Metabolic changes in a contralateral hemisphere after cortex injury assessed by 1H MRS. An animal study.

V. Herynek[1,2], K. Ruzicková[2,3], P. Jendelová[2,3], E. Syková[2,3], and M. Hájek[1]

[1]Department of Diagnostic and Interventional Radiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [2]Center for Cell Therapy and Tissue Repair, Second Medical Faculty, Charles University, Prague, Czech Republic, [3]Institute of Experimental Medicine ASCR, Prague, Czech Republic

INTRODUCTION

Severe brain injury, such as extensive tissue infarction significantly affects not only functioning of the neural tissue directly in the lesion and neighboring structures, but has a huge impact on the whole brain. Changes in the tissue exposed to different types of an experimental lesion have been already studied. Proton MR spectroscopy revealed decrease of N-acetyl aspartate concentration (considered as a marker of viable neurons), lower levels of glutamate (a neurotransmitter), decrease of creatine/phosphocreatine concentrations (energetic metabolism), and increase of lipid content (due to an edema). All these changes are expected in the lesion, however little is known about effect of a severe brain injury on primarily unaffected brain structures. The aim of our study was to monitor also changes in the contralateral hemisphere after an experimental brain injury.

MATERIALS AND METHODS

All experiments were carried out in accordance with the European Communities Council Directive of 24th November 1986 (86/609/EEC).

Experimental animals

Male Wistar rats, 6-8 weeks old at the beginning of the experiment, were used throughout the study. Animals were divided into the following groups: rats with a cortical photochemical lesion (n=21), healthy controls (n=6).

Photochemical lesion

We used a photochemical lesion as a model of thrombotic stroke (1). The rats were anesthetized by isoflorane (2% isoflorane in air). Rose Bengal was injected intravenously into the femoral vein (1mg/100 g). An 1x2 mm area of the skull above the right cortex was exposed to the light from a halogen lamp or a laser beam for 10 minutes. The Rose Bengal is excited and subsequently generates singlet molecular oxygen, which induce photoperoxidative reactions leading to thrombosis and infarction within one hour. The method is virtually noninvasive because the skull is translucent for light at 560 nm, which is needed for photochemical reaction induction.

Magnetic resonance spectroscopy

All MR measurements were performed using a 4.7 T Bruker spectrometer equipped with a homemade surface head coil. The rats were anesthetized by passive inhalation of 1.5 - 2% isoflorane in air. T_2-weighted transversal images were used for localization and positioning of spectroscopic volume of interest (VOI). Spectra were measured using a single voxel STEAM sequence with a water suppression using VAPOR technique (2) and following parameters: TE = 3 ms, TR = 5000 ms, AC = 512, VOI = 2x4x4 mm. The spectra were evaluated using the LCModel (3) to obtain absolute metabolite concentrations. The evaluation included also simulation of signals from macromolecules and lipids.

First spectrum was acquired within 5 days after lesion induction, altogether 2 times within the first ten days, then weekly for up to 60 days. Usually two spectra were acquired (depending on the condition of the animal): from the cortex lesion itself and from the cortex contralaterally.

RESULTS

Measuring of spectra directly in the lesion was complicated due to an edema, which accompanied the lesion and was represented in the spectra by high signals between 0.6 – 1.5 ppm attributed to lipids and macromolecules. The edema gradually decreased, nevertheless in part of the animals we failed to obtain a good spectrum within the first week after lesion creation. We found significantly (Student's t-test) decreased concentration of creatine/phospohocreatine (Cr) and N-acetyl aspartate (NAA) within the first three weeks in the lesion. Concentrations then slowly normalized. In the contralateral hemisphere we observed significantly higher concentrations of glutamate (Glu) and NAA.

DISCUSSION

Low concentrations of Cr and NAA in the lesion are expected, as the tissue is severely damaged. Drop of NAA concentration might be even higher; the method might overestimate its concentration due to lipids, which occur in the spectra when an edema evolved in the lesion. LCModel enables to fit also lipid signals by model data, however due to high error of the fit we cannot completely exclude a contribution of lipids to this signal. More interesting processes are observed in the contralateral hemisphere (increase of NAA and Glu). The uninjured tissue seems to substitute the role of the damaged tissue. Although the function of NAA is not completely clear, signal of NAA is usually considered as a measure of viable neurons, NAA might be important for initiation of protein synthesis, it might play a neuroprotective role by the removal of intracellular water against the water gradient, thus decreasing cytotoxic edema (4). This hypothesis is supported also by significant elevation of Glu (a signaling molecule for excitatory transmission).

CONCLUSION

We monitored an impact of an experimental photochemical lesion on the rat brain using 1H MR spectroscopy. We observed a gradual recovery in the lesion and higher concentrations of glutamate and N-acetyl aspartate in the cortex contralaterally, which probably indicates partial substitution of the function of the damaged tissue by the uninjured one.

Tab.: Concentrations of glutamate (Glu) and N-acetyl aspartate (NAA) measured in the cortex lesion and in the contralateral hemisphere.

Glu	lesion	Contralat.	controls
Day 1-10	7.9 ± 2.2	9.3 ± 1.2*	8.0 ± 1.2
Day 11-20	7.4 ± 1.9	9.4 ± 1.0*	
Day 21-40	8.6 ± 1.6	9.0 ± 0.9*	
Day 41-60	7.0 ± 1.3	9.0 ± 1.7	

NAA	lesion	Contralat.	controls
Day 1-10	6.5 ± 1.7*	8.6 ± 0.7*	7.5 ± 0.2
Day 11-20	6.5 ± 1.3*	8.0 ± 0.7*	
Day 21-40	7.9 ± 1.3	7.8 ± 1.0	
Day 41-60	7.5 ± 1.7	8.6 ± 1.1*	

* significantly differs from healthy controls

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