Localized spectroscopy in the rat brain following hyperpolarized [2-^{13}C]pyruvate injection

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Introduction. The possibility of injecting hyperpolarized ^{13}C labeled molecules into living systems has opened the prospect of detecting metabolites *in vivo* that have not been detectable with conventional NMR techniques. As an example, alanine has been readily observed in tumors following boluses of [1-^{13}C] pyruvate (1). Potential of using hyperpolarized substances in the brain remains to be explored. Last year we presented our first results using [1-^{13}C] and [2-^{13}C] pyruvate in the rat brain (2,3). In the present work, we acquired time courses of [2-^{13}C] pyruvate and its products in the brain and blood, as well as localized ^{13}C-LASER spectra in the brain.

Materials and Methods. Twelve male Sprague-Dawley rats (274 ± 14 g) were used in this study. Four of the rats were fasted overnight before the experiment. All were anesthetized with isoflurane and intubated. Cannulation of the two femoral arteries and of one vein was performed to allow for physiological monitoring, blood gas analysis and hyperpolarized [2-^{13}C] pyruvate solution injection, respectively. Hyperpolarized [2-^{13}C]pyruvate was obtained by DNP technique with OX63 trityl radical and dissolved in 4 ml of a solution containing 40 mM TRIS buffer, 40 mM NaOH and 0.32 mM Na_2EDTA using a HyperSense system. Between 2 and 2.2 ml of the hyperpolarized solution was injected into each animal. NMR experiments were performed on a horizontal 9.4 T Oxford magnet equipped with a Varian INOVA console. Low-flip angle pulse acquire data were acquired in 3 animals (flip angle 4.5º at the center of the coil, TR = 0.75 s). In the 4 fasted animals and in 5 non-fasted animals, a voxel including the whole brain (9 × 5 × 5 mm^3) was acquired using LASER (flip angle 90º, TE = 29 ms) with WALTZ-16 decoupling.

Results and discussion. Unlocalized time courses were obtained for [2-^{13}C]pyruvate, [2-^{13}C]pyruvate hydrate and [2-^{13}C]lactate (a). The formate resonance (169.7 ppm) from the reference is used to define the ppm scale. When several scans were summed, two other small signals were observed at 149 ppm and 86.7 ppm in all rats, corresponding probably to impurities in the pyruvate preparation (b). The spectrum in Figure 1d was acquired from the voxel shown in Figure 1c using ^{13}C-LASER. The good quality of the localization is illustrated by the absence of the formate resonance. In the fasted animals, a signal at 182.8 ppm was visible. This signal was not present in the non-fasted rats, suggesting that this resonance, possibly a carboxyl group coming from a fatty acid, is produced in the liver and transported to the brain.

Conclusion. We have observed an unidentified resonance at 182.8 ppm when the animals were fasted. Further investigation is needed to determine the origin of this signal.

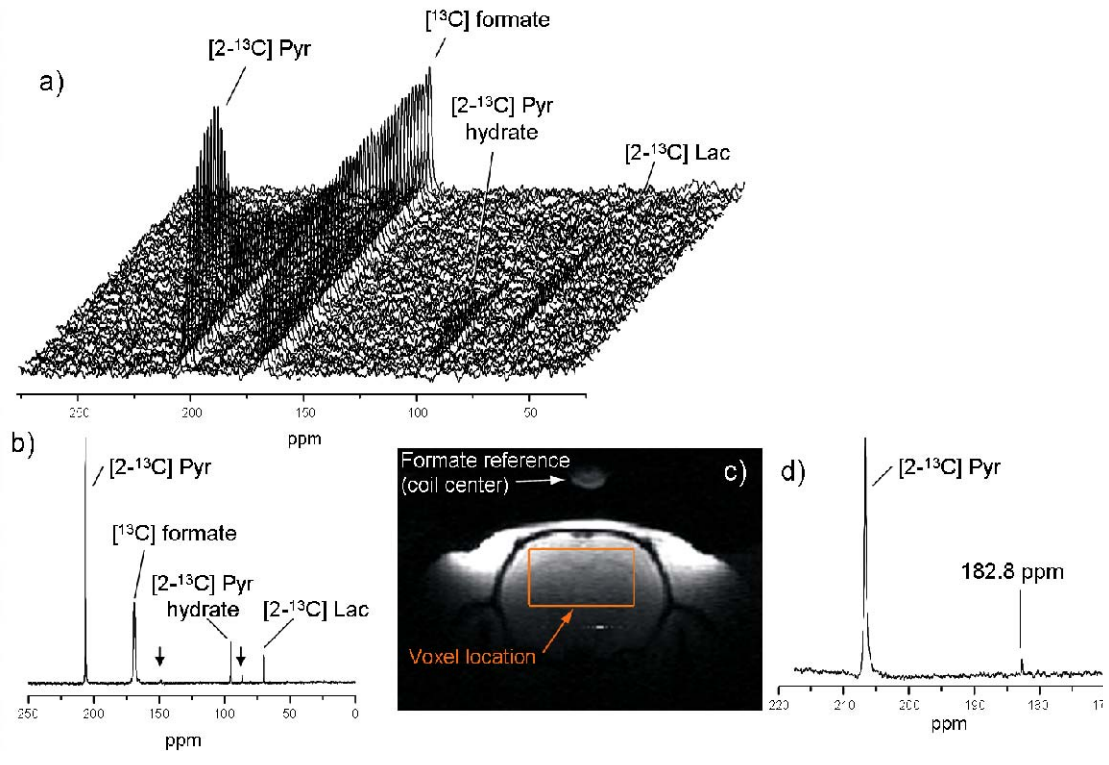

Figure 1. Hyperpolarized [2-^{13}C] pyruvate in the rat brain.
a) Time courses obtained *in vivo* using a low flip-angle pulse acquire acquisition scheme.
b) Sum of 68 scans regrouping 4 dissolutions (3 different rats). The arrows indicate two peaks at 149 and 86.7 ppm, probably corresponding to impurities.
c) Coronal view of the rat brain. A 9 × 5 × 5 mm^3 voxel was positioned in the brain below the sagittal sinus to limit contamination by signals from the blood. (orange box).
d) Spectrum obtained from a fasted rat. The signal at 182.8 ppm was acquired 18 seconds after injection of hyperpolarized solution.

References. 1. Golman K, et al. *Cancer Res 2006; 66:10855-10860.* **2.** Deelchand DK, et al. *Proc Intl Soc Magn Reson Med 2008; 16:3196.* **3.** Iltis I, et al. *Proc Intl Soc Magn Reson Med 2008; 16:1748.*
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