# Quantitative 2-D Proton Spectroscopic Imaging in Children Following Traumatic Brain Injury

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**Introduction**

There are 200,000 children hospitalized for head trauma each year, 30,000 of whom suffer permanent disability. Accurate early prediction of outcomes translates to early implementation of appropriate treatment. Conventional MRI is able to delineate the presence of blood, extra-axial fluid, and major disruption of tissue with any associated cerebral edema. However, the relationship between conventional MRI and patient outcomes following traumatic brain injury (TBI), as measured by neuropsychometric parameters, has been inconsistent across studies[1]. There has been a growing interest in the use of MRS to correlate the outcome of TBI, as a result of closed head injury, with changes in brain metabolites, such as a reduction in NAA reflecting a loss of neuronal and axonal integrity or metabolic state[2]. To this end, we have implemented a chemical shift imaging protocol that quantifies NAA, choline, and creatine in both TBI patients and in normal controls.

**Techniques/Methods**

Using the Philips 1.5 Tesla Gyroscan Intera scanner at Texas Children's Hospital, proton spectra were collected using conventional two-dimensional chemical shift imaging (2DCSI) techniques (TR/TE=1500/60 ms) from left and right fronto-parietal white matter in 7 TBI patients (5F/2M; age at injury, mean=9.6 years, SD=1.78, range=7-12 yr; age at MRS, mean=10.7 years, SD=2.3; post-injury interval, mean=12.8 months, SD=1.1, range=6wk-3yr) and 5 uninjured controls (3F/2M; age, mean=10.62, SD=1.92). The groups did not differ significantly in age, and all but one of the children was right-handed. Fig. 1 displays a typical pair of datasets demonstrating the signal-to-noise ratio of the data. Creatine, choline, and NAA phantoms were prepared and used for creating a basis set for subsequent analysis of the in vivo data with the software package LCModel.

**Results**

The output from the LCModel analysis of each region in each subject (n=12) produced a total of 48 observations. NAA, but not choline or creatine, was marginally lower ($p = 0.07$) in all regions of the TBI group (Table 1, Figure 1) compared to the controls. Higher left than right white matter metabolite concentrations were observed for NAA ($p = 0.02$), choline ($p = 0.04$), and creatine ($p = 0.01$) in both the controls and the patients. Also, the NAA/Cho ratio was significantly higher in the control group than in the TBI group ($p = 0.04$). Metabolite homogeneity tests conducted on a Braino phantom confirmed that asymmetry was not due to any systematic error. The psychometric data (Table 2) demonstrate a statistically significant difference for the three tests administered between the two groups ($p < 0.001$) for all three tests.

**Table 1. Least Square Mean Concentrations of NAA, Choline, and Creatine by Group, Side, and Region**

| | | NAA | | Cho | | Cre | | NAA/Cre | | NAA/Cho | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| TBI (n=7) | FR | 9.63 | 9.21 | 2.26 | 1.88 | 9.94 | 9.46 | 0.98 | 1.00 | 4.37 | 5.01 |
| | PA | 9.83 | 9.35 | 2.09 | 1.92 | 9.86 | 8.92 | 1.02 | 1.05 | 4.73 | 4.99 |
| Control (n=5) | FR | 10.46 | 10.17 | 2.05 | 1.90 | 10.26 | 9.18 | 1.02 | 1.12 | 5.13 | 5.55 |
| | PA | 10.35 | 9.63 | 2.07 | 1.77 | 9.51 | 8.65 | 1.10 | 1.14 | 5.28 | 5.52 |

**Table 2. Psychometric Data**

| | | Test | | |
|---|---|---|---|---|
| Group | Stat | WASI IQ* | WJ-R Math* | CELF Formulated Sentence* |
| TBI | Mean | 85.9 | 84.9 | 92.0 |
| | SD | 10.2 | 6.9 | 11.8 |
| Control | Mean | 115.1 | 115.9 | 117.9 |
| | SD | 12.1 | 14.4 | 8.6 |

* $p < 0.001$

**Discussion**

A TE of 60 ms was chosen to avoid strong macromolecule baselines and coupled spins found at shorter TEs (e.g., 30 ms) and also to minimize T2 weighting and signal loss at longer TEs (e.g., 136 ms). Hemispheric asymmetries in these metabolites have not been reported in children.[3,4] The possibility that these asymmetries were artifacts was ruled out by analysis of data acquired from a uniform solution phantom containing these metabolites. The lower NAA in the TBI group suggests fronto-parietal neuronal and axonal injury consistent with previous research.[5]

**Conclusions**

This research supports prior reports of decreased NAA following TBI and reports a novel observation of L > R hemispheric asymmetry in all metabolites in the frontal white matter of both patients and controls, a finding which appears unrelated to age or gender. The psychometric data clearly shows lower scores in the TBI group than in the controls. The sample investigated was small, but there is ongoing recruitment of children to confirm or refute these observations.

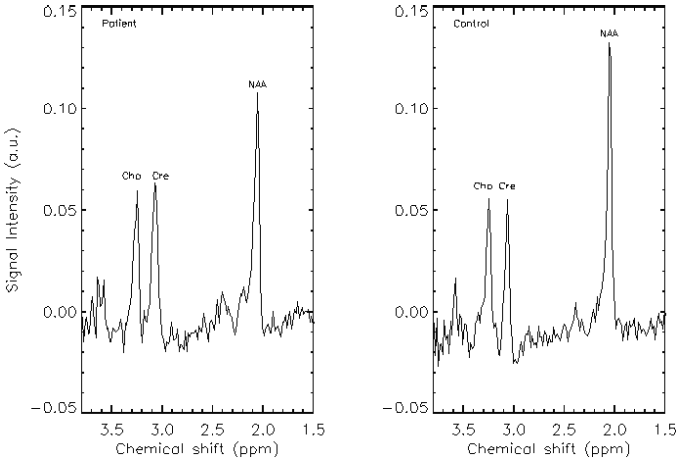


Figure 1: Comparison of average spectra obtained from left frontal lobe of a patient (left plot) versus that of a control (right plot).

**References**

1. Donders J, Strom D: Neurobehavioral recovery after pediatric head trauma: injury, pre-injury, and post-injury issues. J. Head Trauma Rehab. 15:792-803, 2000
2. Friedman SD, Brooks WM, Jung RE, et al: Quantitative proton MRS predicts outcome after traumatic brain injury. Neurology 52:1384-1391, 1999
3. Ashwal S, Holshouser BA, Shu SK, et al: Predictive value of proton magnetic resonance spectroscopy in pediatric closed head injury. Pediatr.Neurol. 23:114-125, 2000
4. Yeo RA, Hill D, Campbell R, et al: Developmental instability and working memory ability in children: a magnetic resonance spectroscopy investigation. Dev.Neuropsychol. 17:143-159, 2000
5. Brooks WM, Stidley CA, Petropoulos H, et al: Metabolic and cognitive response to human traumatic brain injury: a quantitative proton magnetic resonance study. J.Neurotrauma 17:629-640, 2000

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