Characterizing Edema Associated with Cortical Contusion and Secondary Insult Using Magnetic Resonance Spectroscopy

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Summary

It is traditionally believed that edema associated with brain contusion is vasogenic. The objective of this study was to quantify and characterize the edema in cortical contusion coupled with early hypoxia and hypotension.

Sprague-Dawley rats were randomised into six groups: Sham, Trauma moderate (Tm), Trauma severe (Ts), Hypoxia and Hypotension (HH), Tm and Ts with HH (THHm; THHs). Trauma was induced with controlled cortical impact; associated secondary insults lasted 30 minutes. Water content was measured using tissue longitudinal relaxation time (T¹). Apparent diffusion coefficient of water (ADC) was calculated from diffusion-weighted imaging and single voxel spectroscopy.

In the trauma groups ICP increased at 30 minutes post trauma (p < 0.05) and then gradually decreased. Only in the THH groups, ICP showed a trend to continually rise. No ICP variations were seen in the others groups. The increase in water content at 4 hours post trauma was inversely related to ADC variation (p < 0.0001). A significant increase in water content with low ADC, developed in the injured region in Ts, THHm (p < 0.05) and THHs (p < 0.01) compared to Sham. Intracellular water rose in the whole brain in THH groups although more severely in the THHs (p < 0.01). Immediately after trauma ADC fell in the THH groups, but gradually increased in the THHm, whereas there was no recovery in THHs.

The results indicate that the type of edema in the injured area, with and without superimposed secondary insult, is predominantly cytotoxic (cellular). Moreover, secondary insults act synergistically with focal injury to increase cellular water in both injured tissue and remote regions.

Keywords: Traumatic brain edema; secondary insult; water content; diffusion weighted imaging.

Introduction

The nature of edema, vasogenic versus cytotoxic, after traumatic head injury is still controversial and the role of secondary insults to eventually worsen edema is not clear.

Edema surrounding a contusional area has been classified as vasogenic, however recent studies in models of cortical contusion have demonstrated a predominant component of intracellular edema [7]. Secondary insults are common during the acute post-injury phase following a traumatic brain injury. They might increase brain damage and influence a worst outcome [1, 6, 8].

The aim of this study was to quantify and characterize the predominant type of brain edema (vasogenic versus cytotoxic), using MRI techniques, when early secondary insults were superimposed to a focal cortical contusion in rats.

Methods

A model of controlled cortical impact (CCI) [2] was used to induce a lateral cortical contusion in rats. Two different levels of severity of trauma were obtained using a depth of impact of 3 mm and 3.5 mm at a constant velocity of 2.3–2.7 m/sec. Immediately following head injury, 30 minutes of hypoxia (paO2 30–40 mmHg) and hypotension (mean arterial pressure of 30–40 mmHg) were superimposed. Animals were subsequently resuscitated.

We measured water content and ADC by experiments carried out in the MRI. The measurements were obtained in a region of interest (ROI) in the cortex directly under the site of impact, in the homotopic region within contralateral cortex and in the whole brain, at baseline and about 4 hours after trauma. To quantify the edema, precise estimate of longitudinal relaxation time (MRI T¹ weighted imaging) of tissue was converted in percentage of water (water content grams of water / 100 grams of tissue)[3]. Intracellular increase of water was considered as cytotoxic edema whereas an extracellular rise of water was attributed to barrier compromise and vasogenic edema. The apparent diffusion coefficient of water (ADC) was calculated from MRI diffusion weighted imaging (DWI). From previous studies, ADC has been demonstrated to decrease in case of intracellular edema and increase with extracellular accumulation of...
Table 1. Water Content is Expressed in Grams of Water / 100 Grams of Tissue and ADC is 10⁻³ mm²/sec

<table>
<thead>
<tr>
<th>Groups</th>
<th>ROI (injured region)</th>
<th>Whole brain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Water content</td>
<td>ADC</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>10⁻³ mm²/sec</td>
</tr>
<tr>
<td>Sham</td>
<td>1.2 ± 1.03</td>
<td>0.64 ± 0.10</td>
</tr>
<tr>
<td>HH</td>
<td>4.2 ± 2.23</td>
<td>0.62 ± 0.04</td>
</tr>
<tr>
<td>Tm</td>
<td>3.1 ± 1.00</td>
<td>0.56 ± 0.11</td>
</tr>
<tr>
<td>THHm</td>
<td>4.5 ± 3.42*</td>
<td>0.42 ± 0.08**</td>
</tr>
<tr>
<td>Ts</td>
<td>6.3 ± 1.89**</td>
<td>0.39 ± 0.06**</td>
</tr>
<tr>
<td>THHs</td>
<td>7.9 ± 2.98**</td>
<td>0.37 ± 0.10**</td>
</tr>
</tbody>
</table>

* = p < 0.05; ** = p < 0.01 compared to Sham.

Discussion

A fast acquisition (DWI single voxel spectroscopic technique) was used to follow the temporal course of ADC. Eighty-five adult Sprague-Dawley rats were randomized in six groups: Sham, Trauma moderate (Tm) and severe (Ts) Hypoxia Hypotension (HH), Tm and Ts with HH (THHm; THHs).

Technical problems made it impossible to record intracranial pressure (ICP) and cerebral perfusion pressure (CPP) inside of the magnet, so parallel bench studies were carried out to measure those parameters.

All data are shown as mean ± SD. Statistical analysis was performed by means of ANOVA and LSD post hoc test when multiple comparisons were made. Correlation between water map and ADC was analysed by Pearson Product-Moment correlation. Repeated measure analysis was used to follow the temporal course of the ADC and physiology data.

Results

In the trauma groups, ICP increased at 30 minutes post trauma (31 ± 10 mmHg Tm and 21 ± 6 mmHg Ts; p < 0.05), then gradually decreased. ICP showed a permanent trend to rise when trauma was associated with secondary insults (THH groups). No changes were seen in the sham groups.

The increase in water content in the whole brain was inversely related to the variation of ADC (r = 0.70, p < 0.0001) at four hours post trauma. This result suggested a predominant role of intracellular water in the developing edema. A significant increase in water content associated with low ADC was found in the injured region in THHm (p < 0.05) and Ts and THHs (p < 0.01) compared to Sham. In the THH groups the cytotoxic edema was not only confined to regions of trauma, but affected the entire brain. The rise in water content with low ADC was more severe in the THHs when compared to all others groups. (p < 0.01) (Table 1). The analysis of temporal course showed an immediate ADC drop after trauma in the THH groups. ADC was 0.44 ± 0.07 10⁻³ mm²/sec in THHm and 0.32 ± 0.06 10⁻³ mm²/sec in THHs by 30 minutes post-trauma. After this period, ADC recovered to 0.60 ± 0.11 10⁻³ mm²/sec by the end of the study in THHm whereas there was no recovery of ADC values in THHs.

Conclusion

The inverse relation between water content and decreased ADC suggests a predominant role of intracellular water in the developing edema. Moreover, our results show that at 4 hours after a focal traumatic damage, there is an ipsilateral increase of water which is predominantly cellular proportional to the severity of trauma. Superimposed secondary insults increase the amount of edema associated with the mechanical insult. Trauma and secondary insults seem to act synergically to increase cellular edema in the entire brain and is not only restricted to the site of focal injury.

References