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## Asian Pacific Journal of Tropical Medicine

journal homepage: [www.elsevier.com/locate/apjtm](http://www.elsevier.com/locate/apjtm)

Document heading doi:

## MRS and diffusion tensor image in mild traumatic brain injuries

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## ARTICLE INFO

## Article history:

Received 20 November 2011

Received in revised form 15 December 2011

Accepted 5 January 2012

Available online 20 January 2012

## Keywords:

Mild trauma brain injuries

Magnetic resonance spectroscopy

Diffusion tensor image

Fractional anisotropic mapping

## ABSTRACT

**Objective:** To analyze characters of magnetic resonance spectroscopy (MRS) and diffusion tensor imaging (DTI) in the diagnosis of mild traumatic brain injuries (MTBI) in frontal lobe and to compare with conventional magnetic resonance imaging (MRI). **Methods:** A total of 21 patients were selected, who all aged 12–51 years old and had head injury within 72 hours. Computer tomography (CT) and the Glasgow Coma Scale were used to evaluate the degree of injury. All patients were diagnosed as MTBI, and 19 patients underwent conventional MRI, MRS and DTI. The major parameters of MRS were Probe-P sequence  $T_1 = 14$  or 35 ms, and  $T_2$  of single voxel spectrum and chemical shift imaging were included. The major parameters of DTI were diffusion directions =15, b value = 1 000 s/mm<sup>2</sup>. Fractional anisotropic (FA) map and average ADC map were obtained to evaluate DTI result. Positive detection ratio was observed and the imaging changes were compared between injured side and normal side. **Results:** All 21 patients had CT scan and Glasgow scale. A total of 19 patients had conventional MRI, DTI and MRS. Results of CT and conventional MRI showed no significant abnormality in frontal lobe, and Glasgow scale showed mild type. MRS result showed significant decrease in N-acetylaspartate (NAA) and NAA/creatine (Cr) in 13 cases (68.4%) ( $P < 0.001$ ), and increase of lactic acid (Lac) in 7 cases (36.8%). FA mapping of the frontal lobe disclosed significant changes in 7 cases (36.8%), with 5 out of the 7 cases having increase in FA value. And there was no significant difference in average ADC. **Conclusions:** MRS and DTI might be more feasible than other methods, such as CT and conventional MRI in diagnosis of MTBI. The results of MRS were reduced NAA and increased Lac for MRS, and increased FA values for DTI.

## 1. Introduction

Mild traumatic brain injuries (MTBI) is main cause for cognitive deficit. It is characterized as traumatic axonal injury, which causes confusion, disability etc. It is still difficult to find out a non-invasive and special method for diagnosis of MTBI.

Computer tomography (CT), magnetic resonance imaging (MRI) including T2 weighted image (T2WI), T2 star weighted image (T2\*WI) and diffusion weighted image (DWI) have been used to evaluate hemorrhage, edema, and ischemia[2]. As a primary imaging technique, CT is sensitive in detection of intracranial hemorrhage, and is the main method for evaluation of head injury. It can provide important evidence for treatment of emergency neurosurgery diseases[2]. With the rapid development of new techniques and improvement of image quality, MRI has become one of the most important

method for diagnosis of MTBI. Magnetic resonance spectroscopy (MRS) can provide information about local neurons metabolism, and is helpful in prognosis of clinical outcome and selection of treatment strategy[2] This study aims to analyze characters of diffusion tensor imaging (DTI) and MRS, and to compare with conventional MRI (T1, T2, FLAIR).

## 2. Materials and methods

## 2.1. Subjects

A total of 21 cases with head injury admitted from February 1st to August 30th, 2011 were selected. All recruited subjects signed informed consent agreements. All patients had consciousness loss within 30 min, coma within 24 h, slight headache, no obvious abnormality in physical examination of neurological system, and had language reaction. All patients had Glasgow scale and CT. The standard of scale was as following (Table 1), and the result indicated mild type.

Two cases were excluded from further examination,

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Foundation project: This work was supported by the Science Foundation of Haikou Health Bureau (2010-SWY-13-058) and Haikou Science Technology Information Bureau (2009-049-1).

because one patient had metallic artifacts and the another refused.

### 2.2. Checking methods

MRI was performed by a 3.0 Tesla Signa HDx medical MRI scanner (General Electric Co., USA) with twinspeed gradients (maximum gradient strengths of up to  $G_{max} = 50$  mT/m; slew rates 150 mT/m/ms, General Electric Co.). The standard 8 channel high resolution brain coil (HRBRAIN, General Electric Co.) was used as the receiver coils. Main parameters were listed in Table 2.

MRS was performed by PROSE-PRESS method. Multiple voxel spectroscopy (SVS) and chemical shift imaging (CSI) were used. Both were localized at the thalamus level, with the largest slice position at lobus frontalis. Main parameters of SVS were  $TE=35$ ,  $20\text{ mm}^2 \times 20\text{ mm}^2 \times 20\text{ mm}^2$ , and  $NEX=8$ . Main parameters of CSI were  $TE=144$ ,  $10\text{ mm}^2 \times 10\text{ mm}^2 \times 10\text{ mm}^2$ , and  $NEX=8$ .

DTI was conducted by standard DW-SE-EPI sequences ( $TE=85$ ,  $b=1\ 000$ , diffusion gradient direction=6,  $NEX=16$ ,  $128 \times 128$ , and slice=19).

T1/T2/FLAIR/GRE was conducted by standard fast spin echo sequences ( $TE=10/105/125/25$ ,  $IR=2\ 500$ ,  $NEX=2$ ,  $256 \times 256$ , and  $SL=19$ ).

The image results of DTI (FA mapping and ADC mapping) and MRS (SVS and CSI) were analyzed by Spectroscopy Evaluation Software (Advance Workstation version 4.4, General Electric Co.).

Region of interest (ROI) was selected manually under double-blind conditions. References were based on original images of T2WI and T1WI with symmetry position, avoiding large vessels, cerebral spinal fluid, bleeding sites and blood skull at the thalamus level of lobus frontalis. CSI mapping was no less than  $10 \times 10$ , while the voxel size and its mapping were  $12 \pm 3$ .

### 2.3. Statistical analysis

The data were analyzed by t-test method using SPSS16.0 software (SPSS, Chicago, Ill).  $P < 0.05$  was considered as significance.

**Table 1**

Standard of Glasgow Coma Scale.

Points	Eye response	Verbal response	Motor response
1	Not open eyes	No sounds	No movements
2	Open in response to the painful stimuli	Incomprehensible sounds	Extension to painful stimuli
3	Open eyes in response to the voice	Utter inappropriate words	Flexion/Withdrawal to painful stimuli
4	Open eyes spontaneously	Confused	Localize painful stimuli
5	N/A	Oriented, converses normally	Localize painful stimuli
6	N/A	N/A	Obeys commands

**Table 2**

Main parameters of conventional MRI, DTI and MRS.

Sequence	TE(ms)	NEX	Matrix	FOV (mm)	Thickness (mm)	Acquisition time(sec)
T1 FSE	14.7	2	256×256	220×220	5	150
T2 FSE	120	2	256×256	220×220	5	100
T2 FLAIR	125	2	256×256	220×220	5	165
T2* GRE	25	2	256×256	220×220	5	145
DTI(DW-SE-EPI)	Min	2	128×128	220×220	5	109
MRS(PROSE-PRESS)	SVS 35	8	1×1	20×20	20	215
	CSI 144	8	18×18	180×180	10	445

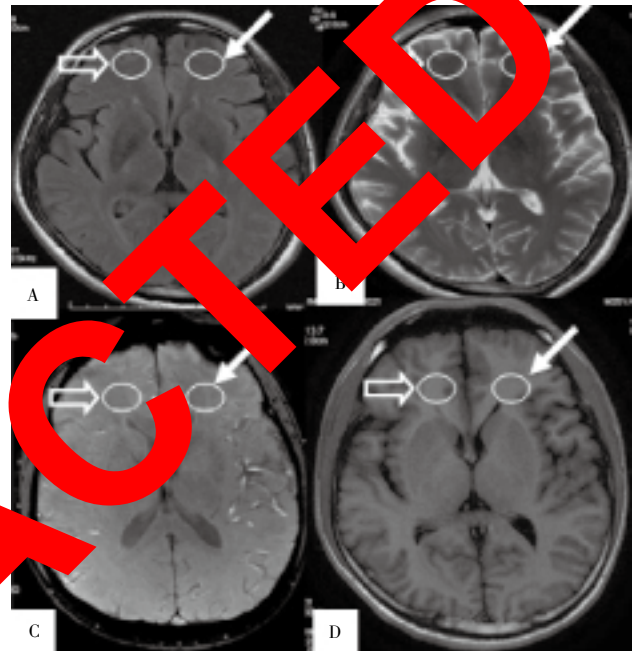
DTI diffusion directions= 6; b value=1 000 sec/mm<sup>2</sup>.

## 3. Results

CT scanning showed no significant abnormalities, without fracture or hemorrhage. Glasgow score was higher than 13.

Results of conventional MRI (including T1, T2, FLAIR, T2\* GRE) showed subcutaneous soft tissue swelling (89.5%), skull fracture (10.5%) and extracranial hemorrhage (15.8%), and no intracerebral hemorrhage (Figure 1 A–D, Table 3).

Results of DTI showed 7 cases had change in fractional anisotropic (FA) (Table 3). FA value of injured side ( $0.48 \pm 0.15$ ) was significantly higher than that of control side ( $0.32 \pm 0.13$ ) ( $P < 0.05$ ). There was no significant difference in ADC value ( $0.78 \pm 0.09$  vs.  $0.72 \pm 0.12$ ,  $P = 0.12$ ) (Figure 2A,B).



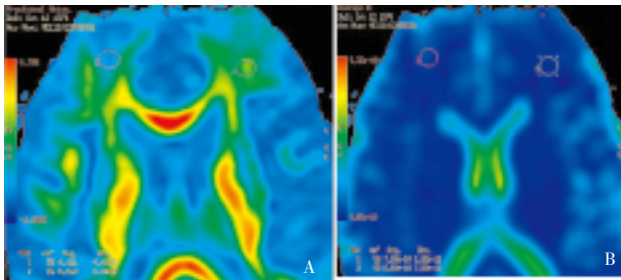
**Figure 1.** Result of conventional MRI.

A, B, C, D were high resolution FLAIR, T2WI, T1WI and T2\* GRE, at lobus frontalis level. ↑ : injured side, ↑ : control side.

**Table 3**Results of conventional MRI, MRS and DTI ( $n=19$ ).

Methods	Positive characters	Control side( $n$ )	Traumatic side( $n$ )	Ratio of positive characters (%)
Conventional MRI	Skull fracture	0	2	10.5
	Extracranial hemorrhage	1	3	15.8
	Intracerebral hemorrhage	0	0	0.0
	Subcutaneous soft tissue swelling	2	17	89.5
MRS	NAA/Cr decrease	0	13	68.4
	Cho/Cr increase	1	3	15.8
	Lac/Cr increase	0	7	36.8
DTI	FA value increase	0	5	
	FA value decrease	0	2	10.5
	ADC value decrease	0	4	21.1

NAA: N-acetylaspartate, Cho: choline, Cr: creatine, Lac: lactic acid.

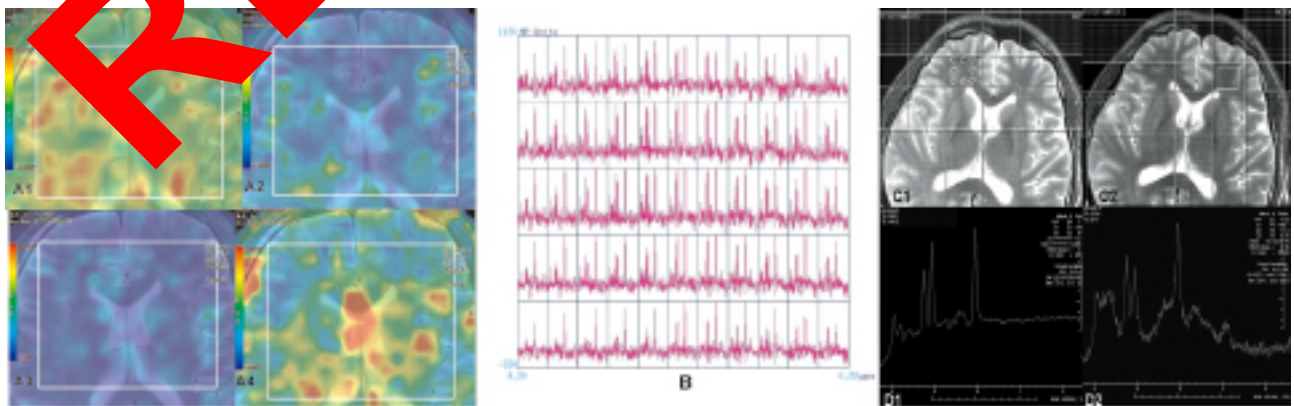
**Figure 2.** Result of DTI.

A and B were separately high resolution FA mapping and ADC mapping, at the lobus frontalis level.

Results of MRS showed reduced N-acetylaspartate/creatine (NAA/Cr) at injured side in 13 cases, increased choline/creatine (Cho/Cr) in 3 cases, increased lactic acid/creatine (Lac/Cr) in 7 cases (Figure 3 & Table 3). FA of white matter in lobus frontalis was significantly decreased ( $P<0.05$ ). Cho/Cr was significantly increased ( $P<0.05$ ). No findings of significant change ( $P=0.02$ )(Table 4).

**Table 4**Results of MRS ( $n=19$ ).

	NAA/Cr	NAA/Cho	Cho/Cr	Lac/Cr
Control side	1.40±0.05	1.09±0.26	1.32±0.19	0.09±0.05
Injured side	1.07±0.05*	1.33±0.28*	1.33±0.24	0.31±0.25*

\*:  $P<0.05$  vs. control.**Figure 3.** Results of MRS.

A1-4: chemical shift image of NAA/Cr, NAA/Cho, Cho/Cr and Lac/Cr; B: the spectroscopy matrix at same position of A; C1, C2 showed the axial positional mapping of single volume spectroscopy; D1, D2: spectroscopy of white matter at deep lobus frontalis.

#### 4. Discussion

MTBI is one of the main causes for post-traumatic complications of head injury, including brain function failure, personality and mental illness[1,2]. Generally MTBI can't be detected by conventional imaging methods[3], positive detection rates of conventional MRI and CT are low. In emergency situations, CT is used as a primary detection method. However, it is limited in range and degree during evaluation of focal axonal injuries, and repeated CT scans might lead to radioactive injuries. It is needful to develop non-radioactive and highly sensitive tools. Until now, MRI is the most suitable candidate imaging method for diagnosis of acute mild brain trauma, because it has high spatial resolution, high contrast to noise ratio, signal-to-noise ratio, and multiple contrast imaging capacity[2].

With the rapid progress of medical imaging technology especially MRS and DTI, chemical components and composition structure of white matter can be furtherly analyzed, and it is possible to make accurate diagnosis, select suitable treatment and make monitoring[4,5]. In this study, in addition to CT and conventional MRI, DTI and MRS were also used to evaluate the sensitivity and characters of main metabolic peak of MRS and FA values of DTI.

The primary results implied that there was no significant

difference between CT and conventional MRI, and there was no positive result of T2\*GRE. It suggests more sensitive method is needed, Susceptibility weighted imaging can improve the sensitivity of MRI in detection of micro hemorrhagic focus, and has advantage in detection of diffusive axonal injury[6]. It is useful in diagnosis of micro hemorrhage in MTBI. However, this technique is not included in our study due to technical limitations.

It is reported that DWI is more advantageous in detection of range and degree than T2WI and FLAIR. ADC value of white matter is significantly decreased in patients with serious brain trauma. DTI, which was developed from DWI, can measure diffusion abilities in specific direction quantitatively, including rate of isotropy and anisotropy. FA value is a widely used indicator of anisotropic diffusion, with values varying between 0 and 1. The FA value of 0 indicates absolutely isotropic diffusion, like in cerebral spinal fluid, and an FA value of 1 indicates maximum anisotropic diffusion, such as white matter fasciculus. Patients with serious axonal injury have decreased FA due to injury and fracture of nerve fiber. It has been proven that DTI is more sensitive than conventional MRI in evaluation of white matter fasciculus injuries, and it is correlated with Glasgow scores positively[7]. In our study, DTI result showed the 36.8% patients had abnormal FA value, while no change occurred in conventional MRI and CT result. Interestingly, this study indicated that FA value increased rather than decreased. This finding is in agreement with Wildes *et al.* They found increased FA, and it may be due to transitory cytotoxic brain edema[8].

<sup>1</sup>H-magnetic resonance spectroscopy (<sup>1</sup>H-MRS) is a non-invasive, and focuses on quantitative analysis of main neurometabolites, including NAA, Cr and Cho. NAA is regarded as a main marker of neuronal cell membrane integrity; Cr is a marker of energy metabolism; and Cho is a marker of cell membrane permeability. Cho will increase while NAA will decrease due to loss of local neurons. In addition, <sup>1</sup>H-MRS can measure the level of Lac, which is a marker of anaerobic metabolism and more increased due to ischemia or inflammation. A lot of researches indicate that neurometabolic disturbance is predictive of long-term cognitive deficit and behavioral defect of MTBI[9,10]. Gasparovic *et al.* found that Cho of gray matter in frontal lobe was correlated with social competence and behavioral problems[11].

In our study, NAA significantly decreased in 68.4% cases within 24 hours post MTBI, and Lac increased in 36.8% cases. Cho was seldom altered, only in 21.1% cases. It is deduced that the main pathological changes are loss of neurons or local anaerobic metabolism indicating cell anoxia. Cell membranes were integrated at the early stage of MTBI. But these resumptons still need further investigation.

In conclusion, MRS is the most sensitive method to evaluate MTBI patients, with the reduced NAA peak and increased Lac at local lobus frontalis. DTI is also sensitive to MTBI and more useful than conventional MRI or CT. FA mapping can partially find nerve fiber injuries, and the characteristic change of FA is increase, not decrease during the first 24 hours of MTBI.

## Conflict of interest statement

We declare that we have no conflict of interest.

## Acknowledgements

This work was supported by the Science Foundation of Haikou Health Bureau (2010–SWY–13–058) and Haikou Science Technology Information Bureau (2009–049–1).

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