Classification of Traumatic Brain Injury Patients Using Multi-parametric Automatic Analysis of Quantitative MRI Scans

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Abstract

Traumatic brain injury (TBI) is ranked as the fourth highest cause of death in the developed world. The majority of patients sustain mild TBI, and a significant number suffer persistent neuropsychological problems. Conventional neuroimaging methods (CT, MRI) do not reveal abnormalities consistent with the cognitive symptoms. Imaging methods offering prognostic information in acutely injured patients are therefore required. Here we applied advanced quantitative MRI techniques (T_1, T_2 mapping and diffusion tensor MRI) in 24 mild TBI patients and 20 matched controls. We applied a support vector machine (SVM) to classify the quantitative MRI data. Univariate classification was ineffective due to overlap between patient and control values, however multi-parametric classification achieved sensitivity of 88% and specificity of 75%. Future work incorporating neuropsychological outcome into SVM training is expected to improve performance. These results indicate that SVM analysis of multi-parametric MRI is a promising approach for predicting prognosis following mild TBI.

1 Introduction

Traumatic brain Injury (TBI) is a major cause of death and disability in adults. Each year in the UK more than 112,000 people are admitted from accident and emergency departments with a primary diagnosis of TBI [1]. TBI is ranked as the fourth highest cause of death in

the developed world, and the number of people sustaining head injuries increases yearly [2]. Computed tomography (CT) is used for initial assessment of TBI patients but CT and conventional MR imaging in mild TBI patients often does not correlate with the severity and longevity of the clinical neurological picture [3]. It has been reported in small cohort studies of TBI that advanced MRI techniques such as diffusion tensor imaging (DTI) and image relaxometry do detect subtle quantitative changes in brain tissue properties [4], but individual measurements do not have prognostic value in individual patients. In view of these previous findings we anticipate that combination of a range of quantitative MRI parameters will be more sensitive in detection of subtle neuronal damage than when using individual parameters. Hence we hypothesised that multi-parametric analysis would offer a better classification of TBI patients than univariate analysis. In order to test our hypothesis we applied a machine learning classification method called Support Vector Machines (SVMs).

SVM works by learning the features which differentiate the groups of a dataset. Once the learning is achieved, the knowledge acquired during the learning can be used to classify any new data. SVM application to biological problems is increasing due to its high accuracy, ability to deal with multi-dimensional and large datasets and the high flexibility in modelling of data from various sources [5].

2 Materials and Methods

2.1 Subjects

A total of 44 subjects were recruited for this study. This comprised 24 mild TBI patients (GCS, 14-15, mean age $38 \pm 15yrs$) and 20 healthy adults (mean age $41 \pm 16yrs$) with no clinical evidence of neurological diseases or prior history of TBI. Scanning for the patient group was performed within 10 days of injury (mean 4.9, range 1-10 days).

2.2 MR Protocol

All images were acquired on a 3.0T whole body Philips Achieva MR System (Philips Medical Systems, Best, NL) using an 8-channel SENSE head coil. The protocol was approved by the local ethical committee and all subjects provided written consent prior to imaging. The following scans were acquired in each subject.

T_1W Imaging: High resolution 3D T_1 weighted anatomical scan (MPRAGE, TR/TE =8.1 / 4.6ms, matrix 150x240 with 240 contiguous slices, 1mm slice thickness, in-plane resolution of 1mm).

T_1 Mapping: A fast quantitative T_1 measurement using a custom inversion recovery prepared EPI sequence (TR /TE=15s /24ms, TIR=0.25 to 2.5s in uniform 12 steps, matrix 128x128, 72 axial slices, isotropic 2mm resolution).

T_2 Mapping: Quantitative T_2 measurement using MSE sequence (TR=4.7s, 8 spin echoes at 20ms spacing, EPI factor 5, matrix 128x128, 72 slices, isotropic 2mm resolution)

Diffusion Tensor Imaging: DTI using SE EPI sequence (SENSE factor 2, TE /TR=71/2524ms, matrix 128x128, 24 slices, 6 mm thickness and 2mm in-plane resolution, 16 diffusions directions, b values 0 and 1000 smm^{-2}).

B_0 Field-map: B_0 Field-map (dual echo 3D GRE sequence TR=27ms, TE=2.6 /6.1ms, matrix 128x128x72, 2mm resolution) which was used to correct the spatial distortion in EPI
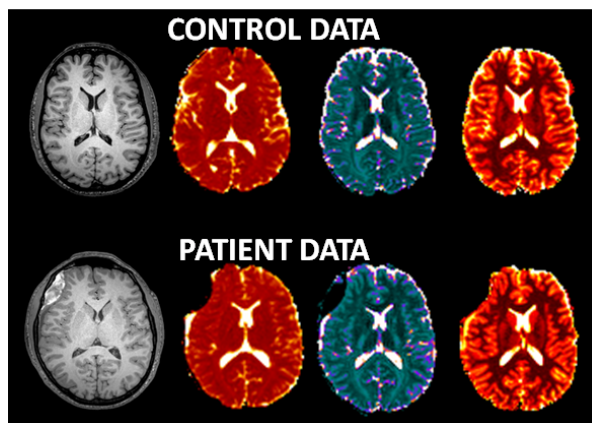
Figure 1: Typical images from quantitative data representing the control and patient population, Columns 1, 2, 3 and 4 are the T_1W, MD, qT_2 and qT_1 images respectively
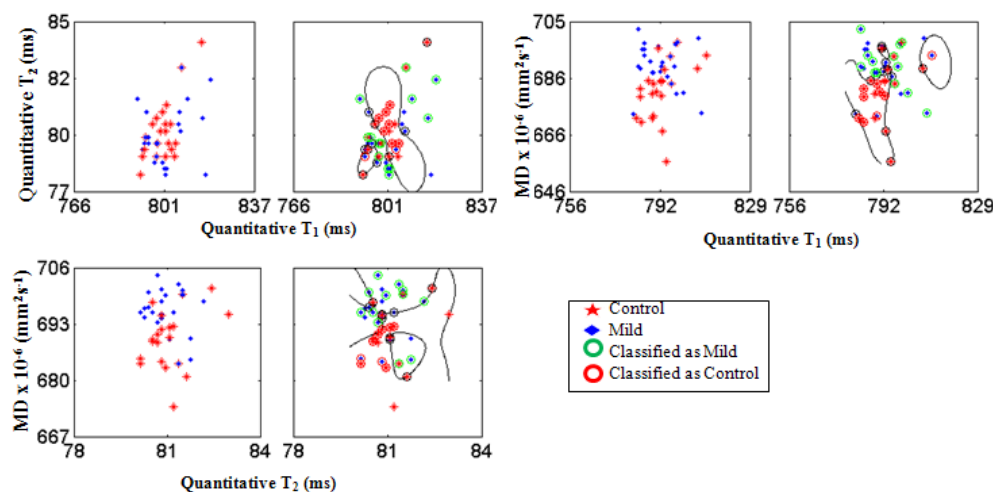
based images.

Figure 2: The scatter plot and SVM results in the Frontal Superior region of white matter. First row represents T_1 against T_2 and T_1 against MD. Second row represents T_2 against MD

2.3 Image Analysis

We applied an automatic image analysis method [6] whereby the whole brain is automatically divided into 16 regions of interest (ROI) for each tissue type. These regions are pairs of right and left inferior frontal lobe, superior frontal lobe, temporal lobe, temporal-occipital lobe, occipital lobe, temporal-parietal lobe, parietal lobe and the cerebellum. In brief, the method uses a standard space brain ROI parcellating the entire brain into 16 chuncks, which is transformed into subject space based on a multi-step registration using the subject's high resolution T_1 weighted anatomical scan. Next, the same anatomical scan is segmented into white matter, grey matter and CSF masks [7] and combined with the brain region template to generate tissue specific anatomical ROIs which are applied to the quantitative images under analysis. Multi-spectral analysis using k-means clustering is applied to the regional quantitative data for removal of partial volume errors in order to improve ROI definitions.

The algorithm was implemented in MATLAB R2009b (The Mathworks Inc., Natick, MA, USA) running on a Linux platform using in-house developed routines but incorporated existing processing methods from the FSL [8] package when appropriate. All segmentation steps were performed using FSL Segmentation Tool (FAST, [7]). Patients with visible lesions were excluded from the analysis.

Quantitative T_1 maps (qT_1) were calculated on a pixel by pixel basis by fitting the acquired data to T_1 inversion recovery curve using the standard 3 parameter fit (Mo, flip angle and T_1) while quantitative T_2 maps (qT_2) were calculated using a 2 parameter (Mo and T_2) monoexponential fit to the acquired data.

DTI data were preprocessed with FDT (FMRIB's Diffusion Toolbox) [9]. Head movement and eddy currents were corrected using 3D rigid body registration to a reference volume. Raw DTI data were brain-extracted using FSL BET tool, and mean diffusivity (MD) images were created by fitting a tensor model to the raw diffusion data using FDT.

The algorithm was then used to automatically determine regional grey and white matter qT_1, qT_2, and MD in each of the 16 target ROIs. Finally, the regional mean values for both grey and white matter were computed in each ROI and used for SVM classification.

2.4   Support Vector Classification of TBI Data

SVM was used to classify the regional mean values computed from qT_1, qT_2 and MD. Each subject's data was divided into the 2 tissue classes with each comprising of 16 x 3 matrices, representing the 16 ROIs and each of the 3 quantitative MRI parameters. These matrices were used as input vectors for SVM. Each of the two groups (mild TBI and control) was divided into 2 mutually exclusive subsets, the training set and the validation set. Selection was done using the holdout cross validation method; this method randomly divides a given dataset into 2 equal groups. Training and classification were evaluated on a regional basis for both white matter (WM) and grey matter (GM) using combinations of qT_1 and qT_2, qT_1 and MD, qT_2 and MD and qT_1, qT_2 and MD. We compared a number of kernel functions using sensitivity and specificity analysis, only the radial basis function gave a desirable result. In view of this finding (no data presented) our implementation used radial basis function.

3   Results and Discussions

Figure (1) shows selections from typical control and patient datasets. Figure (2) shows a representative scatter plot and SVM results. The scatter plots show that there is significant overlap between the 2 groups along each axis but that combination of axes reveals some intra-group relationships. The SVM results on the right hand side of each plots show the separation between groups. We used sensitivity (True positive) and specificity (True negative) to measure the performance of SVM. The average sensitivity (and specificity) for white matter averaged across all the 16 ROIs were 82% (70%) (qT_1 vs qT_2 and qT_1 vs MD), 81% (73%) (qT_2 vs MD) and 83% (68%) (qT_1 vs qT_2 vs MD) while the average sensitivity (and specificity) for grey matter averaged across all the 16 ROIs were 80% (75%) (qT_1 vs qT_2) 87% (79%)(qT_1 vs MD), 88% (75%) (qT_2 vs MD) and 85% (81%) (qT_1 vs qT_2 vs MD). These show that multi parametric analysis using SVM offers a promising tool in to categorising mild TBI.

Epidemiologically, only approximately half of mild TBI patients manifest ongoing neuropsychological problems related to their injury. In view of this approximately 50% of TBI

population are expected to be indistinguishable from normal controls and this could cause misclassification. We believe that this may be a significant contributing factor to the low specificity of our analysis. Our future work will include follow up studies in order to identify the mild TBI patients who have fully recovered without any neuropsychological symptoms which will help us to redefine the groups which could lead to improved specificity.

4   Conclusions

We have shown that a multi-parametric analysis of quantitative MRI data can be used to separate mild TBI patients from the control group. Our results show that SVM can detect changes in normal appearing tissues in some patients suffering mild TBI as compared with the control group. These changes may represent damage to neuronal tissue and further work is needed to determine whether this is responsible for the cognitive and affective symptoms commonly seen following mild head injury, which include memory loss, inability to concentrate, irritability and depression

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