STRUCTURAL BRAIN DIFFERENCES BETWEEN PATIENTS WITH NON HEPATIC LIVER CIRRHOSIS AND HCV-PATIENTS WITHOUT LIVER CIRRHOSIS

P. Raab[1], K. S. Blum[1], A. B. Tryc[2], A. Goldbecker[2], A. Tabesh[3], H. Lanfermann[1], and K. Weißenborn[2]

[1]Neuroradiology, Hannover Medical School, Hannover, Germany, [2]Neurology, Hannover Medical School, Hannover, Germany, [3]Radiology, New York University, New York, United States

Objective

Both, hepatic encephalopathy in patients with liver cirrhosis and Hepatitis-C Virus - Infection associated encephalopathy (1,2) share distinct neuropsychological features such as deficits in attention, memory and higher executive function. Thus, we were interested to find out if the two disorders show similar or different microstructural alterations in magnetic resonance imaging. ^{1}H-MR-Spectroscopy (MRS) and Diffusion Kurtosis Imaging (DKI)(3) were used to answer this question. DKI estimates the non-Gaussian diffusion pattern of water and can be interpreted as a measure of tissue structure complexity.

Methods

In this IRB approved and patient consented study we included 11 patients with chronic HCV infection but only mild liver disease, 13 patients with liver cirrhosis (MELD-score range: 7,4-22,2) not being caused by HCV infection and 18 healthy controls. Five patients were diagnosed with HE (mHE – HE III, PHES range -4 to -15). The DKI technique acquires data with diffusion encoding in 30 directions and uses 6 different b-values up to 2500 sec/mm² (dual spin echo diffusion sequence, TR 2300ms, TE 109 ms, parallel imaging factor 2, averages 2, field of view 256 mm², matrix 128², slice thickness 4mm, gap 4mm, scanning time 16min 20 sec), a 1,5T scanner was used. A T2-weighted sequence (TR 5250 ms, TE 115 ms, FOV 256 mm², Matrix 384², scanning time 2 min) was used as an anatomic reference with identical slice positioning. Diffusion data analysis was performed using an algorithm developed by A. Tabesh (4), resulting in parameter maps for mean diffusivity (MD) and mean kurtosis (MK) as well as their radial and axial derivatives and fractional anisotropy (FA). ImageJ was used for ROI placements and evaluation (basal ganglia, thalamus, rostrum and splenium of corpus callosum, deep frontoparietal white matter). A 2D-CSI-spectroscopy was performed (TE 30msec, TR 1500msec, matrix 16x16, FOV 160, 1,5cm slice thickness), the slice was angulated axially containing the thalamus and the head of the caudate nucleus. LCModel was used for spectroscopy analysis. Group data were compared using the Mann-Whitney test (SPSS 18).

Results

The cirrhotic patient group showed significantly lower mean kurtosis (MK, p=0,005) and higher mean diffusivity (MD, p=0,026) in the basal ganglia compared to the HCV patients, significantly lower MK (p=0,014) and radial kurtosis (p=0,034) in the rostrum of the corpus callosum and lower MD (p=0,026) and axial diffusivity (p=0,04) in the splenium of the corpus callosum. The data with significant differences between the patient groups were almost always on opposite sides of the normal controls data (except for MD (basal ganglia)). There was no difference in the supratentorial white matter. Compared to normal controls, non hepatitic cirrhotics show higher diffusivities (p=0,034) and HCV patients show higher MK values (p=0,008) in the basal ganglia (Fig. 1) as well as lower FA values in the thalamus (p=0,048) for HCV patients. In the basal ganglia we found significantly elevated glutamine/glutamate resonances (p=0,001) and reduced inositol (p=0.002) in the cirrhosis group compared to normal controls and HCV patients. HCV patients showed slightly higher choline resonances compared to normal controls (p=0,039).

Conclusions

DKI detects structural differences of the brain between patients suffering from HCV-encephalopathy and patients with liver cirrhosis and mild grades of HE, indicating a different cause for the cognitive deficits in both disorders, especially because the signicantly different parameters are mostly lying on opposite sides of the normal control data. The MD and MK changes and metabolic differences of the basal ganglia in the cirrhotics group can be explained by increased water content in this region and compensation mechanism due the increased ammonia levels in cirrhosis, leading to a reduced tissue structure complexity. The higher MK values in the basal ganglia of HCV patients combined with the increased choline signals compared to controls might reflect an increased difference between cellular microcompartments, maybe due to microglial activation caused by the HC virus (5). The data also indicate different microstructural changes regarding rostrum and splenium of the callosum between HCV patients and non hepatitic cirrhotics – in the rostrum changes in myelin integrity vs. axonal changes in the splenium.

References

1. Weissenborn K, Krause J, Bokemeyer M, Hecker H, Schuler A, Ennen JC, Ahl B, Manns MP, Boker KW. Hepatitis C virus infection affects the brain-evidence from psychometric studies and magnetic resonance spectroscopy. J Hepatol 2004;41(5):845-851.
2. Forton DM, Thomas HC, Taylor-Robinson SD. Central nervous system involvement in hepatitis C virus infection. Metab Brain Dis 2004;19(3-4):383-391.
3. Jensen JH, Helpern JA, Ramani A, Lu H, Kaczynski K. Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic resonance imaging. Magn Reson Med 2005;53(6):1432-1440.
4. Tabesh A, Jensen JH, Ardekani BA, Helpern JA. Robust estimation of kurtosis and diffusion tensors in diffusional kurtosis imaging. 2010; Stockholm, Sweden.
5. Bokemeyer M, Ding XQ, Goldbecker A, Raab P, Heeren M, Arvanitis D, Tillmann HL, Lanfermann H, Weissenborn K. Evidence for neuroinflammation and neuroprotection in HCV infection-associated encephalopathy. Gut 2010.
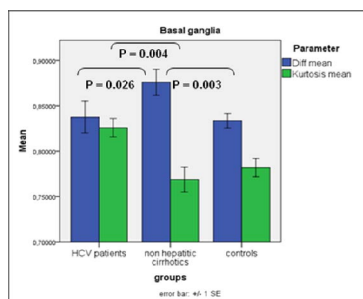
Figure 1.
Diagram showing the significant differences for DKI data in the basal ganglia between the HCV and cirrhosis groups. For comparison the mean data for normal controls are shown as well.