Detection of Tissue Changes in Traumatic Brain Injury Patients Using Automatic Regional Analysis of Quantitative MR Scans

B. S. Aribisala[1], C. J. Cowie[1,2], J. He[1], J. Wood[1], D. A. Mendelow[2], P. Mitchell[2], and A. M. Blamire[1]

[1]Institute of Cellular Medicine, Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle upon Tyne, England, United Kingdom, [2]Department of Neurosurgery, Newcastle General Hospital, Newcastle University, Newcastle upon Tyne, England, United Kingdom

Introduction

Traumatic brain injury (TBI) is a major cause of death and disability with more than 112,000 people per year in the UK admitted with a primary diagnosis of head injury. Around 90% of these admissions are classed as mild (Glasgow Coma Scale 14 – 15) [1], but a significant proportion of these patients have ongoing symptoms which do not correlate with conventional MRI or CT findings. Here we investigated a cohort of patients with mild TBI using multi-parametric, quantitative MRI to assess whether it is a more sensitive technique for detecting parenchymal damage.

Methods

Patients: Twenty subjects with history of mild TBI (GCS, 14-15, mean age 38±15 yrs) were scanned within 10 days of injury (mean 4.9, range 1 -10 days) and compared against 20 healthy adults (41±16 yrs) with no clinical evidence of neurological diseases.

MR Protocol: Subjects were imaged using a 3.0T whole body system (Philips Achieva) equipped with an 8-channel head coil. Scan data included (a) *T_1 weighted anatomical scan* (SENSE factor 2, TE/TR=4.6/8.3ms, matrix 256x256x180, 1x1x1 mm^3), (b) *quantitative T_1 measurement* using a custom IR-EPI sequence (SENSE factor 2, TE/TR=24/15000 ms, TI=0.25-2.5s in 12 steps, matrix 128x128x72, 2x2x2 mm^3), (c) *quantitative T_2 measurement* using a MSE sequence (TE/TR=20ms/4.7s, 8 echoes, echo spacing 20 ms, matrix 128x128x72, 2x2x2 mm^3), (d) *DTI* (SE EPI sequence, SENSE factor 2, TE/TR=71/2524ms, matrix 128x128x24, 2x2x6 mm^3, 16 directions, b value 1000 smm^{-2}) and (e) *3D dual echo field map* (SENSE factor 1.5, TE_1/TE_2/TR=2.5/5.8/27ms, matrix 128x128x72, 2x2x2 mm^3) which was applied to all EPI data to correct for spatial distortion.

Image Analysis Algorithm: We applied our previously proposed method whereby the whole brain is automatically divided into 16 regions of interest (ROI) for each tissue type [2]. This analysis method operates in patient space and was demonstrated to significantly reduce partial volume errors compared to the same analysis performed in standard space [3]. In brief, the method uses a standard space brain ROI template which is transformed into patient space based on a multi-step registration using the patient's high resolution T_1 weighted anatomical scan. Next, the same anatomical scan is segmented into white matter, grey matter and CSF masks [4] 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 is applied to the quantitative data to improve classification [5].

Scan Analysis: Quantitative T_1 and T_2 times and mean diffusivity (MD) values were calculated on a pixel by pixel basis and subsequently analysed to determine the grey and white matter T_1, T_2 and MD histograms for each of the ROIs. Patients whose lesions were still visible after brain extraction and segmentation were excluded from the analysis. Group comparisons were made by t-test although heterogeneity of patient injury is expected to influence the power of such group statistics. We therefore determined the Z-score for each individual ROI in each patient against the mean and the standard deviation of the control group. In each patient the number of ROI with $Z > 1.65$ ($p<0.05$) were counted and the patient was considered abnormal if at least 3 out of 7 regions had significant Z scores ($p<0.05$ correct for multiple comparisons).

	Controls Group- (T_1 and T_2 in ms, MDx10^{-6} mm^2s^{-1})						**Patients Group** - (T_1 and T_2 in ms, MDx10^{-6}					
ROI	T_1WM	T_2WM	MDWM	T_1GM	T_2GM	MDGM	T_1WM	T_2WM	MDWM	T_1GM	T_2GM	MDGM
Right Fron. Sup.	813 ±34	84 ±5	680 ±31	1164 ±51	90 ±5	822 ±39	819 ±46	83 ±4	**708 ±24***	1181 ±109	91 ±5	814 ±57
Left Fron. Sup.	811 ±33	84 ±5	673 ±29	1158 ±46	90 ±5	824 ±48	817 ±45	83 ±4	**701 ±21***	1181 ±84	91 ±4	824 ±72
Right Temp.	805 ±29	78 ±2	830 ±26	1216 ±36	90 ±3	770 ±125	818 ±36	78 ±2	842 ±41	**1279 ±116***	**94 ±6***	808 ±54
Right Occi.	804 ±40	82 ±2	775 ±21	1038 ±62	81 ±3	846 ±38	811 ±36	82 ±4	779 ±36	**1140 ±163***	**86 ±6***	836 ±38
Right Temp. Par.	794 ±30	81 ±2	781 ±25	1251 ±22	90 ±3	926 ±47	798 ±38	80 ±2	793 ±26	**1275 ±58***	91 ±4	918 ±62
Left Temp. Par.	806 ±46	80 ±2	764 ±24	1250 ±23	91 ±3	919 ±37	806 ±44	80 ±3	**781 ±23***	1271 ±35	91 ±2	927 ±58
Left Parietal	819 ±34	84 ±2	749 ±37	1182 ±40	86 ±4	873 ±43	818 ±45	**82 ±2***	763 ±25	1207 ±58	87 ±5	875 ±56

Results and discussions

Significant group differences ($p<0.05$) were found in White matter T_2 (left parietal), White matter MD (left frontal superior, left temporal parietal and right frontal superior), Grey matter T_1 (right temporal, right occipital and left temporal parietal) and Grey matter T_2 (right temporal and right occipital). Values for T_1WM, T_1GM, T_2GM and MDWM were elevated in **almost all ROI** in the patients compared to controls (table). Z-score analysis of individual ROI data showed areas of significant difference in most patients.

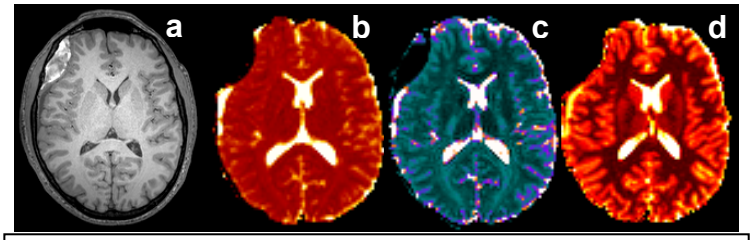

Fig. : (a) Anatomical T_1W image, (b) MD, (c) and (d) quantitative T_2 and T_1 images

However, 12 patients had significant Z-scores for at least 3 regions in T_1GM with 4 patients having significant Z-scores in 6 of 7 regions.

Conclusions

We have shown that a fully automatic real space method of analysing quantitative MR parameters can be used to detect changes in normal appearing tissues in patients suffering mild TBI. 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 (data collected but not presented).

References: [1] NICE, Clinical Guideline 56. Head Injury: Full Guideline. 2007, NIH and CE, [2] Aribisala et. al., ISMRM 2008,3043, [3] Aribisala et. al., ISMRM 2009,4771 , [4] Zhang et. al.; *IEEE Trans. on Medical Imaging*, 20(1):45-57, 2001, [5] Aribisala et. al., ISMRM 2009, 4872.

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