In Vivo ^{13}C Spectroscopy of Human Brain on a Clinical 3T Scanner Using [2-^{13}C]Glucose Infusion

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INTRODUCTION

[1-^{13}C]glucose is commonly used in human brain ^{13}C MRS studies. It was reported in a recent monkey brain study that using [2-^{13}C]glucose has important advantages for in vivo ^{13}C spectroscopy (1). The kinetics of ^{13}C label incorporation from [2-^{13}C]glucose into glutamate C5, glutamine C5 and GABA C1 are identical to those from [1-^{13}C]glucose into glutamate C4, glutamine C4 and GABA C2, respectively. Because the carboxylic and amide carbons have very weak long-range ^{1}H-^{13}C couplings, broadband decoupling can be achieved using pseudo noise waveforms with low RF power (1, 2). In addition, contamination from subcutaneous lipid signals is no longer an issue because lipids do not resonate in the vicinity of glutamate C5, glutamine C5 or GABA C1. Here we report, for the first time, in vivo detection of the metabolism of [2-^{13}C]glucose in the carboxylic/amide carbon region of the human brain. The study was performed on a standard clinical 3 Tesla scanner.

METHODS

Experiment setup: ^{13}C spectroscopy experiments were performed on a standard GE 3 Tesla MRI scanner. The standalone proton decoupler, ^{13}C TR switch, preamplifier and filters were provided by GE. Pseudo noise decoupling waveforms were generated from the decoupler with bi-level outputs: low level pulsing during relaxation to generate NOE enhancement and high level pulsing during data acquisition for proton decoupling. The duration of noise waveform repetition unit was 1.2 ms. Output level switching was triggered by a TTL signal from the MR scanner. RF coil assembly included a single-loop ^{13}C surface coil (dia. = 7 cm) and a quadrature proton surface coil mounted on a half cylindrical tube (dia. = 20 cm). The coil was placed underneath the human head. ^{13}C spectra localized by the surface coil were acquired in the occipital lobe region. A one pulse sequence was used with spectral width = 5 kHz, number of points = 1024, acquisition time = 204.8 ms, TR = 4 s, and NS = 64. A 500 μs nominal 45° hard pulse was used for ^{13}C excitation. The decoupling power forwarded into proton RF coil was 15 W during the decoupling and 0.5 W during NOE. After considering the loading effect, about 75% of the forwarded power was deposited into subject's head. Due to the hardware limitation, only first order B_0 field shimming was performed through proton channel using a localized PRESS sequence on a single voxel of 5x5x5 cm^3 in the occipital lobe region anterior to the ^{13}C coil.

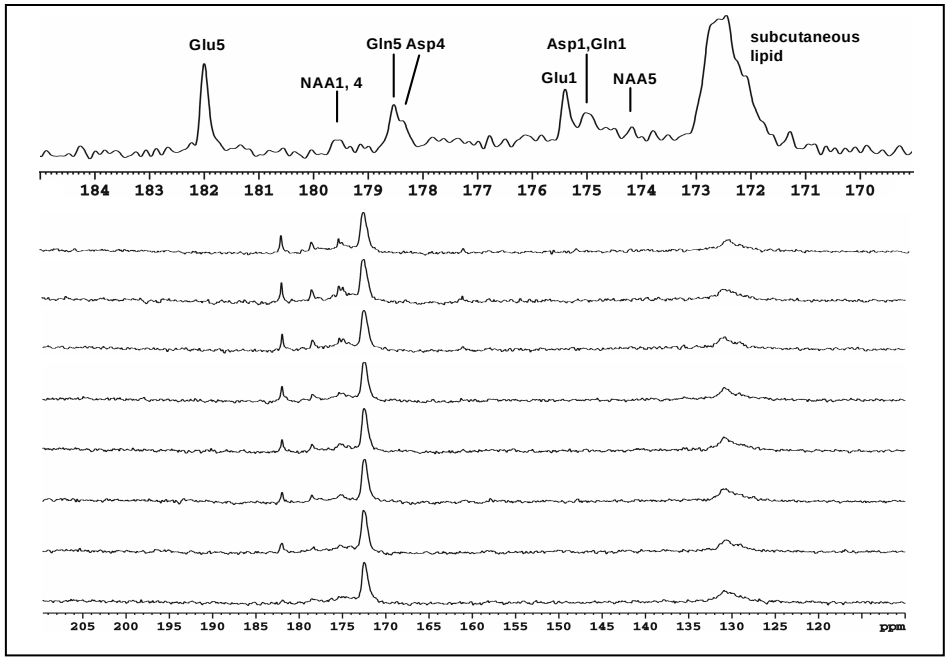
[2-^{13}C]glucose infusion protocol: Two healthy male and one female volunteers (60-67 kg) were examined. Glucose infusion began with a bolus injection of 60 mL solution containing 33.3% [2-^{13}C]glucose solution within 10 min via the antecubital vein. After the bolus injection, a solution containing 14% [2-^{13}C]glucose was continuously infused using an MR-compatible infusion pump. The blood sample was withdrawn from the opposite anticubital vein for monitoring glucose level at 5-10 minute intervals. The glucose level was maintained at ~180 mg/dL by adjusting infusion rate.

RESULTS

Time-course spectra from one subject are shown in the figure below. Each spectrum has a total NS of 128 acquired in 8 minutes. The expanded spectrum on the top was averaged for 24 min before the end of infusion. The time-course spectra were processed using LB = 4 and GB = 0.5 and the expanded spectrum was processed using LB = -1 and GB = 0.2. Resonances from several key metabolites are indicated. Glutamate C5, glutamine C5 and aspartate C4 are spectrally resolved. Resonances from glutamate C1, glutamine C1, aspartate C1, NAA C1, C4 and C5 were also detected.

DISCUSSION

^{13}C labels from [2-^{13}C]glucose are primarily incorporated into glutamate C5 (and glutamine C5 via the glutamate-glutamine cycle) during the first turn of the TCA cycle. Also, glutamate and glutamine C1 and C5 peaks are not contaminated by the strong subcutaneous lipid peak at 172-173 ppm, which is a significant advantage over the method using [1-^{13}C]glucose and detecting glutamate and glutamine C3 and C4 peaks. Additional advantage is the substantial reduction of averaged decoupling power deposition. Although only first order shimming was used, glutamine C5 was resolved from aspartate C4. The spectral resolution and SNR can be largely improved if higher order B_0 shimming can be performed in the local space. Furthermore, SNR can also be improved using infusion of [2-^{13}C]glucose with higher concentration. Our numerical analysis of the two-compartment model of the glutamate-glutamine cycle shows that the glutamine C5-to-glutamate C5 ratio is relatively constant after the initial infusion period. The magnitude of this ratio, because of astroglial isotopic dilution, is very sensitive to changes in the rate of the glutamate-glutamine cycling flux. Therefore, the glutamine C5-to-glutamate C5 ratio can be used as a surrogate marker for the rate of glutamate-glutamine cycling flux in clinical studies when relatively long scan time to measure the full labeling kinetics is difficult.



REFERENCE

(1) S. Li, *et al*. MRM 57:265 (2007). (2) S. Li, *et al*. ISMRM Proceeding 2007, Abstract 535.