Substructural segmentation based on regional shape differences

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Abstract. This article presents a method for the segmentation of substructures based on exploratory factor analysis. In this approach, a high-dimensional set of shape-related variables is examined with the purpose of finding clusters with strong correlation. This clustering can potentially identify regions that have anatomic significance and thus lend insight to morphometric investigations. **Methods:** The information about regional shape is extracted by registering a reference image to a set of test images. Based on the displacement fields obtained form image registration, the amount of pointwise volume enlargement or reduction is computed and statistically analyzed with the purpose of extracting a reduced set of common factors. **Experiments:** The effectiveness and robustness of the method is demonstrated in a study of the human corpus callosum anatomy, based on a sample of 84 right-handed normal controls. **Results:** The method is able to partition the structure into regions of interest that present correlated shape variation. The confidence of results is evaluated by analyzing the statistical fit of the model.
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1 Introduction

An important problem related to medical image analysis is extraction of relevant shape-related information from the large amount of data provided by imaging modalities. The data should not only be represented in a manageable way, but also facilitate hypothesis-driven explorations of regional shape differences and allow the segmentation of regions of interest. Segmentation is even more difficult when there is no clear information about borders or textures within a specific structure. This work presents a novel method for the segmentation of substructures based on the correlation among morphometric variables. Shape variation analysis has been frequently addressed as a step performed after segmentation. In this work, we aim to invert this order: the information obtained from shape analysis is be used to segment the structure into regions of interest. Our approach is based on the analysis of high-dimensional sets of vector variables obtained from non-rigidly registering or deforming an image, taken as a reference, so as to align its anatomy with the subject anatomy of a group, depicted in MRI studies. The result of registration is a set of displacement fields from which the amount of volume enlargement or reduction at each point of the image can be computed and statistically analyzed with the purpose of extracting a reduced set of common *factors*. We demonstrate the exploratory potential of the method in a study of the human corpus callosum and compare these results with the ones obtained by principal component analysis.

Principal component analysis (PCA) has been one of the most relevant mathematical frameworks used o describe general shape variation. Cootes *et al.* [2] applied the theory of PCA to build a statistical shape model of organs based on manually chosen landmarks. The organs were first segmented and represented as a set of labeled points located at particular regions in order to outline their characteristic shape. The model provided the average positions of the points and the principal modes of variation computed from the dataset. Le Briquer and Gee [7] applied the method to analyze high-dimensional displacement fields obtained from registering a reference image volume of the brain to a set of subjects, based on the elastic matching framework [1]. The analysis provided the inference of morphological variability within a population and was the basis for the construction of a statistical model for the brain shape, which

could be used as prior information to guide the registration process and perform automatic segmentation.

Davatzikos *et al.* [4] showed how the results obtained from matching boundaries of structures could be interpolated to determine an estimate for the displacement field. The method was useful in the registration of structures such as the corpus callosum, whose contour was of more interest than its inner texture. Further analysis on the gradient determinant of the resulting displacement fields showed the amount of area enlargement/reduction while deforming the reference image to match the images in the study. The method was applied to a small set of images of the human corpus callosum, revealing gender-related morphological differences. Using the same dataset, Machado and Gee [9] performed elastic matching to both the boundary and the interior of the structure. Based on the displacements fields obtained from image registration, the method was able to reproduce Davatzikos' results and additionally determine the principal modes of callosal shape variation between sexes. By determining the effect size of the gradient determinant, regions that presented gender-related shape differences could be visualized, but were not used with the purpose of segmentation.

The major objective of PCA is to represent data in a new basis whose axes correspond to the principal modes of the sample variance. However, when the purpose is to explore the covariance among the variables, factor analysis (FA) may be considered an appropriate alternative [15]. On exploring the morphology of a specific structure, one may be concerned with the relationship between shape-related variables within regions of interest. FA may reveal aspects about the correlation between those regions and facilitate interpretation. Nonetheless, the use of FA in morphometry has been restricted to the representation of gross measurements and landmarks, regardless of exploring the relationship between pointwise shape-related variables, as the ones obtained from image registration. Marcus [11] compared the application of PCA and FA on a set of length measurements for several hundreds skeletons of birds. The extracted factors were interpreted as general features related to the overall size of the subjects. Reyment and Jöreskog [14] presented a thorough discussion on the factor analysis of shape-related landmarks. Scalar features such as the distances between landmarks in the carapace of ostracod species were considered in the analysis. Some of the resulting factors were interpreted as shape-changes in specific regions of the shell, location of eye tubercles and valves. Other factors, however, were related to global features such as the dimensions and curvature of the shell.

Stievenart *et al.* [16] applied FA to study the correlation among parts of the corpus callosum, whose boundary curvature was measured at 11 different positions. The results revealed 3 factors that explained 69% of the variation of the original curvature values. The first and second values were clearly related to the curvature of the isthmus and posterior region of the splenium, respectively. Another relevant work on the factor analysis of the corpus callosum was presented by Deneberg *et al.* [5], in which the callosal structure was divided into 100 segments taken along equally spaced intervals of the longitudinal axis. Although the structure partitioning criteria was arbitrary and deliberately chosen to result on transversal segments, the study was able to identify regions in the corpus callosum, particularly the isthmus, which presented morphological differences related to gender and handiness.

2 An overview of principal components and factor analysis

In this section, we present the main concepts of PCA and FA and discuss the most relevant differences between the methods.

2.1 Principal component analysis

In PCA, a p-dimensional set of original variables, $\mathbf{y} = (y_1, \ldots, y_p)^T$, is rotated in order to find the orthogonal axes along which the data is maximally spread out. The new p-dimensional basis $\mathbf{z} = (z_1, \ldots, z_p)^T$ is achieved by multiplying the original variables by an orthogonal matrix $\mathbf{B}$:

$$\mathbf{z} = \mathbf{B}\mathbf{y}. \tag{1}$$

Each new variable z, or *component*, is a linear combination of the original variables $\mathbf{y}$. The covariance matrix for the data in the new basis $\mathbf{z}$, denoted as $\mathbf{S}_z$, can be expressed in terms of the sample covariance matrix $\mathbf{S}$. From Eq. 1,

$$\begin{aligned} \mathbf{S}_z &= cov(\mathbf{z}) \\ &= cov(\mathbf{B}\mathbf{y}) \\ &= \mathbf{B}cov(\mathbf{y})\mathbf{B}^T \\ &= \mathbf{B}\mathbf{S}\mathbf{B}^T. \end{aligned} \tag{2}$$

The covariance matrix for the sample in the original basis, $\mathbf{S}$, can be derived from Eq. 2:

$$\mathbf{S} = \mathbf{B}^T\mathbf{S}_z\mathbf{B}. \tag{3}$$

Since the sample covariance matrix $\mathbf{S}$ is real-valued and symmetric, it has real eigenvalues and orthonormal eigenvectors can be chosen, so that it can be written as

$$\mathbf{S} = \mathbf{Q}\mathbf{\Lambda}\mathbf{Q}^T, \tag{4}$$

where $\mathbf{Q}$ is the matrix whose columns are the orthonormal eigenvectors of $\mathbf{S}$ and $\mathbf{\Lambda}$ the diagonal matrix with the corresponding eigenvalues. In PCA, the rotation of axes brings the new components $\mathbf{z}$ to be uncorrelated, so that the covariance matrix $\mathbf{S}_z$ is also diagonal. Comparing Eq. 3 and

Eq. 4, it can be seen that $\mathbf{S}_z$ is the diagonal matrix of eigenvalues $\mathbf{\Lambda}$ and the transformation matrix $\mathbf{B}$ is the transpose of the eigenvector matrix:

$$\mathbf{B} = \mathbf{Q}^T. \tag{5}$$

2.2 The factor analytic model

The purpose of FA is to explore the correlation among the variables of a problem. Similarly to PCA, FA is a powerful method of data reduction, which makes it possible to manage the large amount of information obtained from image registration. A fundamental feature of FA is that, in addition to data reduction, it may favor data interpretation. In this work, we show how the factors obtained in the analysis of shape-related variables can be associated to specific regions of interest in the images.

In FA, the p-dimensional set of original standardized variables, $\mathbf{y}$, is represented as linear combinations of m hypothetical constructs called *factors*:

$$\mathbf{y} = \mathbf{A}\mathbf{f} + \boldsymbol{\epsilon}, \tag{6}$$

where $\mathbf{f} = (f_1, \ldots, f_m)^T$ is a vector of *common factors*, $\boldsymbol{\epsilon} = (\epsilon_1, \ldots, \epsilon_p)^T$ are the *unique factors* or residual terms which account for the portion of $\mathbf{y}$ that is not common to other variables, and $\mathbf{A} = ((a_{11}, \ldots, a_{1m})^T, \ldots, (a_{p1}, \ldots, a_{pm})^T)^T$ is the *loading* matrix. The coefficients a_{ij}, called *loadings*, express the covariance between variable y_i and factor f_j. The factor analytic model imposes certain assumptions on $\mathbf{f}$ and $\boldsymbol{\epsilon}$. Since the expected value $\mathcal{E}(\mathbf{y})$ is the null vector, $\mathcal{E}(\mathbf{A}\mathbf{f} + \boldsymbol{\epsilon})$ must also be $\mathbf{0}$. It is assumed that $\mathcal{E}(\boldsymbol{\epsilon})$ is $\mathbf{0}$. In order for the factors to account for all the correlation among the variables $\mathbf{y}$, the covariances among unique factor terms and common factors are 0. The covariances among unique factor terms are represented by the diagonal matrix $\mathbf{\Psi} = diag(\psi_1, \ldots, \psi_p)$. Factors are uncorrelated, so that the corresponding covariance matrix is the identity. It should also be noticed that FA, as well as PCA, can be completely modeled from the information represented in the covariance matrix. In other words, FA is implemented in the context of the classical assumption of Gaussianity. Determining if the data fit a multivariate Gaussian distribution is an additional aspect of the problem, since the population parameters should be estimated from the sample. In order to justify the choice of a specific model, a test of Gaussianity should be made (e.g. forth-order cumulants [3, 8]), so that the results can be considered reliable.

Considering the assumptions in the factor analytic model, the variance σ_i^2 of a given variable y_i can be decomposed into components due to the m common factors, $a_{i1}^2 + \ldots + a_{im}^2$, called the *communality*, and a *specific variance* ψ_i:

$$\sigma_i^2 = \sum_{j=1}^{m} a_{ij}^2 + \psi_i. \tag{7}$$

The population covariance matrix $\mathbf{\Sigma}$ can be determined from Eq. 6. Since $\mathbf{A}\mathbf{f}$ and $\boldsymbol{\epsilon}$ are uncorrelated, the covariance matrix of their sum is the sum of the covariance matrix of each term. Also, since $cov(\mathbf{f}) = \mathbf{I}$, the relationship between $\mathbf{\Sigma}$, $\mathbf{A}$ and $\mathbf{\Psi}$ can be written as

$$\begin{aligned} \mathbf{\Sigma} &= cov(\mathbf{A}\mathbf{f} + \boldsymbol{\epsilon}) = cov(\mathbf{A}\mathbf{f}) + cov(\boldsymbol{\epsilon}) \\ &= \mathbf{A}cov(\mathbf{f})\mathbf{A}^T + \mathbf{\Psi} = \mathbf{A}\mathbf{A}^T + \mathbf{\Psi}. \end{aligned} \tag{8}$$

The parameters of FA can be estimated from the sample, by replacing the population covariance matrix $\mathbf{\Sigma}$ in Eq. 8 by the covariance matrix $\mathbf{S}$ obtained from the dataset:

$$\mathbf{S} \approx \hat{\mathbf{A}}\hat{\mathbf{A}}^T + \hat{\mathbf{\Psi}},$$

where $\hat{\mathbf{A}}$ and $\hat{\mathbf{\Psi}}$ are estimations for the loading matrix and unique factor covariance matrix, respectively, since they are computed from the sample. Many techniques have been proposed to determine $\hat{\mathbf{A}}$. The simplest one (principal factor method) neglects $\hat{\mathbf{\Psi}}$ and factors $\mathbf{S}$ using spectral decomposition:

$$\begin{aligned} \mathbf{S} &\approx \hat{\mathbf{A}}\hat{\mathbf{A}}^T \\ &\approx \mathbf{Q}\mathbf{\Lambda}\mathbf{Q}^T \\ &\approx (\mathbf{Q}\mathbf{\Lambda}^{1/2})(\mathbf{Q}\mathbf{\Lambda}^{1/2})^T, \end{aligned}$$

where $\mathbf{\Lambda}^{1/2} = diag(\sqrt{\lambda_1}, \ldots, \sqrt{\lambda_p})$ is the diagonal matrix with the square root of the eigenvalues of $\mathbf{\Sigma}$ and $\mathbf{Q}$ is the matrix of the corresponding eigenvectors. The loading matrix can then be estimated based on the sample covariance matrix as

$$\hat{\mathbf{A}} = \mathbf{Q}\mathbf{\Lambda}^{1/2}. \tag{9}$$

An important property of the loading matrix $\mathbf{A}$ is that it can be rotated and still be able to represent the covariance among factors and original variables [6]. The rotation of loadings plays an important role in factor interpretation, as it is possible to obtain a matrix that assigns few high loading for each variable, keeping the other loadings small. If such matrix is obtained, each variable will be related to a single factor or at least to few ones. Since the variables are related to pixels in the image, the resulting factors can be visually identified as regions in the structure.

2.3 Differences between FA and PCA

Although the main objective of PCA and FA is data reduction, they differ fundamentally on two aspects: the algebraic model of the transformation and how data reduction is achieved. In the factor analytic model, the original variables are represented as a linear combination of new variables (factors), while in PCA, the new variables (principal

components) are linear combinations of the original variables. In PCA, data reduction is achieved by changing the basis of the variable space, so that the new orthogonal axes represent most of the variance embedded in the dataset. The objective of PCA can be defined as maximizing the variance of a linear combination of the original variables. Data reduction is obtained (with possible loss of information) by ignoring the axes in which the data present small variance. In contrast, FA aims to find a new low-dimensional set of non-observed variables that maximally represents the covariance (or correlation) among the original variables.

PCA and FA are frequently mistaken as a single model due to the fact that the most commonly applied method to estimate the loadings, described in Section 2.2, uses the eigendecomposition of the covariance matrix. In this case, the models would be identical if the covariance matrix for the factors could not be assumed to be the identity and the loading matrix further rotated. In PCA, the model must represent both the diagonal and off-diagonal elements of the covariance matrix, so the diagonal elements of $\mathbf{S}$ must be 1, otherwise the analysis of variance will not be properly performed. In contrast, the aim of FA is to represent only the off-diagonal elements that account for the correlation among variables. By neglecting the specific variance matrix $\hat{\mathbf{\Psi}}$, the factor analysis of the covariance matrix is performed by placing communalities in the diagonal elements. In this case, the recovered covariance matrix $\hat{\mathbf{A}}\hat{\mathbf{A}}^T$ will have its off-diagonal elements affected. Hence, it is important to measure this error in order to have a robust estimation of whether the data fit the model. Other techniques such as the *principal factor* and *maximum likelihood* methods can also be used for determining the loading matrix [6]. These methods have, nevertheless, the drawback of requiring inverting the covariance matrix. When the number of variables is greater than the number of subjects in the sample, as it is the case of morphometry studies, the covariance matrix is always singular.

In PCA, data reduction is obtained after the computation of $\mathbf{B}$ by eliminating the components that do not contribute significantly to the representation of variance. In principle, the dimension of the new basis $\mathbf{z}$ is the same of $\mathbf{y}$, so data reduction is achieved by discarding components, with possible loss of information. In fact, since PCA is directed to the representation of variance, the covariance information is guaranteed to be preserved only if all components are kept. Furthermore, data reduction is possible only when the original variables $\mathbf{y}$ are correlated. In the case of independent variables, all the eigenvalues will have similar values. This contrasts with FA, in which dimension reduction is accomplished during the computation of $\mathbf{A}$. The number of factors to be considered must be chosen in order to compute the loading matrix. As a consequence, the elements of $\mathbf{A}$ changes as the number of factors m considered in the analysis varies. As in the case of PCA, in which the number of components to be kept should also be defined, the number of factors must also be chosen. The results of FA should therefore be evaluated by analyzing the statistical fit of the data.

3 Methods

The rationale for structural shape characterization is to provide a quantitative description of the morphometric differences between structures that present a gross common anatomy. Shape description can be achieved by taking a reference image and warping it as to align its anatomy with the anatomy of each individual in the study. The spatial transformation obtained in the warping process can be analyzed and yields immediate knowledge about the anatomic variation among the subjects of the sample.

3.1 Image Registration

Image registration aims to determine a correspondence between each voxel in the reference image to a voxel in the test image. Registration may be performed by first applying rigid transformations (translation and rotation), in order to approximately register corresponding features, and then warping the template to match the subject. Image volumes may be described as continuous media to which a constitutive model will be prescribed. The linear elasticity model [1], in which the image is deformed as an elastic body, guarantees smoothness to the deformation, so that neighboring structures in the reference image will be matched to neighboring structures in the subject's image, preserving the gross anatomy common to the majority of individuals in the population.

3.2 Jacobian Analysis

When the reference image is warped to match a subject image, some regions may get enlarged and some may be reduced. It is possible to determine the amount of scaling applied to an infinitesimal area around each point of the reference image, by computing the Jacobian determinant of the spatial transformation. In the case of two-dimensional images, the displacement vector field from the reference to subject i, $\mathbf{u}_i$, can be decomposed into its components u_i and v_i. Similarly, a voxel $\mathbf{q}$ can be expressed in terms of its coordinates (x, y). The Jacobian determinant $J_i(\mathbf{q})$ is defined as the determinant of the gradient of the mapping function $\mathbf{q} + \mathbf{u}_i(\mathbf{q})$. The set of pointwise Jacobian determinants is the input to FA and PCA. Since the result of image registration is a smooth displacement field, it is expected that the factors be correlated to the Jacobian determinants of neighboring points.

3.3 Statistical fit of the factor analytic model

Another important issue that affects FA is the number of factors to be considered. Harman [6] presented a comprehensive discussion on how to determine the number of factors that best represent a data set. Machado *et al.* [10] proposed an iterative algorithm for choosing which factors to retain by evaluating the number of observed variables associated to each factor. In the experiments, only those factors with correlation greater than 0.5 with at least 2 variables were considered informative. The initial number of factors (number of columns in $\mathbf{A}$) was determined as the number of eigenvalues greater than 1, since they accounted for the variation of at least one variable. The number of factors was reduced, at each iteration, by discarding factors which did not present high correlation to at least two variables. Convergence was achieved when the same number of factors was determined at two consecutive iterations.

In this work, we also discuss the influence of the choice of the number of factors in the results, based on the quantitative analysis of the statistical fit of the model. A straightforward way to analyze whether the loading matrix $\hat{\mathbf{A}}$ is a good estimate of the correlation between factors and variables is to compute the distribution of the correlation residuals. The recovered correlation matrix $\hat{\mathbf{A}}\hat{\mathbf{A}}^T$ should be a good approximation to $\mathbf{S}$. Let r_{jk} be the observed correlation between variables y_j and y_k, $j \neq k$, and $\hat{r}_{jk}$ be the corresponding recovered correlation determined as

$$\hat{r}_{jk} = \sum_{i=1}^{m} a_{ji} a_{ki}.$$

The residual correlations $r_{jk} - \hat{r}_{jk}$ should have a distribution similar to that of a zero correlation, whose standard deviation is computed as

$$\sigma_{r=0} = N^{-\frac{1}{2}}.$$

The loading matrix $\hat{\mathbf{A}}$ can be considered a good approximation if the standard deviation for the residuals is smaller or equal to $\sigma_{r=0}$.

4 Materials

The MRI images used in the experiments are normal controls recruited at the Mental Health Clinical Research Center of the University of Pennsylvania. The images were acquired on a GE 1.5 Tesla instrument, using a spoiled GRASS pulse sequence optimized for high resolution, near isotropic volumes (flip angle = 35^o, TR = 35 ms, TE = 6 ms, field of view = 24 cm, 0.9375 $\times$ 0.9375 mm^2 in-plane resolution, 1.0 mm slice thickness, no gap). The images were obtained in the axial plane and the midsagittal slice extracted and reformatted into 256 $\times$ 256 8-bit images.

The sample used in the study is composed of 42 male and 42 female right-handed controls. The age of the subjects is in the range of 19 to 68 years (mean$\pm$S.D.,30.4$\pm$11.8) for males and 18 to 68 years (26.5$\pm$9.0) for the females. The sample was chosen in order to provide an approximated distribution of age and race for both groups and to guarantee a minimum influence of these features in the analysis. No expressive correlation was detected, in the sample, between gender and age (0.18) and between gender and race (0.06).

5 Experimental Procedure

The images were first segmented by supervised thresholding. The process was performed twice by a single rater who was blind to subject gender. The reliability of the segmentation was measured by computing the intraclass correlation coefficient (ICC) based on the area of the corpus callosum. The ICC value for the dataset was 0.888. Additionally, the same dataset was segmented by a second rater who was also blind to demographic information. Using the adaptive K-means clustering algorithm of Pappas [12], the images were partitioned into white matter, gray matter and cerebrospinal fluid components, from which the corpus callosum structure was extracted by manual delineation. The interrater variability, measured based on the ICC was 0.884.

Global registration was performed by translating and rotating each callosal structure to align with the template, without scaling, through landmark matching. A set of three landmarks were manually chosen in each subject and in the template: the intersection of the subject's callosum boundary to its minimum enclosing rectangle at the most inferior point of the splenium, the most anterior point of the genu and the most superior point of the callosum body. The rigid transformation for each subject was achieved by jointly minimizing the distance between the subject's landmarks and the corresponding points at the template. The process was repeated three times by a single rater, over all the dataset, yielding ICC values greater than 0.980 for all coordinates.

Local registration was performed by warping the template to match each globally aligned subject callosum. The displacement fields obtained from image registration were the basis for the computation of the Jacobian determinants. Vector $\mathbf{y}$ was formed by the determinant of the Jacobian matrix at each of the 851 pixels in the callosal template and used as input to FA and PCA. Since the methods assume that the variables fit Gaussian distributions, a test of normality was performed by estimating the skewness and kurtosis of the distribution for the populations. With a level of significance of 0.01, there were no evidences to reject the hypothesis of normality for 71.4 % of the variables, based on the skewness, and for 86.2% of the variables, based on

the kurtosis of the distribution.

After determining the loading matrix $\hat{\mathbf{A}}$ (Eq. 9), it was rotated in order to maximize the variance of the squared loadings in each column, so that each variable presented high loading for fewer factors (*varimax* algorithm) [14].

6 Results

The algorithm used to determine the number of factors, described in Section 3.3, took 9 iterations to converge from 78 to 11 factors with correlation magnitude greater than 0.5 among at least 2 variables. With a level of significance of 0.01, a correlation coefficient magnitude of 0.5 computed for the sample gives an estimation that the population correlation coefficient, ρ, is in the confidence interval of $0.257 < \rho < 0.683$. The value of 0.5 is also sufficient to reject the hypothesis that $\rho = 0$ with level of significance $\alpha < 0.001$. Fig. 1 shows the 11 resulting factors. Each variable is assigned to the factor for which it presents the greatest absolute loading. For each factor, the regions in the callosal structure that have loading values greater than 0.5 are shown in white and the regions that have loadings smaller than -0.5 are shown in black. The results of PCA are shown in Fig. 2. The principal modes of variance are ordered from left to right, top to bottom, by the amount of variance they represent. Each variable is assigned to the mode for which it presents the greatest absolute coefficient value. Variables with positive coefficient values are shown in white and the ones with negative values are shown in black. The 11 first components acounted for 64.3% of the total variance. The contribution of each component is given in Table 1.

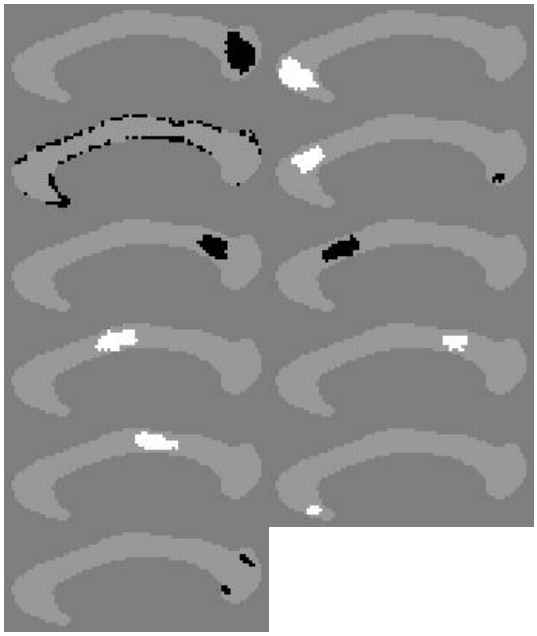

Figure 1: Results of factor analysis. Factors are numbered left to right, top to bottom, starting from factor f_0. For each factor, the variables that present loading values greater than 0.5 are shown in white and the variables that present loadings smaller than -0.5 are shown in black.

7 Discussion

The use of FA as a statistical model may be questionable when the interpretation of the factors is not straightforward. Since factors are non-observed variables, they should have a natural meaning in order to provide new information about the data, otherwise the method would serve only as a data reduction tool. In the case of morphological studies, the factors are visually interpreted as regions in the structure, showing its ability to serve as a segmentation method. This property was explored by Denenberg *et al.* [5], who applied FA to the study of the corpus callosum by partitioning the structure into segments, following the callosal axis at equally spaced intervals. The width of each interval, together with other scalar variables such as the callosal area, perimeter and axis length were examined. Factor analysis were based on the principal component method with oblique rotation and the criterion for retaining factors was similar to the one used in our study: eigenvalues should be greater than unity and the loading value greater than 0.6 for a variable to be assigned to a given factor. The main problem on the experimental procedure is that no registration was performed and, consequently, a precise correspondence between segments and substructures of the corpus callosum could not be established. The splenium, for instance, is a region that varies substantially with respect to length, so that one specific segment may be located at the splenium of one subject and at the isthmus of another. This may explain why 3 out of the 7 factors revealed in the analysis were located between segments number 77 and 99. Compared to the results of our study, they correspond to factor number 0, which encompasses the splenium region. The remaining factors determined in Denenberg's study correspond to factors number 4, 8, 5 and 1, respectively related to the isthmus, posterior midbody, rostral body and genu regions of the corpus callosum (see Fig. 1).

The results of the exploratory FA presented in our study are also in accordance with the topology proposed by Witelson [17], regarding the subdivision of the callosal structure. Fig. 3 shows a schematic of the callosal midsagittal plane subdivisions, in which 7 regions of interest are defined. Compared to the factors depicted in Fig. 1, it is possible to relate the rostrum with factor number 9, the genu with factors 1 and 3, the rostral body with factor 5, the anterior midbody with factor 6, the posterior midbody with factor 8, the isthmus with factors number 4 and 7, and the

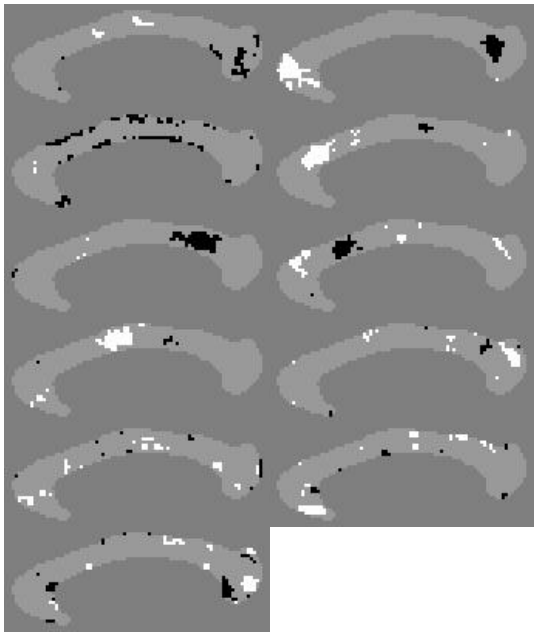

Figure 2: Results of principal component analysis. Modes of variance are ordered left to right, top to bottom, according to the amount of variance they represent. Each variables is assigned to the mode for which it presents the greatest coefficient value. Variables with positive coefficient values are shown in white and the ones with negative values are shown in black.

splenium with factors 0 and 10. Factor number 2, which represents the contour of the callosal structure, is probably related to error in the segmentation and registration steps — in the elastic matching model, the choice of the stiffness parameter may hinder perfect matching of high-frequency details in the boundary. In the case of factor number 9, related to the rostrum, it may reflect error in the segmentation step, as this part of the corpus callosum is frequently linked to the fornix.

A comparison between the results of FA and PCA can be done based on Fig. 1 and 2. Is is clear that FA provides results that can be interpreted as regions in the structure that present correlated shape variation. Since the purpose of PCA is to represent the variance of the dataset, the morphological meaning of the results, in this case, is not straightforward.

The impact of parameter m (number of factors) was investigated by choosing different values, computing the corresponding loading matrix and analyzing the statistical fit of the model. Table 2 shows the average magnitude, mean and standard deviation for the analysis of the correlation residual at different values of m. Since the expected standard deviation for a zero correlation distribution for the same sample size is given as $\sigma_{r=0} = 1/\sqrt{84} = 0.109$, all analyses with the number of factors greater than or equal to 4 were acceptable. The analysis based on the 11 factors determined by the iterative algorithm presented about half the expected standard deviation, showing the satisfactory statistical fitness of this representation.

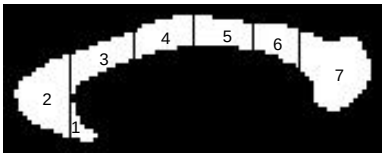

Figure 3: Topology of the corpus callosum, adapted from Witelson(1989) and projected at the template used in the study. The regions of the callosal structures are the rostrum(1), genu(2), rostral body(3), anterior midbody(4), posterior midbody(5), isthmus(6) and splenium(7).

8 Conclusion

A novel approach to morphometry was presented, in which the relationship among parts of anatomies were explored. The method is based on the factorial analytic model, in which the covariances between variables are represented by a new variable set of lower cardinality. Applied to high-dimensional vector representations of the anatomy, the method is able to provide concise description and allow exploratory analysis of the correlation between regions of interest. The application of this approach to the study of the human corpus callosum revealed strong agreement with previous published results and was able to segment regions of interest within the structure.

The current results are preliminary in nature and much work remains, including studies relating the effect of smoothness in the spatial and intensity transformation and their impact on the correlational structure modeled by the factors, a careful examination of the anatomy underlying the factors for a given study and the implications for the particular condition being investigated.

The application of FA to high-dimensional representations of the anatomy are particularly advantageous, since the method circumvents much of the controversy addressed to it, with respect to the number of factors considered and their interpretation [13]. The factors can be visually identified as regions that embed strong correlation. The final number of factors to be used in the model can be related to the desired degree of details in the analysis and, consequently, to its completeness: reducing the number of factors results on larger regions with coarser correlation, whereas a larger number of factors may represent smaller regions with stronger correlation. The ability of FA to provide prior

Table 1: Variance acounted for each component.

comp.	var.
z_0	15.30
z_1	12.10
z_2	9.74
z_3	6.07
z_4	5.07
z_5	3.67
z_6	3.31
z_7	2.58
z_8	2.39
z_9	2.15
z_{10}	1.91

Table 2: Statistical fit of the model. For each number of factors m, the table shows the average magnitude, mean and standard deviation of the correlation residual distribution.

m	av. magn.	mean	std. dev.
3	0.0814	0.0193	0.1130
4	0.0706	0.0107	0.0970
5	0.0619	0.0101	0.0831
6	0.0552	0.0082	0.0751
7	0.0500	0.0078	0.0677
8	0.0463	0.0055	0.0630
9	0.0425	0.0018	0.0588
10	0.0398	0.0005	0.0549
11	0.0376	0.0004	0.0517
13	0.0303	0.0003	0.0468
78	0.0000	0.0000	0.0022

modeling and the effectiveness of factors as discriminant variable sets are a vast field for future work.

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