

Magnetic Resonance Spectroscopic Imaging is Sensitive to Severity in Traumatic Brain Injury

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Introduction

Traumatic brain injury (TBI) results in long term, often severe, deficits in cognitive functioning and yet magnetic resonance imaging often reveals a largely-normal radiological picture inconsistent with individual behavioral impairment. Several proton magnetic resonance spectroscopy (¹H-MRS) studies have shown altered neurometabolite concentrations including N-acetylaspartate (NAA), choline (Cho), and myo-inositol (mIns) providing an opportunity to investigate various molecular and cellular mechanisms non-invasively following human traumatic brain injury (TBI). Most of these studies have employed single voxel MRS to examine a relatively small sample of brain tissue [1,2]. Others have used multi-voxel spectroscopic imaging to acquire data but have only reported results from a number of discretely selected voxels [3]. One study found minimal widespread metabolite changes in whole brain metabolites from mildly injured patients [4]. The overall aims of the current study were to determine whether neurochemical markers of brain injury averaged across a large sample of brain 1) were sensitive to overall injury and 2) could discriminate levels of severity of brain injury.

Methods

We used magnetic resonance spectroscopic imaging (STEAM, TE=20ms, TR=1500ms, 15mm slice, 16*16 phase partitions) to examine a rectangular slab of tissue encompassing frontal, parietal, and occipital lobes superior to the lateral ventricles in 27 patients following TBI (mean time from injury=25.5±19.4 days). The mean Glasgow Coma Score (GCS; maximum recorded first 24 hours post injury) was 7.7 (range 3-14). Patients with GCS<11 were classified as severe (mean=4.5; time from injury 35.5±29.7 days; n=13) and those with GCS>10 as mild/moderate (mean=14.5; time from injury 17.2±27.4 days; n=14). We compared patients with 26 age-, sex-, and education-matched, uninjured controls.

MRSI data were zero-filled in both spatial directions and analyzed using LCModel. For each voxel that was determined to be greater than 50% tissue from corresponding T1-weighted imaging, NAA/Cre, Cho/Cre, mIns/Cre, and Gln/Cre ratios were calculated. Voxels with >50% white matter were classified as white matter (~109 per subject) and those <50% as gray matter (~110 per subject). Average metabolite ratios for whole slice, WM, and GM were calculated.

Results

Averaged across the whole slab, NAA/Cre was lower and Cho/Cre and mIns were higher in TBI patients than uninjured controls as shown in Table 1 below. Similar observations were also noted for white and gray matter voxels.

Table 1	Whole brain		White matter		Gray matter	
	Uninjured (n=26)	TBI (n=27)	Uninjured (n=26)	TBI (n=27)	Uninjured (n=26)	TBI (n=27)
NAA/Cre	1.16±0.07	1.06±0.09 ⁺	1.11±0.09	1.04±0.08 ⁺⁺	1.12±0.08	1.08±0.09
Cho/Cre	0.23±0.02	0.26±0.05 ⁺	0.25±0.02	0.28±0.05 ⁺	0.21±0.02	0.24±0.04 ⁺⁺
mIns/Cre	0.53±0.07	0.59±0.09 ⁺⁺	0.53±0.07	0.61±0.10 ⁺⁺	0.52±0.06	0.57±0.07 ⁺
Gln/Cre	0.66±0.08	0.71±0.12 ⁺	0.57±0.07	0.62±0.11 ⁺	0.73±0.10	0.78±0.14

+ indicates P<0.05, ++ indicates p<0.01 (TBI vs. uninjured control)

When patient data were separated by severity of injury, it was revealed that most effects were due to the patients with more severe injury (See Table 2). This was consistent for metabolites measured in both white and gray matter. We also found that Cho/Cre measured in gray matter of mildly injured patients was elevated compared with controls (p=0.01). mIns/Cre in both gray and white matter of severely injured patients was elevated compared with mild (p=0.01).

Table 2	Uninjured (n=26)		Mild/moderate TBI (n=14)		Severe TBI (n=13)	
	White matter	Gray matter	White matter	Gray matter	White matter	Gray matter
NAA/Cre	1.11±0.09	1.12±0.08	1.06±0.08	1.10±0.09	1.02±0.08 ⁺⁺	1.06±0.10 ⁺
Cho/Cre	0.25±0.02	0.21±0.02	0.28±0.06	0.24±0.05 ⁺	0.28±0.03 ⁺⁺	0.24±0.03 ⁺⁺
mIns/Cre	0.53±0.07	0.52±0.06	0.56±0.08	0.54±0.05	0.66±0.09 ⁺⁺	0.61±0.07 ⁺⁺
Gln/Cre	0.57±0.07	0.73±0.10	0.59±0.10	0.75±0.13	0.65±0.11 ⁺	0.81±0.15 ⁺

+ indicates P<0.05, ++ indicates p<0.01 (TBI vs. uninjured control)

Discussion

Magnetic resonance spectroscopy of a large slab of normal-appearing brain generally provides a similar metabolic picture to that obtained by more focal approaches. That is, NAA/Cre is generally lower and Cho/Cre and mIns/Cre are significantly higher in both whole brain and in each of white and gray matter of patients following traumatic brain injury. Subsequent analyses showed that mild/moderate patients were not significantly different from uninjured controls except for Cho/Cre in GM but not WM. All metabolites measured in severely injured patients were significantly different from control values. Finally, mIns/Cre in both WM and GM discriminated mild/moderate patients from severe.

The observation that Cho and mIns measures discriminated different patient severity indicates that different molecular and cellular mechanisms might be important in understanding recovery from these forms of injury. For example, elevated mIns indicates a substantial glial response in the severely injured patients. On the other hand, elevated choline might implicate membrane injury present in less severely injured individuals. However, it should be noted that the mildly injured patients were scanned rather earlier in their recovery phase than the severe patients. Given the temporal evolution of NAA and Cho over periods up to six months after TBI [5], some of the effects reported might be due to changing values.

Future studies are required to explore the relationships between levels and temporal evolution of these metabolite markers of injury and longer term cognitive outcome and recovery.

References

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