Chronic hepatitis C: T2 and metabolic changes in the brain

V. Herynek[1], M. Dezortová[1], P. Taimr[2], M. Hájek[1]

[1]MR Unit, Department of Diagnostic and Interventional Radiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [2]Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction

Hepatitis C (HCV) represents a serious liver disease which subsequently affects metabolism of a whole body. Approx. 75-80% of infected patients may suffer from chronic HCV and consequently liver cirrhosis. HCV caused liver cirrhosis is one of the most common indications for liver transplantation. HCV treatment still remains troublesome. In spite of the fact the combination therapy (pegylated interferon and ribavirin) is currently at our disposal, the sustained response is achieved in no more than 50-60% of patients. One possible explanation of failing of antiviral therapy in some HCV patients might be viral persistence outside the liver, which could be resistant to contemporary treatment modalities. HCV-RNA virus could also persist in the brain tissue. While hepatic encephalopathy has been long recognized as a disorder associated with cerebral metabolic changes, HCV infection is also being associated with changes in the brain. HCV-infected individuals may have deficits in cognitive functions and also abnormalities on MR spectroscopy have been recently described [1].

The aim of this study was to reveal possible metabolic and T2 relaxation changes in the brain of HCV-infected patients.

Methods

8 patients (age 38 ± 13 years) with a chronic hepatitis C infection were scanned. In four of them a mild cirrhotic conversion of the liver tissue was already proved. Hepatic encephalopathy has not been clinically detected in any of the patients. A control group of 22 age-matched healthy volunteers (age 40 ± 13 years) was scanned using the same protocol.

We used a Siemens Vision imager 1.5 T with a standard head coil. Localization for T2 relaxometry and 1H MR spectroscopy was performed using T2-weighted axial, coronal and sagittal sets of images. T2 was measured using a CPMG sequence with 16 echoes, echo-spacing 22.5 ms, recovery time TR = 2000 ms, slice thickness 5 mm. A single tilted axial slice through the anterior and posterior commissures was used. This slice included the basal ganglia, thalamus, and frontal white matter. T2 values were evaluated in the whole slice, i.e., a T2 map was calculated on a pixel-by-pixel basis by 3-parameter fitting using a home made software Chrobak. Values of T2 were obtained from the globus pallidus (GP), anterior putamen (Put), head of the caudate nucleus (CN), thalamus (Th) and frontal white matter (WM). Occipital WM was not included in the selected slice.

MRS was performed using a single voxel technique. We used a STEAM sequence, TR=5000 ms, TE=10 ms, mixing time TM=15 ms, 64 acquisitions. The voxel was positioned in the basal ganglia (BG, volume of interest VOI=10 ml) and occipital periventricular white matter (WMo, VOI=3.4 ml) (spectra could not be obtained from the frontal white matter, evaluated by relaxometry, due to problems with shimming). Absolute metabolite concentrations were evaluated using LCModel software 6-1.0 [2].

Results

We found a significant decrease of the T2 relaxation time in the gray matter (Put, CN, Th) in HCV patients with cirrhosis compared to patients without cirrhosis. However, there is no difference between averaged T2 values in patients and controls (age-related T2 changes did not influence these results) in the gray matter. Decrease of T2 was found also in the frontal white matter in HCV patients. For the T2 results see Tab. 1.

MRS revealed lower concentration of NAA in the basal ganglia. No statistically significant changes in metabolite concentrations compared to the controls were found in the occipital white matter (see Tab. 2). No difference between HCV patients with and without cirrhosis was found.

Tab. 1: T2 relaxation time in HCV patients compared to controls (mean ± SD)

	GP (ms)	Put (ms)	CN (ms)	Th (ms)	WM (ms)
all HCV patients	**67.5±2.9**	**79.0±3.0**	**87.6±3.1**	**82.8±2.0**	**75.9±1.8***
non-cirrhotic patients	69.1±2.0	81.5±2.2+	89.8±2.1+	84.3±1.0+	75.8±2.0
cirhotic patients	65.8±2.8	76.5±0.8	85.3±2.1	81.3±1.6	76.1±1.6
controls	**67.3±2.9**	**80.1±3.6**	**89.3±3.6**	**82.1±1.8**	**77.9±1.8**

*significant difference between patients and controls, p<0.01
+significant difference between patients with and without cirrhosis, p<0.05

Tab. 2 Selected metabolite concentrations (in mM) in HCV patients and controls in the basal ganglia (BG) and occipital white matter (WMo) (mean ± SD)

	Choline	Creatine	Inositol	N-acetyl aspartate	glutamine/ glutamate
HCV patients – BG	1.6±0.6	8.6±1.7	3.8±1.2	7.1±1.5*	7.5±2.7
controls – BG	1.9±0.7	9.6±1.9	2.9±1.9	11.1±2.0	8.5±5.3
HCV patients – WMo	1.7±0.4	6.9±1.0	4.3±1.8	11.0±1.1	10.2±2.6
controls - WMo	1.5±0.5	5.7±1.6	3.5±1.9	9.9±3.0	9.0±4.3

*significant difference between patients and controls, p<0.01

Discussion/Conclusion

In accord with the results obtained on patients with severe cirrhosis [3,4] we found significant decrease of T2 relaxation times in the gray matter in cirrhotic patients, although hepatic encephalopathy has not been detected in any patient yet. However, observed T2 changes could be a marker of an initial stage of encephalopathy. Similarly decreased N-acetyl aspartate concentration in the basal ganglia indicates an emerging brain tissue impairment.

A significant decrease of T2 in the white matter indicates possible brain damage associated with HCV infection. Some authors described a decrease of NAA or an increase of choline/creatine ratio in the white matter associated with HCV infection [1], however we observed no significant changes in relevant metabolite concentrations compared to the control group. The spectra quantification might be affected by observed relaxation time changes, nevertheless as we use a short echo sequence, the possible error is not substantial.

References

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