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Application of Proton MRSI to assess metabolic status of the brain in post traumatic brain injury depression

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Introduction

Traumatic brain injury (TBI) survivors often suffer multiple neuropsychiatric sequelae (McAllister, 1992). Estimates of the prevalence of depression rang from 13% at 1 year after trauma (Deb et al, 1999) to 60% at 8 years (Hibbard et al, 1998). Depression can contribute to disability after TBI by interfering with rehabilitation and exacerbating cognitive deficits. Post TBI depression can be divided into early onset / transient depression (1 to 3 months after injury) which lasts for a few days to weeks, and late onset / persistent depression (several months after injury) which may last for months afterwards (Jorge et al, 1993). Early onset depression is associated with lesions in the left dorsolateral frontal and/or left basal ganglia regions, but this association is lost 3 months after injury. These results suggest that early-onset transient depression is associated with disrupted brain physiology associated with the injury, whereas late-onset depression may be a psychological reaction to physical and cognitive impairment. To date there are no published results of MRS in post-TBI depression, however preliminary MRS studies in major depression, bipolar disorder, panic disorder, or obsessive-compulsive disorders have reported alterations in brain levels of NAA, myo-inositol, Cho, and gamma-aminobutyric acid (Kumar et al 2002; Moore et al 2002). We hypothesized that TBI depressed subjects would have decreased NAA/Cho and/or NAA/Cr ratios in the frontal gray matter (GM) and basal ganglia compared to controls as these regions have been implicated in structural imaging studies of the pathogenesis of post-TBI depression (Jorge 2004).

Methods

All TBI depressed subjects underwent a complete neuropsychiatric evaluation and MR scanning. Inclusion criteria included age 18 years or older, date of TBI between 3 and 24 months of MRS study, no history of mood disorder prior to TBI, Mini Mental State Examination (MMSE) > 24, stable medical history prior to injury, sufficient cognitive capacity to provide consent. Depressed subjects were required to meet DSM-IV criteria for Major Depressive Episode, and to have met these criteria only in the period after TBI. Age-matched subjects (+/- 7 years) with history of TBI who did not meet or never met the DSM-IV criteria for major depressive episode were recruited. Proton MRSI was performed using a multi-slice spin-echo sequence with outer volume suppression (Duyn et, 1993). Three oblique axial slices were acquired with a 15 mm thickness and a gap of 2.5 mm (TR/TE= 2000/280 ms, acquisition matrix 28x28x256, FOV=24 cm). Metabolite ratios NAA/Cho, NAA/Cr and Cho/Cr were calculated from ROIs- frontal white matter, frontal gray matter, basal ganglia and thalamus, from both hemispheres. Figure 1 shows the MRSI voxel locations and representative spectra from ROIs. Independent t test was used to determine the difference in these ratios between TBI depressed subjects and controls (P-value < 0.05).

Results

Table 1 shows the mean metabolite ratios for various ROIs from control and TBI subjects with p values ($p < 0.05$). NAA/Cho and/or NAA/Cr ratios were significantly decreased in the TBI depressed group compared to normal controls in the frontal GM, basal ganglia, and the thalamus. Frontal gray matte showed significant change ($p = 0.009$) in NAA/Cho ratio compared to subcortical regions (basal ganglia, $p = 0.091$; thalamus, $p = 0.049$). No difference between the two groups was noted in the frontal white matter. There was no significant difference between the TBI depressed subjects and the normal controls in the Cho/Cr ratio in any of these regions.

Discussion

Frontal gray matter, basal ganglia and thalamus were the regions which showed significant change in NAA related ratios indicating diffuse axonal injury or metabolic depression in cortical/subcortical regions. These results indicate that post TBI depression is mainly due to diffuse neuronal injury in cortical/subcortical region. This finding is supported by results that indicate no significant change in Cho/Cr ratios in these patients. Also, frontal white matter region showed no significant change in metabolite ratios. We conclude that diffuse neuronal injury in frontal cortical and subcortical regions may be associated with post-TBI depression.

Table 1: Comparison of metabolite ratios for TBI depressed and control subjects from 4 ROIs.

	Frontal White Matter			Frontal Gray Matter		
	Depressed TBI Mean (SD)	**Non-depressed TBI Mean (SD)**	**p**	**Depressed TBI Mean (SD)**	**Non-depressed TBI Mean (SD)**	**p**
NAA/Cho	1.62 (.43)	1.57 (.25)	p=0.853	1.65 (.25)	2.40 (.43)	**p=0.009**
NAA/Cr	1.95 (.56)	3.10 (1.08)	p=.067	1.68 (.70)	2.69 (1.05)	p=0.113
Cho/Cr	1.30 (.38)	1.89 (.99)	p=0.252	1.39 (.39)	1.06 (.21)	p=0.13
	Basal Ganglia			**Thalamus**		
NAA/Cho	1.43 (.35)	1.45 (.29)	p=0.918	1.32 (.19)	1.61 (.20)	**p=0.049**
NAA/Cr	1.73 (.28)	2.46 (.65)	**p=0.050**	1.88 (.17)	2.04 (.75)	p=0.658
Cho/Cr	1.21 (.36)	1.54 (.62)	p=0.32	1.57 (.17)	1.32 (.29)	p=0.139

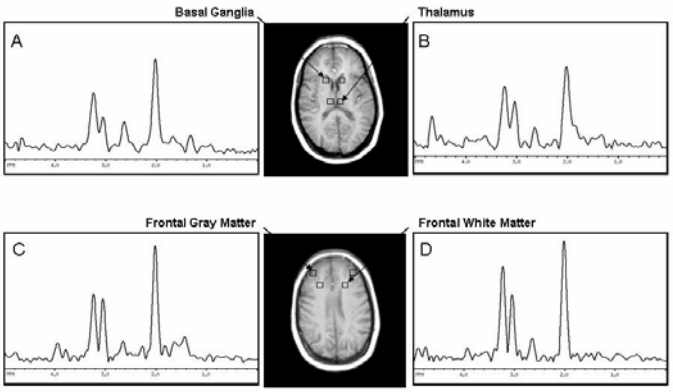

Figure 1: T1-weighted MR image with 4 ROIs – A, Basal Ganglia, B, Thalamus, C, Frontal Gray Matter, and D, Frontal White Matter with representative MR spectra from these regions.

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