Hyperpolarized ^{13}C acetate detection in the rat brain in vivo

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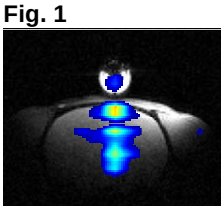
Introduction

^{13}C MRS in conjunction with infusion of a labeled compound has become a very important tool to investigate brain energy metabolism in vivo. However, due to the limited SNR of ^{13}C MRS, such studies of label kinetics require infusion of a tracer over hours, to allow observation of the complete turnover of label until a static state is reached. Hyperpolarization of metabolites labeled with ^{13}C carbon isotopes allow to enhance the MRS signal by a 10000fold for a short time. 1-^{13}C-Acetate is known as a suitable precursor to investigate glial metabolism and can be hyperpolarized [1]. The aim of this study was to investigate the feasibility to study acetate metabolism in the rat brain with infusion of hyperpolarized 1-^{13}C-acetate.

Fig. 1



Materials and Methods

Three Male Sprague-Dawley rats (w = 354 ± 47 g) were anesthetized using 1.5% isoflurane and a femoral vein was catheterized for injection. Animal physiology was monitored. A surface coil consisting of a quadrature proton coil and a single 3-loop carbon coil was placed on top of the rat head and the animal positioned in a Varian Inova 9.4T 31 cm bore actively-shielded animal spectrometer.

10 seconds after injection of the hyperpolarized solution of 1-^{13}C-Acetate (procedure and hardware are described elsewhere [1,2]) 20 spectra were acquired with a 45^0 BIR4 and a repetition time of 3 s. One additional experiment was performed in the same manner to prove the localization of signal in the rat brain using spectroscopic imaging with a spin echo EPI sequence derived from FASTESTMAP [3].

The acetate decay was corrected for magnetization loss due to preceding RF pulses.

To find the T1 representing best the decay of the acetate signal, the first quarter, the first half, the first three quarters and all data points were fitted with a monoexponential curve. This resulted in T1 values ranging from 12 to 17 s. This lead to the assumption, that two mechanisms has to be expected to cause the observed signal to decay over time, i.e. T1 relaxation and label efflux out of the acetate pool. Hence the signal curve was fitted with a biexponential function.

Fig. 2

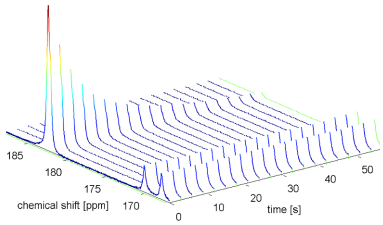
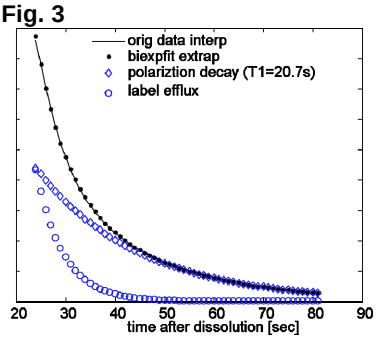


Fig. 3



Results

Fig. 1 shows the twofold interpolated and smoothed metabolic map of acetate localizing the acquired signal mainly in a central vessel and in the brain tissue. The 20 acquired spectra summed over the three experiments show the decay of acetate signal (182.6ppm) (Fig. 2) including the doublet arising from the formic acid reference at the RF coil center.

The biexponential fit of the decay (Fig. 3) yielded a T1 of 21 s and another exponential rate λ = 0.1 min. The separated exponential decays are added to the plot (diamonds & circles), demonstrating that one of the curves better fits the first half of the decay whereas the other exponential better represents the second half. The T1 in vivo was shorter than in vitro (T1~35s, data not shown). Assuming that the latter exponential decay is due to label efflux out of the acetate pool only ([ace] = 0.6 µmol/g), this yields an apparent efflux rate of V_{ex}= [ace] / λ =6.5 µmol/(g*min).

Fig 4 summarizes the summed spectra of all three rats in four stacked spectra resulting from the sum of subsequent five spectra. The extra line at 174.1 ppm marks a label at a currently unassigned peak. The following plot in Fig. 5 demonstrates that the signal at 174.1 ppm is decaying slower than that of acetate. For better visualization the acetate signal has been scaled down by a factor of 100.

Fig. 4

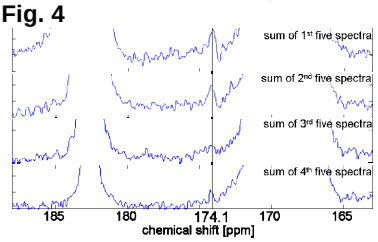
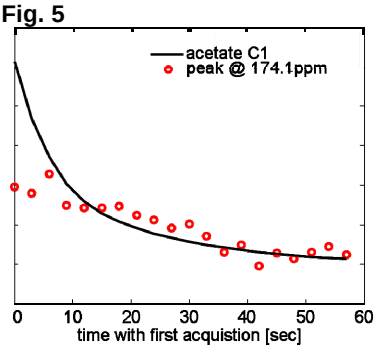


Fig. 5



Discussion & Conclusions

The study demonstrated the feasibility to investigate glial metabolism with infusion of hyperpolarized 1-^{13}C-acetate. An enhanced signal of the infused acetate could be detected in the brain. Localization was confirmed by spectroscopic imaging. Furthermore it was found that the decay of the signal is caused not only by the T1 relaxation but also on other mechanisms, which could be related to label flow kinetics. However, if this decay is interpreted as an efflux V_{ex} and calculated as described above, it is much higher than reported values of fluxes involved in brain metabolism. Thus this interpretation could indicate that more complex mechanism of label fluxes, such as label recirculation.

An unexpected peak was found at 174.1 ppm. Its signal is decaying at a slower rate than the acetate signal.

References

[1] Comment, ISMRM 2007, 369; [2] Comment, Conc Magn Reson 31B (2007) p. 255; [3] Cunningham, JMR 187(2) (2007), p. 357

Acknowledgements

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