Artificial Neural Network analysis of differences in fiber tracks between term and preterm children

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Introduction:

In most DTI investigations of cerebral white matter, scalar DTI parameter maps are analyzed between some patient and control groups using voxel based analysis techniques. This reveals information about local differences in the white matter between those groups. However, tractography is essential to investigate actual morphological differences and brain connectivity. For example, low FA may be caused by less densely packed axons or increased complexity as a result of crossing fibers. Besides, thinning of a white matter pathway can be identified more precisely using tractography. More importantly, tracts need to be constructed to understand actual brain connectivity. Voxel-based morphometry (VBM) analysis of FA images between groups will result in some clusters of voxels that are different between the groups. In some cases it is not possible to identify precisely which brain connectivity is affected by looking at the location of these clusters on FA or orientation color maps. For instance, when two different fiber tracts run in parallel in close proximity, one needs to construct the affected tract to understand where it connects. Analysis of differences in specific fiber tracts is more complicated than VBM analysis of FA maps. Once a specific fiber tract is constructed for all subjects, a set of parameters such as volume, density or mean tract FA can be generated and statistically analyzed between groups. This will be informative in cases where the whole tract morphology is affected. However, in some cases only a segment of the tract might be affected. Therefore, group differences in the distribution of DTI parameters along the tracts must be investigated. One approach is to normalize the lengths of the fiber tracts across subjects and run a T-test at each location on the tract across the subjects. This is not much different from VBM approaches. Here, we developed an Artificial Neural Network based analysis (ANN), to select a set of features that can achieve the highest differentiation power between the two groups. Once these sets of features are found, inferences about the morphological differences in fiber tracts can be made. Compared to traditional statistical analysis method (logistic regression modeling), ANN was found to have higher prediction rates in complex and non-linear relationships among a large number of variables.

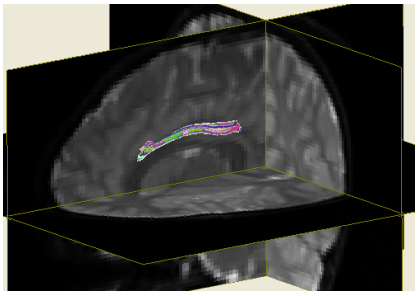

Fig.1. Segment of left cingulum used in ANN analysis and the plots in Fig. 2.

Methods:

As an example, we investigated the differences in left cingulum between a group of preadolescent children who were born prematurely and age-matched controls who were born at full-term. The data were acquired using a 3T Philips Achieva system. The study was approved by the IRB of the university and written consents were obtained from the parents. DTI images were acquired using SE-EPI with 32 gradient directions with b=800 and a single acquisition with b=0. 60 axial slices were collected to cover the whole brain with FOV=224*224mm^2 and 1.75*1.75*2mm^3 voxel size, NEX=1. TR=9290ms and TE=55ms were used with SENSE=2.4. Left cingulum between anterodorsal edge of the genu and posterior edge of the splenium was generated for each subject in their native space (Fig.1). 20 tracts were generated for analysis (10 term, 10 preterm). Since the length of this segment was slightly different for each subject, they were all normalized to 100 sample points linearly. Since the difference in the lengths were relatively small, nonlinear normalization was not deemed necessary. Moreover, a bias toward a group was not expected due to this normalization since the mean and standard deviation of the lengths of the tracts were similar (33±1.5 and 32.75±1.42 pixels for the preterms and terms, respectively). FA distribution along the length-normalized cingulum was averaged for each group and shown in Fig.2. First, the 100 FA values for each subject were down-sampled to 20 *features* by averaging every other five FA values and entered in the input layer for ANN. This was done because the number of features should be equal to or smaller than the number of subjects for more robust estimation. A three-layer back-propagation neural network, known as multi-layer perceptrons (MLP) ANN was utilized to obtain the *optimal classifiers* (*Liu H. and Motoda H., 1998, Kluwer Acad. Pub.*). The three-layer topology has an input layer, one hidden layer, and an output layer. The number of nodes in the input corresponds to the number of input variables. The output layer contains one node with values from 0 to 1 where 0 means control group (term) and 1 means preterm. The number of hidden nodes is usually determined by a number of trial-and-error runs. Each parameter set was first normalized to have zero mean and unit variance before training. Forward search strategy was applied to find the optimal feature subset, which was obtained when the trained classifier produced the least error rate. The specific structure of the neural network was determined by selecting the one leading to the best performance. To explore the best discrimination performance, the entire dataset was used in training using leave-one-out cross validation. The features that yielded maximum discrimination capability were selected using the ANN software.

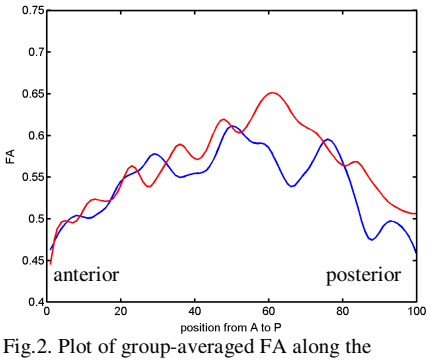

Fig.2. Plot of group-averaged FA along the cingulum segment shown in Fig.1. Red and blue lines are the plots for term and preterm children, respectively. The standard deviation was 0.045. The error bars were excluded for clarity.

Results and Discussion:

When the selected classifier contained both *features* 13 (average of FA between 61-65 in Fig.2) and 14 (average of FA between 66-70) were selected as classifiers, the area under the ROC curve was 92.2%. Since the *features* 13 and 14 are the averages of 5 FA values each, the ANN was applied the second time to the original 10 FA values. This second step gave us a more precise feature selection. When the four FA values between points 63-66 were selected as the classifiers, we obtained 86% sensitivity and 91% specificity. This region corresponds to the anterior part of the posterior cingulum, where the fibers are more tightly organized in the middle, more linear and compact sections of this tract, thus the FA reaches the peak values in the control group. However, it does not show the same peak in the preterm group, which can be interpreted as reduced axonal density. These results suggest that the FA values in a particular segment of cingulum clearly differentiate the two groups and ANN provides a robust and accurate method to identify them. Once the *optimal classifier* set is found for any tract analysis, inferences can be made about which part of the tract is different and the morphological changes that led to those differences in DTI parameters. It should be noted that multiple DTI parameters per tract (e.g. FA and λ1 together) could be entered as features and ANN can identify the combination of those parameters in specific anatomic locations that best differentiates the morphological differences of the tract between the groups.