Downfield Spectra at Ultrahigh Field

A. Henning[1], A. Fuchs[1], C. Boesch[2], P. Boesiger[1], and R. Kreis[2]

[1]Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland, [2]Department of Clinical Research, University Berne, Berne, Switzerland

Introduction

MR spectroscopy is one of the most promising applications for 7T human MR systems. Profiting from SNR gain as well as increased spectral resolution, detection and quantification of an increasing number of metabolites as compared to lower field strength becomes feasible. While these advantages have been exploited for the upfield part of the human cerebral ^{1}H spectrum [1], the downfield part (5 -10ppm) is still poorly characterized.

In this work, 7T downfield spectra from the human periventricular white matter are presented, compared to corresponding spectra recorded at lower field strength and characterized regarding contributing metabolites and relaxation behaviour and in view of chemical exchange. Both - protons bound to carbon atoms in aromatic compounds, as well as amide protons can be observed. Additional metabolites in comparison to the upfield spectrum such as ATP and homocarnosine (hCs) should be detectable; the amide protons of the NH_2 group in glutamine (Gln) should allow its unambiguous distinction from glutamate. Potentially, additional resonances visible in the downfield part as well as changes in the chemical exchange rates of amide protons and the chemical shift of the imidazole ring resonances of hCs might become important disease markers. Prominent examples are the accumulation of phenylalanine in neuronal tissue of patients suffering from phenylketonuria or of Gln in hyperammonemia [2,3,4].

Materials and Methods

Spectra were recorded on a 7T Philips Achieva scanner using a transmit-receive head coil and compared to previously published spectra recorded on a 3T Siemens Trio and a 1.5T GE Signa scanner [5]. Data acquisition at 7T was performed with STEAM using broadband frequency modulated excitation pulses [6], which enabled a minimized chemical shift displacement at short echo times (TE_{min} = 18 ms). To avoid perturbation of the downfield spectrum by gradient induced water sidebands a B_1- and T_1- insensitive eight-pulse VAPOR water suppression scheme was applied [7]. Third-order localized shimming based on FASTERMAP was available. 7T spectra obtained in four healthy subjects are presented. Baseline corrections and elimination of residual water by HLSVD was applied in some spectra.

Results and Discussion

In contrast to 1.5T and 3T, at 7T the macromolecular baseline appears less prominent at the minimal echo time of 18 ms due to the overall shortening of T_2 relaxation times. Hence, the reduced macromolecular signal, with main peak intensity between 7 and 9 ppm [3], and the intrinsically larger spectral separation render the downfield resonances better distinguishable at 7T for TE 20 ms. This effect is especially obvious for the most prominent downfield peak of the NAA amide proton at 7.82 ppm ***(Figure 1***). The reproducible spectral features observed at 7T are illustrated in **Figure 2**, where the results from three volunteers are presented. They include two peaks at 5.9 ppm and 6.1 ppm, which are ambiguous at lower field strength. While the resonance at 5.9 ppm presently remains unassigned, the one at 6.1 ppm can be tentatively attributed to ^{1}CH of ATP Ribose [8]. The 7T spectrum also shows peaks that occur at the positions expected for the adenosine resonances of ATP: ^{2}CH (8.22 ppm), ^{8}CH (8.514 ppm) and NH_2 (6.755 ppm). However, the two peaks at 8.2 ppm and 8.4 ppm are best discernable at 3T. The peak at 6.8 ppm seems to have two components with slightly different relaxation behaviour (c.f. spectra at TE 40ms at 1.5 and 3T, **Figure 3**). It can be due to ATP (6.755 ppm) and also to a Gln amide proton (6.816 ppm) ***(Figures 2 & 3)***. The second amide resonance of Gln expected at 7.52 ppm is missing at all field strengths, which can be explained by its exchange with (suppressed) water that occurs faster than for the proton at 6.8 ppm [9]. The resonance at 7.07 ppm has been assigned to hCs previously and shows a pH dependent chemical shift. However, the hCs concentration is with 0.2-0.6 mM comparatively low and hence its intensity cannot be fully explained by hCs. If exchange with water does not prevent detection, two amide peaks of glutathione (GSH) might contribute: the ^{9}NH proton (7.15 ppm [8]) of the glycine moiety would overlay with this hCs peak (7.08 ppm), while the cysteine ^{6}NH at 8.18 ppm could explain the intensity differences between the two ATP singlets at 8.22 and 8.51 ppm. Amide protons of hCs would occur at 6.4 ppm (ambiguous peak at 7T) and at 7.88 ppm where it would be overlaid by NAA. The further hCs imidazole resonance at 8.08 ppm fits with a long TE peak at lower fields, but has no striking counterpart at 7T. Other remarkable field dependences occur for the relaxation behaviour of the peak at 7.27 ppm and the NH peak of NAA. At 7T, the 7.27 ppm peak, which is possibly due to a NH of PCr, is relaxed already at TE = 36ms, while at 1.5 T it is still visible at TE = 120 ms [5]. One might be tempted to speculate about PCr binding to creatine kinase leading to partial immobilization in this context. The NAA peak, on the other hand, shows apparently faster relaxation at low fields (± decayed at 60 ms at 1.5T, but prominent > 50 ms at 7T). Peak overlap may partly explain this puzzle.

In summary, the downfield part of the spectrum, as obtained at very high fields, is better resolved than at lower fields and yields relevant facts to clarify peak assignments. Field-dependent relaxation behaviour is evidenced and promises to provide information on molecular mobility and milieu.

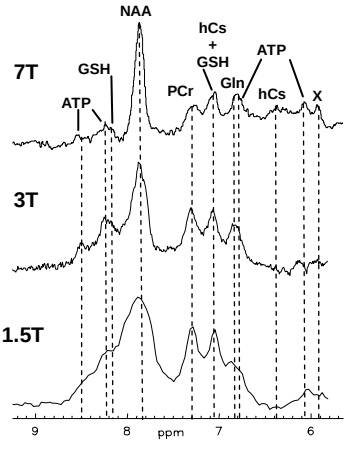

Figure 1: *Downfield spectra from the human periventricular white matter at different field strengths: different resolution and baseline, but reproducible spectral patterns, (TE = 18-20 ms, average of 3 volunteers each).*

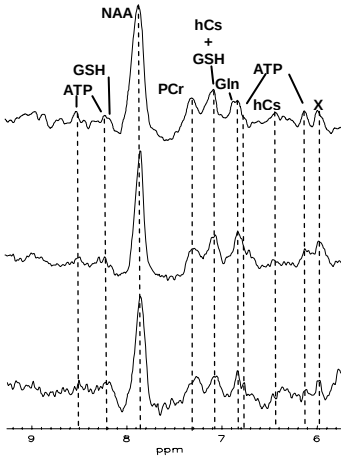

Figure 2: *Downfield spectra from the human periventricular white matter at 7T: reproducible spectral patterns between 5.8 ppm and 9.2 ppm for three healthy volunteers.*

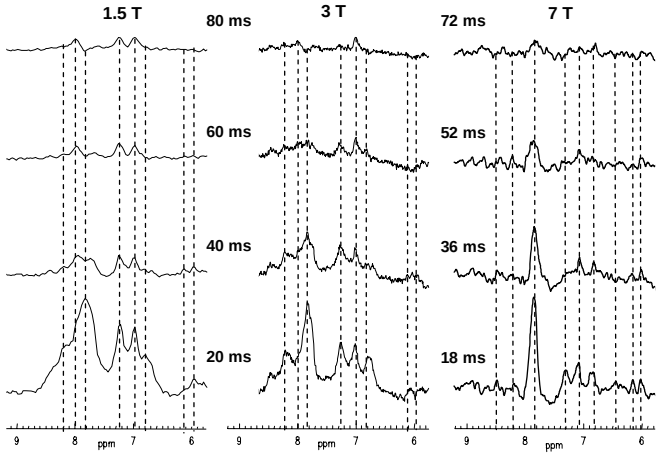

Figure 3: *T_2 relaxation behaviour of the various downfield resonances at 1.5T, 3T and 7T (TE = 20 – 80 ms at 1.5T and 3T, and TE = 18 – 72 ms at 7T; TR= 2 – 3s).*

[1] Tkac I et al., Magn Reson Med (46):451-456; 2001. [2] Kreis R et al, Proc ISMRM (5):24; 1998.
[3] Kreis R et al., Proc ISMRM (11):303; 2004. [4] Mori s et al, Proc ISMRM (4): 536 1997.
[5] Kreis R et al., Proc ISMRM (14):2636; 2006. [6] Henning A et al., Proc ISMRM (15):776; 2007.
[7] Tkac I et al., Magn Reson Med (41): 649-56; 1999. [8] Govindaraju V et al., NMRB (13): 129; 2000.
[9] Kanamori K et al.. JMR B (107):107;1995. *Supported by the Swiss National Science Foundation*