Diffusion Weighted MRI of Closed Head Injury and Treatment with PEG (polyethylene-glycol) in Rats

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Introduction

In United States, traumatic brain injury (TBI) is a leading cause of death and disability for children and adults; with ~1.5 million Americans injured each year[1]. TBI is associated with increased intracranial pressure caused by a combination of vasogenic (or extracellular) and cytotoxic (or intracellular) edema, which leads to cellular damage and death. Measurements of water apparent diffusion coefficient (ADC) by diffusion weighted MRI (DWI) may be useful in detection of focal and diffuse tissue damage and in differentiating the edema type caused by TBI. Water ADCs have been suggested to increase with vasogenic edema and decrease with cytotoxic edema[2]. It has been recently demonstrated that PEG (polyethylene glycol) fuses and repairs damaged cell membranes in dogs with spinal cord injury[3]. The main objectives of this study were to apply water ADC measurements: (a) for detection and differentiation of the type of edema that develops in a rat TBI model, and (b) to examine the protective effects of PEG treatment after TBI.

Methods:

Fisher Rats weighing 400-500 g were divided control (n=6), injury only (n=8) and injury with treatment (n=10) groups. A new impact-acceleration closed head injury model was used[4]. The animals in the treated group received PEG by *i.v.* injection within a few hours of injury. MRI experiments were performed using a 9.4- T, 31-cm horizontal bore Varian system equipped with a 12-cm ID with gradient coil capable of generating 38 gauss/cm. RF excitation and reception were performed using a 63 mm quadrature coil tuned to 400 MHz for ^{1}H. Rats were anesthetized with 4% isoflurane and 99% medical air for the MRI study. Temperature was maintained at 37° C inside the bore. A two-dimensional multi-slice DWI sequence with two isotropic gradient fields of 5 msec duration each, separated by 12 msec was used. Image data were collected at four b values of 0, 200, 500 and 1200 seconds/mm^2. Other parameters used were as follows: 24 axial slices, 0.5 mm thickness, 0.25 mm gap, 256 x 128 data points over a field-of-view of 5 x 5 cm^2, TR/TE 4000/22 msec and NEX=1. Total image data collection time was 34 min 14 sec. The data set were zero-filled to 512^2 points, Fourier transformed, and converted into a readable format using BROWSER (Varian Image processing software). T_2-weighted MRI was acquired with the following parameters: TR/TE 2000/30 msec, 4 min 12 sec scan time for slice selection. ADC maps were calculated for three midline sections in the center of brain where cortex, corpus collaseum, hippocampus and thalamus can be differentiated. Statistical analysis was performed using ANOVA.

Results and Discussion:

The representative T_2-weighted images and water ADC maps for control, injury-only and PEG-treated groups are shown in Figure 1. The ADC maps of the injury-only group show diffuse hypo intense areas in the cortex, hippocampus and thalamus compared to the control group. The ADC values are similar in the PEG-treated and control groups. The average ADC values for the three groups in the cortex, hippocampus and thalamus are shown in Figure 2. In the control group, the water ADC values (10^{-3} mm^2/sec) of the cortex, hippocampus and thalamus were 0.79 ± 0.02, 0.80 ± 0.04 and 0.75 ± 0.03, respectively. The ADC values of injury-only group at the 7th day post-injury in the three regions were 0.74±0.05, 0.75±0.05 and 0.70±0.05, respectively. The PEG-treated animals showed a significantly higher ADC compared to the injury-only group. The ADC values of PEG-treated group were 0.80±0.04, 0.82±0.06 and 0.77±0.05, respectively.

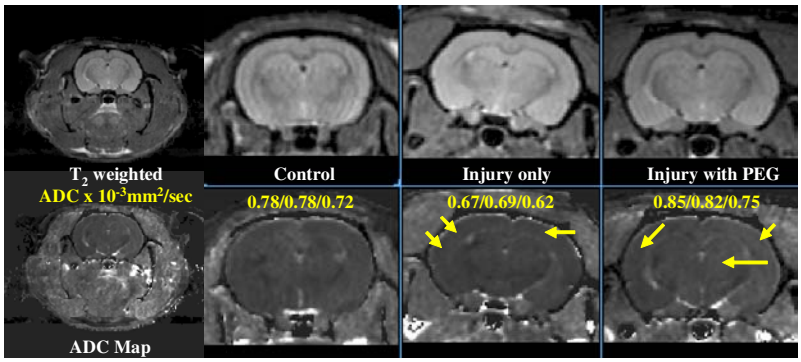

Fig 1. T_2 -weighed images and ADC maps of the control, injury-only and PEG treatment groups of rat brain at the 7th day post-injury or post-treatment

The decrease in water ADC in the injury-only group suggests that TBI caused cytotoxic edema 7 days after the trauma. After the tissue injury, cellular ATP levels may be depressed, resulting in a decrease in Na^+/K^+ ATP pump activity and an increase in intracellular sodium. The increase in cellular osmotic pressure due to increased ion concentration can cause the water to migrate from the fast diffusing extracellular space into the slower diffusing intracellular space, resulting in the observed decrease in water ADC. PEG treatment attenuated the decrease in water ADC caused by TBI, suggesting that the treatment prevents the cells from developing cytotoxic edema.

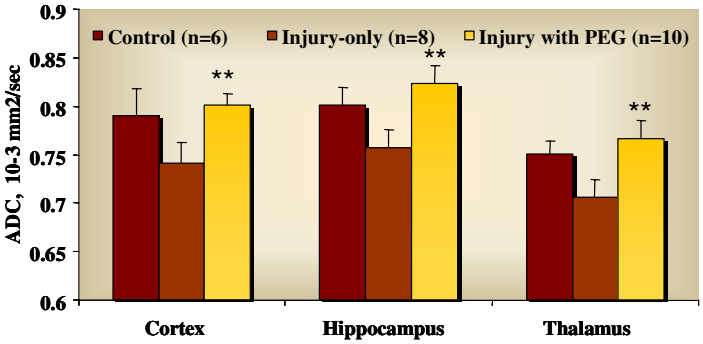

Fig. 2. The mean ADC values of cortex, hippocampus and thalamus of the rat brain for control, injury-only and injury with PEG treatment groups at the 7th day post-injury or post-treatment. ** represents significance with respect to injury only group. Values shown are mean ±standard error of the means.

Conclusion:

In summary, water ADC is decreased after TBI, suggesting that cytotoxic edema plays an important role in its pathophysiology. Unchanged water ADC in the PEG-treated group demonstrates the protective effects of the therapy.

References:

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