In vivo DNP-enhanced 13C labeled acetate brain studies in a 9.4T animal scanner

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Introduction

^{13}C MRS label experiments are widely used to investigate brain metabolism *in vivo*. Nevertheless, because of the low sensitivity, application of conventional ^{13}C MRS is limited to the measurement of label in highly concentrated compounds such as Glutamate. Hyperpolarization by means of Dynamic Nuclear Polarization (DNP) provides a way to increase the signal of ^{13}C tracer by several thousand-fold. The injection of such a DNP-enhanced label allows for the measurement of low ^{13}C concentration in tissue and potentially to follow its metabolism provided the signal is measured from a ^{13}C resonance with sufficiently long T_1. Acetate, which is readily taken up by the brain, is thus an excellent candidate for the study of glial metabolism, with low concentrations of metabolic products. The goal of the present study was to establish the feasibility of DNP-enhanced 1-^{13}C acetate infusion in animals placed in a narrow-bore high-field imager and the subsequent detection of a largely increased ^{13}C signal in the *in vivo* rat brain.

Methods

The carbon nuclear spins of a glassy frozen 1-^{13}C labeled sodium acetate solution were dynamically polarized in a 3.35T field and at a sample temperature of 1.2K [1]. The obtained low-temperature maximum polarization on the 1-^{13}C of sodium acetate was about 10% corresponding to a factor 125 larger than the equilibrium value at the same field and temperature. The polarization time constant was about 400 seconds, which means that about 99% of the maximum polarization value was obtained after 30 minutes of microwave irradiation. Once polarized, the sample was rapidly dissolved with water vapor using a procedure similar to the one developed by Ardenkjaer-Larsen *et al.*[2]. The final sodium acetate concentration of the solution before injection was 0.3M and contained ~2mM of TEMPO (2,2,6,6-Tetramethylpiperidoxyl) free radical that provided the paramagnetic centers needed in the initial DNP process. The solution was then blown with He gas into a home-built injection pump through a 6m long PTFE tube. The pump was placed close to the animal in the scanner magnet. It is designed to separate the He gas from the liquid solution prior to injection into the animal, so as to obtain a highly reproducible remote injection of DNP-enhanced solutions into anesthetized rats, and to avoid unnecessary loss of polarization.

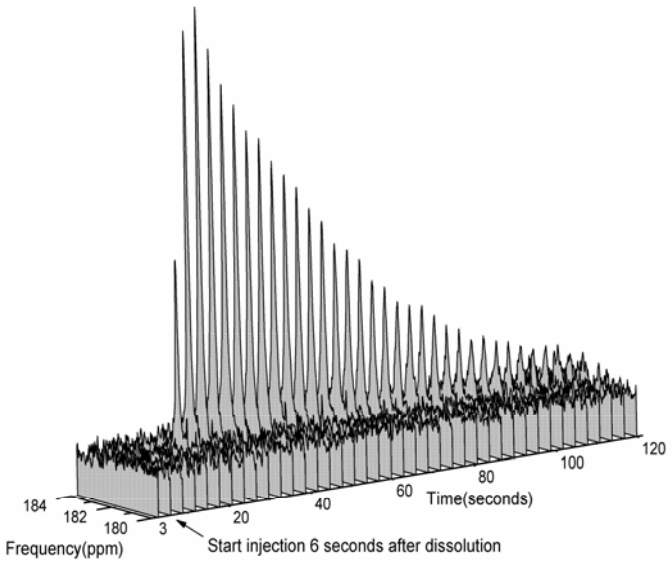

Figure 1. Time evolution of the *in vivo* rat brain ^{13}C signal after injection of the DNP-enhanced ^{13}C-labeled acetate solution.

Results and Discussion

The injection of 2.5ml of 0.3M acetate solution into the femoral vein of several Sprague Dawley rat was started exactly 6 seconds after the dissolution. A ^{13}C spectrum of the rat brain was acquired with a 10 mm diameter surface coil every 3 seconds with an adiabatic 10 degree BIR-4 pulse. The time evolution of the ^{13}C signal is shown in Fig.1. A strong signal at the frequency of the carboxyl ^{13}C of sodium acetate was detected 15 seconds after the injection. The characteristic decay time of the signal was found to be on the order of 30 seconds. Since the actual time evolution of the acetate concentration in the brain is not known, it was not possible to determine the *in vivo* enhancement factor of the signal. However, the enhancement was found to be larger than 2500 when the solution was injected into a phantom, the theoretical maximum value being of the order of 10000.

Conclusions

These results show that a highly enhanced carboxyl ^{13}C signal from sodium acetate can be obtained by DNP using a widely available free radical. The *in vivo* characteristic decay time of this ^{13}C signal should be sufficient to allow the study of brain metabolism. It was demonstrated that such a study can be performed in narrow bore experimental MR scanner without the need of moving the animal and with complete remote control of the injection procedure and that therefore recording high resolution ^{13}C spectra of brain metabolites is feasible in rodents at high fields.

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