Hyperpolarized ^{13}C MRS in the Rat Brain: Spatial Origin of Signals

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Introduction

The low sensitivity of ^{13}C spectroscopy can be enhanced using dynamic nuclear polarization (DNP) technique (1). Detection of [1-^{13}C]pyruvate and its metabolic products have been reported in kidney, liver, muscle (2,3), and brain (4). In this work, we investigate the spatial origin of [1-^{13}C]pyruvate and [1-^{13}C]lactate signals in rat brain.

Methods

A mixture of [1-^{13}C]pyruvic acid and OX63 trityl radical was hyperpolarized by DNP (Hypersense, UK) for 90 min in a field strength of 3.35 T at approximately 1.4 K (5). 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 under isoflurane anesthesia.

In vivo decoupled-^{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) with a small sphere placed inside filled with ^{13}C labeled formic acid. Spectra were acquired with two pulse sequences: pulse-acquire with 4.5° and 90° pulse angle and LASER sequence (6) adapted for ^{13}C spectroscopy.

Results

All spectra, acquired with different pulse sequences and from different brain regions, were obtained 9 s after beginning of an injection of hyperpolarized solution. Figure 1A shows a spectrum obtained with a small flip angle (4.5° at the coil center) pulse-acquire sequence. The intensity of [1-^{13}C]lactate signal is 16% of [1-^{13}C]pyruvate signal. Figure 1B shows a spectrum obtained with a pulse-acquire sequence where an adiabatic 90° BIR4 pulse was used. [1-^{13}C]alanine and ^{13}C-labeled bicarbonate are detected in this experiment. The intensity of [1-^{13}C]lactate signal is 52% of [1-^{13}C]pyruvate signal. Figure 1C shows a spectrum obtained from the brain (VOI of 400 μL) with LASER sequence adapted for ^{13}C spectroscopy where the same BIR4 pulse as in Figure 1B was used for excitation. The intensity of [1-^{13}C]lactate signal is 163% of [1-^{13}C]pyruvate signal. Figure 1D shows a spectrum obtained from the skin (VOI of 200 μL) with the same sequence used to obtain spectrum in Figure 1C. The intensity of [1-^{13}C]lactate signal is 10% of [1-^{13}C]pyruvate signal.

Discussion and Conclusions

The ratio of intensities of [1-^{13}C]lactate to [1-^{13}C]pyruvate are very similar for spectra obtained using a small flip angle and from the skin voxel suggesting that information obtained using small flip angles with surface coil is mostly coming from the skin. With larger, adiabatic pulse, signal is a mix of signal coming from skin and brain tissue including blood. When signal is localized in the brain, the ratio of [1-^{13}C]lactate to [1-^{13}C]pyruvate drastically changes. This suggests that the large part of [1-^{13}C]lactate signal comes from brain tissue.

We conclude that when using surface coil with small flip angle pulse-acquire, the ^{13}C information obtained is mainly reflecting the metabolism of [1-^{13}C]pyruvate within the subcutaneous fat and veins.

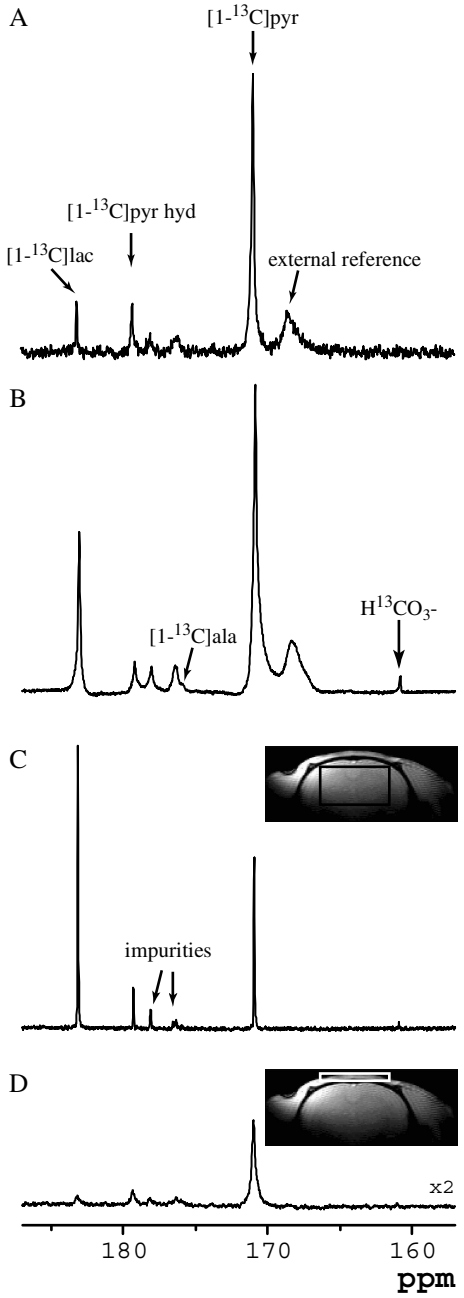

Figure 1. Single-shot ^{1}H decoupled ^{13}C spectra acquired from the rat 9 s after beginning of injection of hyperpolarized solution with (a) small angle pulse-acquire, (b) 90° BIR4 pulse-acquire, (c) LASER sequence (brain voxel), (d) LASER sequence (subcutaneous fat voxel). To better see the resonances, vertical scale was increased two times as compared to spectrum in (c).

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