}$  which maximizes the ratio of the determinant of the between-class scatter matrix to the determinant of the within-class scatter matrix (Fisher's criterion) by  $\phi_{MLDA} = \text{eigenvector}(\mathbf{S}_w^{*-1} \mathbf{S}_b)$ .

Afterwards, the reduced data matrix  $\mathbf{X}_r$  is multiplied by  $\phi_{MLDA}$  to compute the MLDA classification vector. Every input image is now represented by one classification score. Each of the two groups (patients and healthy controls) can be now represented by the average classification score of subjects from the group. A boundary between the two groups is computed using an arithmetic mean in Thomaz *et al.* [10]. Here, the following formula for the weighted mean is used to calculate the boundary:

$$\frac{\bar{z}_1 SD_2 + \bar{z}_2 SD_1}{SD_1 + SD_2}, \quad (2)$$

where  $\bar{z}_1$  is the mean classification score for the group 1,  $\bar{z}_2$  is the mean classification score for the group 2 and  $SD_1$  and  $SD_2$  are the group standard deviations [2].

A new image, which is supposed to be classified is reduced by the matrix of eigenvectors  $\mathbf{V}_j$  of pPCA and eigenvectors  $\phi_{MLDA}$  of MLDA and then classified into one of the groups depending on whether its classification score falls above or below the boundary.

### 3 Experiment and Results

The classification algorithm built up from the pPCA and the modified MLDA was tested in an experiment with 49 MRI brain data of first-episode schizophrenia patients and 49 brain images of sex- and age-matched healthy control subjects. The classification efficiency is evaluated with the leave-one-out cross-validation technique while using various input image data and MLDA designed by Thomaz *et al.* [10] versus the modified MLDA.

Table 1: Efficiency of classification with various input images and classification methods.

Image data	Classification method	Accuracy (in %)	Sensitivity (in %)	Specificity (in %)
GM density images	MLDA	77.6	79.6	75.5
GM density images	Modified MLDA	78.6	81.6	75.5
Deformations	MLDA	75.5	71.4	79.6
Deformations	Modified MLDA	77.6	87.8	67.3
Intensity images	MLDA	62.2	57.1	67.3
Intensity images	Modified MLDA	72.4	93.9	51.0

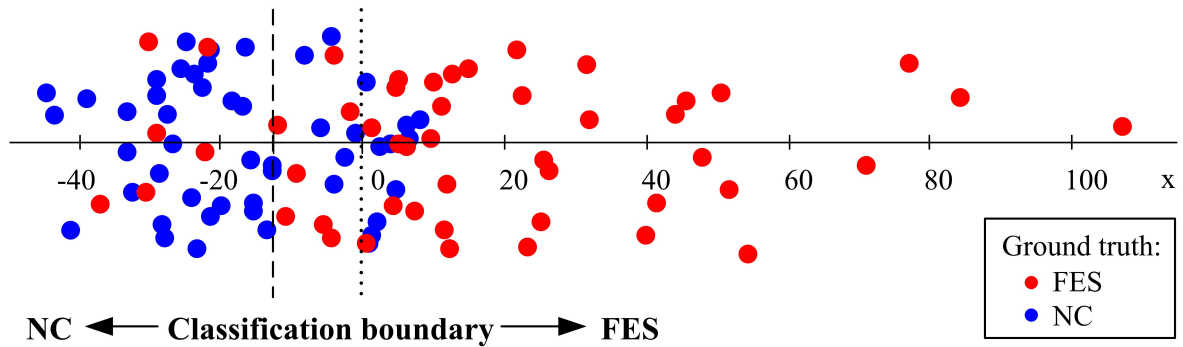


Figure 1: MLDA classification. Red dots stand for classification scores of first-episode schizophrenia patient (FES) images and blue dots stand for classification scores of healthy control (NC) images. The dashed line represents the classification boundary of the original MLDA and the dotted line represents the classification boundary of the modified MLDA. Images left of the boundary will be classified as NC and images right of the boundary as FES. It is obvious that the modified MLDA enables classification with higher sensitivity (it means more FES are classified correctly using the modified MLDA) and lower specificity (it means fewer NC are classified correctly using the modified MLDA) than the original MLDA.

According to the Tab.1, the modified MLDA improves accuracy and sensitivity in the classification of all image data, when compared to MLDA designed by Thomaz *et al.* [10]. The table also shows that the highest accuracy was achieved in the classification based on the GM density images. The second best accuracy was obtained in the classification based on the deformations and the worst accuracy in the case of the original MRI intensity images.

The results of classification based on deformations using MLDA designed by Thomaz *et al.* [10] and the modified MLDA are showed in Fig.1 for illustration. The figure demonstrates that the modified MLDA leads to the classification with higher sensitivity and lower specificity than the original MLDA. The increase of sensitivity is more important than the decrease of specificity here because the proportion of correctly classified patients is more crucial than the proportion of correctly classified controls in diagnostics.

## 4 Conclusions

Classification of 3-D MRI deformation data and gray matter density images into a group of first-episode schizophrenia patients and a group of healthy controls is described here. The first part of the classification algorithm performs data reduction with the use of pPCA, which

is based on the covariance matrix of persons and enables reduction with no loss of information important for classification. The second part is represented by modified maximum uncertainty linear discriminant analysis (MLDA). The presented modification of MLDA enables classification with higher sensitivity and accuracy than the original MLDA. The highest accuracy was achieved in classification based on GM density images. The accuracy of classification based on GM density images and deformations was higher than the accuracy of classification based on intensity images. The efficiency of the proposed classification algorithm is comparable with other recent studies which deal with classification of schizophrenia patients and is significantly better than the efficiency of the classification by chance.

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