Semi-quantitative Assessment of Inflammation in dMRI Using Data-Mining Techniques

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Introduction

Dynamic contrast-enhanced MRI (dMRI) is a method that enables quantitative measures of tissue vasculature such as perfusion and permeability to be obtained. Such an approach requires knowledge of other parameters such as an arterial input function and an adequate model to fit derived contrast agent concentration kinetics. An alternative approach is to identify contrast agent enhancement profiles typical of, for example, pathological tissue, and use these to identify similar tissue. Here, we introduce a method derived from data-mining and unsupervised-learning, developed to automate the identification of a specific dynamic contrast enhanced MRI profile within a group of subjects, hence obviating the need for laborious manual intervention, highly accurate regions or detailed prior knowledge.

Method

Inspection of a single example dataset is performed to locate a suitable ROI which contains a representative time response. Analysis of the ROI is performed with singular-valued decomposition (SVD). This has several advantages including that the desired target signal can be obtained even in the presence of severe noise, and that the ROI need not be a homogenous class. In addition, unlike the mean of an ROI, the SVD is robust to spatial variations in the location of the ROI borders. The largest SVD component is then used as the 'template' with which to search through all other subjects in order to locate those voxels with a similar time-response. The search is performed via a voxelwise normalized cross-correlation, and the resulting data is thresholded to obtain a map of voxels considered to be most similar to the template. The number of thresholded voxels can then be used as an indicator of disease extent.

Results

Control and meningitis-infected rats (n=41 data sets) displaying intracranial enhancement (image matrix size 128 x 128, 3 slices), were investigated using a dMRI protocol with 100 time points to assess the blood-brain-barrier (BBB) integrity via gadolinium (GdDTPA, 0.5 mmol/kg) enhancement kinetics. An approximate enhancement-ROI was obtained from one subject, the SVD calculated and the major component, demonstrating the target time-response, extracted (Figure 1). Cross-correlation was then performed on all data sets, and the results, with the threshold set at 0.5 normalized correlation, are shown in Figure 2 for high and medium disease-severity, and also for a control. The same images were rated for disease severity by a blinded clinician, assessing both the clinical images and motor performance of the subjects. Significant correlations were found for a number of clinical and para-clinical measurements and the voxel count. Bacterial counts in the CSF were shown to be correlated with the number of voxels, significant at the 0.05 level (2-tailed Spearman).

Conclusion

A method of performing a semi-automatic classification analysis upon a large data set is demonstrated. The technique has the advantage of robustly extracting a template from a potentially heterogeneous, very noisy and/or poorly defined ROI, and then automatically locating similar time-response signals in the other subjects. The results show this approach to be an effective method of automatically generating suitable quantitative indices, such as disease extent or progression. In this case, the extent of BBB breakdown, i.e. the number of extracted voxels, is shown to correlate highly with, for example, bacterial counts in the CSF suggesting that this approach may also provide insight into the evolution of disease processes and may be used to assess specific therapeutic strategies.

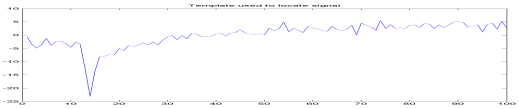

Figure 1. The template, or target, time response obtained via an SVD of an ROI drawn in approximately the correct area of a known responder. This is then used to locate voxels in the other subjects that have a similar time response.

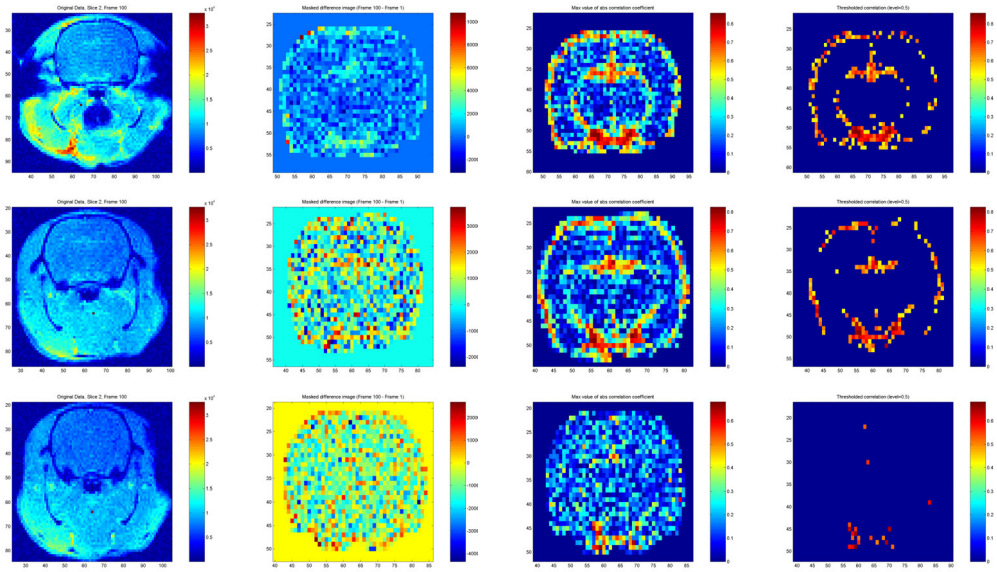

Figure 2. Four stages of the process (columns) performed upon 3 example datasets (rows). From left to right, the first column shows the last (100th) frame of an original transversal scan of the brain. From here, the data has been spatially masked via an automatic morphological routine tuned to extract only the brain tissue. For comparison with column 3, column 2 contains the difference between the first and last frames. Column 3 contains the maximum correlation coefficient obtained via cross-correlation with the template. Finally, the correlation coefficient is thresholded at 0.5 in order to obtain a quantitative measure of activated voxels. The top row is a subject with a high degree of infection, the middle row a medium degree, and the lower row is a control. Note how the difference images in column 2 offer no information about disease severity, yet the structural pattern and number of voxels shown in columns 3 and 4 show good correlation.