H-MRS study of the neurochemical effects of interferon-α treatment in patients with chronic hepatitis C

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Introduction

People with chronic hepatitis C virus (HCV) infection commonly experience neuropsychiatric side effects, particularly during treatment with interferon-alpha (IFN-α). Proton magnetic resonance spectroscopy (MRS) studies have revealed changes in cortical neurochemistry during HCV infection including elevated choline which are thought to reflect a central inflammatory response [1,2]. However, the effect of treatment on these measures has not previously been described. The recent development of the SPECIAL sequence [3] allows for resolution of an increased range of metabolites than have previously been studied in hepatitis C infection. The current study aimed to clarify the cortical neurochemistry of chronic HCV infection and the effect of treatment with IFN-α.

Methods

Patients with chronic HCV infection, without evidence of cirrhosis, starting treatment with IFN-α were compared to healthy controls. Healthy controls were observed at a single time point, while the patients were each observed at two time points - pre-treatment and after four-six weeks treatment. All experiments were performed on a 3 Tesla Siemens TIM Trio scanner with a body coil transmitter and a 12-channel head receiver array. First, a three-plane localizer image was obtained followed by a high-resolution, whole brain T_1-structural image. A 2 x 2 x 2.5 cm voxel was manually placed in the posterior cingulate cortex (PCC), and localized spectra were obtained using the SPECIAL sequence [3] (TR/TE = 3000/8.5 ms, 192 averages). Spectral analysis was performed using LCModel, and basis sets were obtained by quantum mechanical simulation of all of the relevant metabolites under the relevant pulse sequences and echo-times. All subjects provided informed written consent to participate in the study, and full approval was obtained from the appropriate local ethics committee.

Results

Initial results from 6 patients and 6 controls are described. Measures referenced to tissue water (Figure) suggest that HCV infection is associated with elevated choline and decreased phosphoethanolamine (PE). Glutathione (GSH) also appears elevated in some individuals. These findings tend to normalise with IFN-α treatment. No difference in N-acetylaspartate (NAA) or myo-inositol (mI) is apparent between groups.

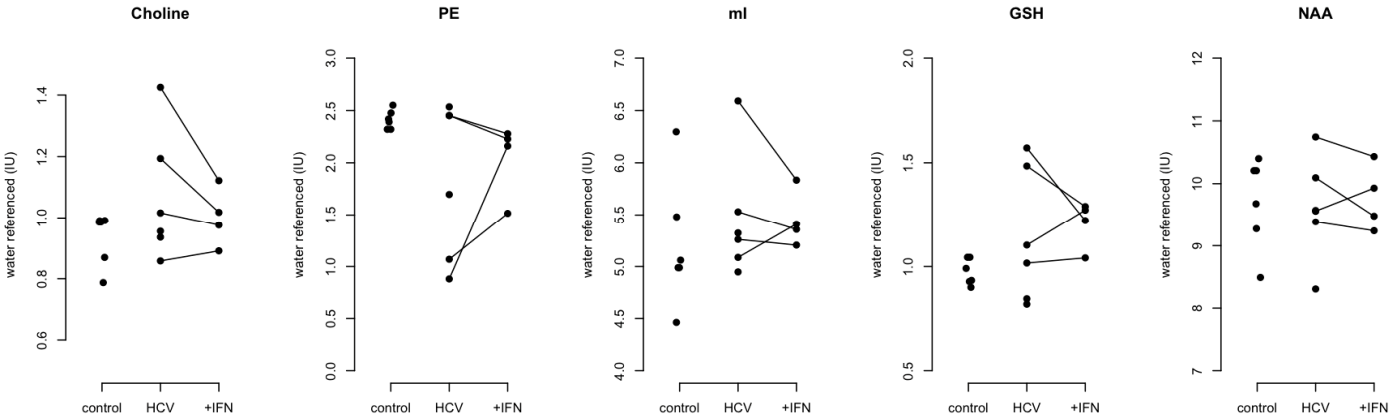

Figure – Levels of choline, PE, mI, NAA, and GSH referenced to water. Data from controls, HCV patients at baseline and during IFN-α treatment.

Discussion

Elevation of choline and decreased PE in chronic HCV infection suggest alterations in membrane turnover consistent with an inflammatory response. The elevation in levels of the antioxidant, GSH, may be an adaptive response to increased oxidative stress, which has been observed in liver in HCV infection. Substantial overlap is observed between patients and controls on all measures. This suggests that abnormalities may be present in only a subset of cases.

References.

1 Forton et al. *Lancet* 2001;358:38-9.
2 Bokemeyer et al *Gut* In Press
3 Mekle et al *Magn Reson Med*. 2009;61:1279-85.