Hyperpolarized ^{13}C MRS in the Rat Brain: Spectral Improvements with ^{1}H Decoupling

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Introduction

Most *in vivo* studies using the dynamic nuclear polarization (DNP) technique (1) to enhance sensitivity of ^{13}C have been utilizing molecules with ^{13}C labeled quaternary carbons. In the most often used [1-^{13}C]pyruvate, ^{13}C labeled carbon does not have any ^{1}H attached to it and experiences only small *J*-coupling with ^{1}H's three bonds away. In case of [2-^{13}C]pyruvate and [1-^{13}C]lactate, ^{13}C labeled carbon also does not have any ^{1}H attached to it, but it is *J*-coupled to ^{1}H's which are two bonds away. The *J*-coupling structure can be very useful for providing qualitative molecular structure information. However, for *in vivo* application, this splitting structure is undesirable since *J*-splittings distribute signal intensity over many smaller peaks and therefore reduce detection sensitivity. In this work, we investigate the effects of heteronuclear *J*-coupling on hyperpolarized [1-^{13}C]pyruvate and [2-^{13}C]pyruvate signals and their metabolic products.

Methods

A mixture of [1-^{13}C]pyruvic acid and OX63 trityl radical and and [2-^{13}C]pyruvic acid and OX63 trityl radical were hyperpolarized by DNP (Hypersense, UK) for 90 min in a field strength of 3.35 T at approximately 1.4 K (1). The sample was then dissolved in 40 mM TRIS buffer, 40 mM NaOH and 0.32 mM Na_2EDTA solution to produce 4 mL of hyperpolarized solution at a concentration of ~35 mM. *In vivo* experiments were performed using a 9.4-T/31-cm bore magnet equipped with a Varian INOVA spectrometer. Fasted male Sprague-Dawley rats were injected intravenously with approximately 2.2 mL of hyperpolarized [1-^{13}C]pyruvate or [2-^{13}C]pyruvate under isoflurane anesthesia.

In vivo ^{13}C NMR spectra were acquired using a coil assembly consisting of a ^{1}H quadrature surface coil (two loops of 14 mm diameter) and an inner ^{13}C linearly polarized surface coil (12 mm diameter). A small sphere filled with ^{13}C labeled formic acid placed at the center of the coil served as external reference. Decoupled and undecoupled spectra were acquired one after another 10 s after injection of a hyperpolarized [1-^{13}C]pyruvate solution with LASER sequence (2) adapted for ^{13}C spectroscopy and using a 45° BIR4 pulse for excitation. The ^{1}H decoupling was performed using WALTZ-16.

Results and Discussion

Figure 1 shows representative spectra obtained with ^{1}H decoupling from 400 µL voxel placed in the rat brain. Table 1 reports the effects of decoupling on linewidths. The linewidth of [1-^{13}C]pyruvate signal was narrower by 1.2 ± 0.3 Hz with decoupling and [1-^{13}C]lactate signal by 6.3 ± 0.6 Hz.

Table 1. Effects of decoupling on linewidths reported in Hz (4 animals, 10 dissolutions).

Undecoupled linewidths		Decoupled linewidths		Difference in linewidths	
[1-^{13}C]pyr	[1-^{13}C]lac	[1-^{13}C]pyr	[1-^{13}C]lac	[1-^{13}C]pyr	[1-^{13}C]lac
7 ± 1	12.8 ± 0.9	6 ± 1	6.4 ± 0.6	1.2 ± 0.3	6.3 ± 0.6

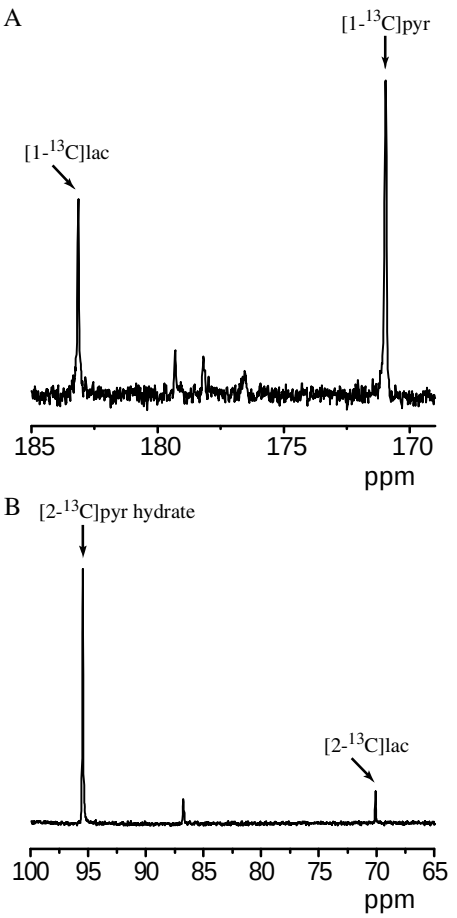

Figure 1. Representative localized spectra obtained after injection of hyperpolarized (a) [1-^{13}C]pyruvate and (b) [2-^{13}C]pyruvate solutions with ^{1}H decoupling from 400 µL brain voxel (LASER, T_R = 0.75 s, T_E = 27 ms, lb = 1 Hz).

The effect of decoupling on SNR was difficult to determine *in vivo* due to the loss of magnetization caused by a 45° BIR4 excitation pulse. Therefore, to obtain information about effects of decoupling on SNR simulations were performed using values of long-rage *J*-couplings and assuming a linewidth of 6 Hz, consistent with *in vivo* data. The effects of decoupling on SNR are reported in Table 2. There was almost no improvement in SNR for [1-^{13}C]pyruvate signal. Decoupling improved SNR for [1-^{13}C]lactate signal by 50%. The improvement in SNR was even greater for [2-^{13}C]pyruvate and [2-^{13}C]lactate signals. The larger improvement for [2-^{13}C]lactate signal was expected due to the large value of one bond *J*-coupling. The improvement in the linewidth in the simulations was consistent with experimental data (Table 1).

Table 2. Effects of decoupling on SNR reported as ratio of decoupled to undecoupled SNR.

[1-^{13}C]pyr	[1-^{13}C]lac	[2-^{13}C]pyr	[2-^{13}C]lac
1.01	1.51	1.85	2.61

Conclusions

^{1}H decoupling significantly improved the linewidth and signal-to-noise ratio of [1-^{13}C]lactate, [2-^{13}C]pyruvate and [2-^{13}C]lactate. Negligible improvement was observed for [1-^{13}C]pyruvate, consistent with very small three bond *J*-coupling.

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