# Thalamic Metabolic Characterization of Human Mild Traumatic Brain Injury

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***BACKGROUND AND PURPOSE:*** Although mild traumatic brain injury (mTBI) comprises 85% of all brain trauma (1) it has received significantly less attention than the rarer/much rarer moderate and severe forms of the disease. Due, perhaps, to its largely MRI-invisible pathology, early mTBI findings correlate only weakly with clinical outcome (2). A year post injury 55% of patients suffer any of several postconcussion syndrome symptoms (3), some of which point to the thalamus (Fig. 2). Surprisingly, although MRI-occult injury may be probed with proton MR spectroscopy ($^1$H-MRS), to our knowledge the only TBI $^1$H-MRS study of the thalamus was in vegetative patients, not mTBI, which accounts for most of head trauma injuries. Thus, the aim was to study thalamic metabolite levels due to mTBI.

***METHODS:*** 20 closed head mTBI (Glasgow Coma Scale score of 15-13) patients, 19 – 59 years old, 0 – 7 years post injury and 13 age and gender matched controls were scanned at 3 Tesla. MRI was used to guide a $10_{AP}\times8_{LR}\times6_{IS}$ cm$^3$ volume of interest (VOI), excited with TE=135 ms PRESS with water suppression. A $16_{AP}\times16_{LR}\times6_{IS}$ cm$^3$ field of view (FOV) containing the VOI was partitioned into $1.0_{AP}\times1.0_{LR}\times0.75_{IS}$ =0.75 cm$^3$ voxels with 8$^{th}$ order Hadamard spectroscopic imaging and $16_{AP}\times16_{LR}$ 2D chemical-shift imaging (CSI) matrix (4). Relative *N*-acetylaspartate (NAA), Choline (Cho) and Creatine (Cr) levels were estimated from their peak area using parametric spectral modeling and least-squares optimization (5) (Fig. 1). In-house software averaged the metabolite levels and spectra in the thalamus (Fig. 2). Mixed model regression was used to compare patients and controls with respect to the mean absolute metabolite levels within the thalamus.

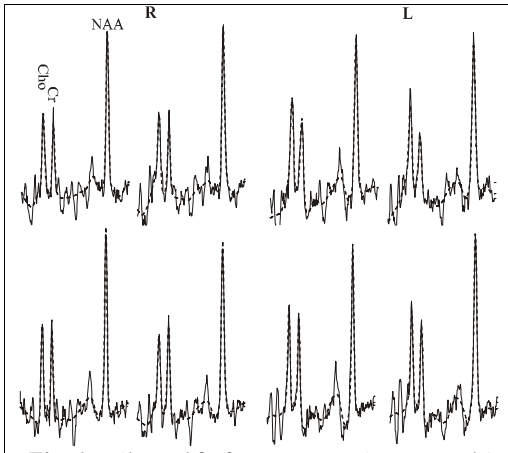


***Fig. 1.*** *Bilateral 2×2 spectra matrix extracted from the left (L) and right (R) thalami (solid lines) of a patient. Each spectrum is superimposed with its fitted model functions (dashed lines) for NAA, Cr and Cho (5). Note the SNR and spectral resolution as well as the quality of the fit to the selected resonances of interest and accounting for the baseline.*

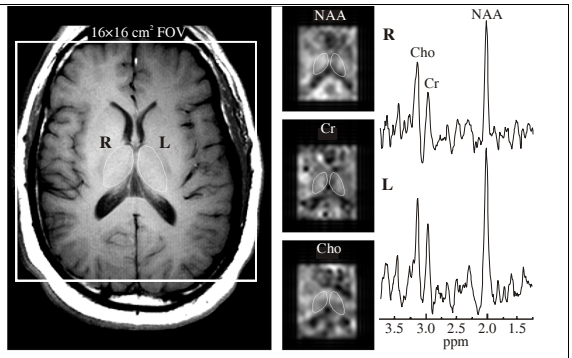


***Fig. 2.*** *Axial T1 image of a patient superimposed with the $16_{LR}\times16_{AP}$ cm$^2$ MRS FOV. The manually-outlined thalami were transcribed by our software onto the corresponding regions of the three metabolic maps and each metabolite's level, standard deviations and spectrum in that region computed. Average spectra from the left and right thalamic regions are shown. Note the quality of the maps and similarity of spectra.*

***RESULTS****:* The fact that thalamic metabolite concentrations of the patients do not significantly differ from the controls: NAA: 9.60±0.34 versus 10.08±0.30 (mean±standard error), Cr: 5.44±0.19 compared with 5.62±0.18, Cho: 2.03±0.10 versus 2.08±0.09 mM, indicates that mTBI-induced changes are under ±13.0% for NAA (range between dashed lines in Fig. 3), ±13.5% for Cr and ±18.8% for Cho.

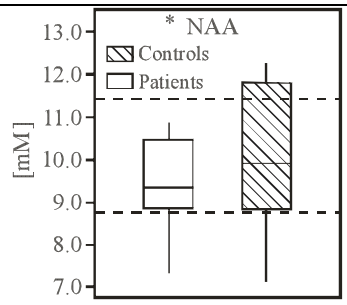


***Fig. 3.*** *Box plot displaying 25%, median and 75% (box), 95% (whiskers) and outliers (*) range of the variation of the absolute thalamic NAA concentration in patients and controls. Note that any thalamic metabolite change imparted by mTBI is likely to be within the ranges marked with dashed lines. Also, although not statistically different, the patients' NAA levels are confined to the lower half of the controls', which may suggest a degree of neuronal dysfunction.*

***DISCUSSION AND CONCLUSION:*** Based on this study any deviation of thalamic metabolite levels caused by mTBI is likely to lie within the calculated limits. For example, the NAA mean of the mTBI patients is not likely to be lower or higher by more than 13.0% of healthy controls'. These established intervals give the likely range of any thalamic metabolic abnormalities caused by mTBI and, thus define the minimum sensitivity needed to resolve them. Moreover, these limits might be used as additional indicators of "mildness" or "severity" of TBI and thus could guide clinical decisions about individual patient treatment or prognosis. The intervals might also be useful in constructing animal models of mTBI.

The small magnitude of metabolic changes in mTBI combined with the heterogeneity of head trauma injury mechanisms may reduce the sensitivity of any technique to find significant differences in mTBI cohorts of this size. Increasing the sensitivity, *e.g.,* by averaging several follow-up studies, a larger cohort and more sensitive MR instrumentation, could alleviate this.

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