Neurometabolites Alteration in the Acute Phase of Mild Traumatic Brain Injury (mTBI): An In Vivo Proton Magnetic Resonance Spectroscopy (1H-MRS) Study

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Rationale and Objectives: Magnetic resonance spectroscopy is a noninvasive imaging technique that allows for reliable assessment of microscopic changes in brain cytoarchitecture, neuronal injuries, and neurochemical changes resulting from traumatic insults. We aimed to evaluate the acute alteration of neurometabolites in complicated and uncomplicated mild traumatic brain injury (mTBI) patients in comparison to control subjects using proton magnetic resonance spectroscopy (1H magnetic resonance spectroscopy).

Material and Methods: Forty-eight subjects (23 complicated mTBI [cmTBI] patients, 12 uncomplicated mTBI [umTBI] patients, and 13 controls) underwent magnetic resonance imaging scans with additional single voxel spectroscopy sequence. Magnetic resonance imaging scans for patients were done at an average of 10 hours (standard deviation 4.26) post injury. The single voxel spectroscopy adjacent to side of injury and noninjury regions were analysed to obtain absolute concentrations and ratio relative to creatine of the neurometabolites. One-way analysis of variance was performed to compare neurometabolite concentrations of the three groups, and a correlation study was done between the neurometabolite concentration and Glasgow Coma Scale.

Results: Significant difference was found in ratio of N-acetylaspartate to creatine (NAA/CR + PCR) ($\chi^2(2) = 0.22$, $P < .05$) between the groups. The sum of NAA and N-acetylaspartylglutamate (NAAG) also shows significant differences in both the absolute concentration (NAA + NAAG) and ratio to creatine (NAA/NAAG + PCR) between groups ($\chi^2(2) = 4.03$, $P < .05$) and ($\chi^2(2) = 0.79$, $P < .05$), NAA values were lower in cmTBI and umTBI compared to control group. A moderate weak positive correlation were found between Glasgow Coma Scale with NAA/CR + PCR ($\rho = 0.38$, $P < .05$ and NAA + NAAG/CR + PCR ($\rho = 0.45$, $P < .05$)), whereas a moderate correlation was seen with NAA + NAAG ($\rho = 0.38$, $P < .05$).

Conclusion: Neurometabolite alterations were already apparent at onset of both complicated and uncomplicated traumatic brain injury. The ratio of NAA and NAAG has potential to serve as a biomarker reflecting injury severity in a quantifiable manner as it discriminates between the complicated and uncomplicated cases of mTBI.

Key Words: Neurometabolite; mild Traumatic Brain Injury (TBI); Magnetic Resonance Spectroscopy (MRS); N-acetylaspartate (NAA); Glasgow Coma Scale (GCS).

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INTRODUCTION

Dysregulated metabolites-induced cellular energy crisis is a common occurrence in traumatic head injury (1). The cascading events post trauma may lead to terminal membrane depolarization with excessive release of excitatory neurotransmitters (2), lysis of the cell membranes and apoptosis, disrupting various neural connectivity networks and consequently affecting neurocognitive function or performance (1). Injury severity in mild traumatic brain injury (mTBI) could be categorized into complicated or...