Serial proton MRS of the human brain after oral administration of ^{12}C and ^{13}C enriched glucose

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Introduction:

Recent progress in MR technology has resulted in improved reproducibility of MR spectra. The goal of this study was to demonstrate that the uptake of glucose (Glc) and its breakdown in the human brain can be monitored with standard ^{1}H MRS on clinical MR scanners.

Methods:

After a baseline MRS study, regular glucose (three subjects, four studies, 1.1 – 1.8 gr/kg body weight) or U-^{13}C enriched glucose (one subject, two studies, 0.9 gr/kg) was orally administered. MR spectra were acquired up to ≈100 min after glucose administration. Subjects fasted 4-12 hours for the regular glucose studies and 12 hours overnight for ^{13}C glucose studies. All studies were carried-out on a clinical MR system (Philips, Achieva 3.0T, Best, The Netherlands) using an eight-channel head coil. Single-voxel PRESS spectra (TR=2s, TE = 35ms, 128 averages, 10-15cm^{3}) of occipital grey matter (GM) and parietal white matter (WM) were acquired and fully automated LCModel software (S. Provencher Inc.) was used for processing and quantitation.

Results:

Oral ^{12}C Glc administration resulted in increased tissue Glc concentrations. When ^{13}C enriched Glc was used, ^{13}C label replaced ^{12}C and resulted in an apparent reduction of the ^{1}H MRS detectable breakdown products of glucose such as glutamate (Glu) (**Fig. 1, 2**).

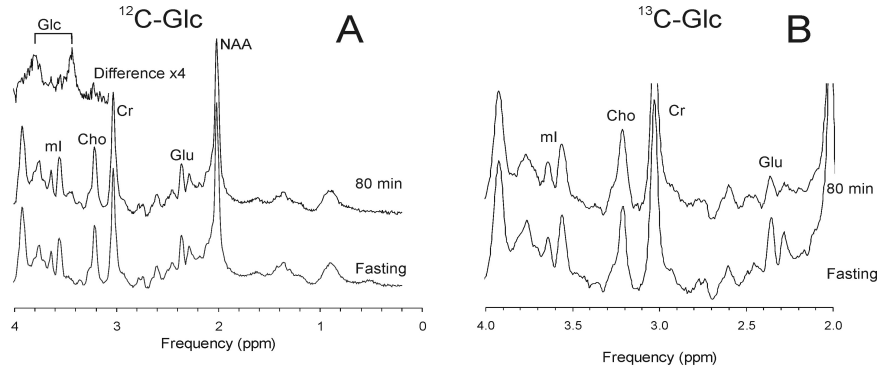

Fig. 1A: *A grey matter spectrum obtained 80 min after ^{12}C Glc administration showed increased Glc levels when compared with the baseline scan (small insert: difference spectrum).* ***B:*** *When ^{13}C Glc was administered, ^{13}C label accumulated in breakdown products of Glc, such as glutamate (Glu). Due to heteronuclear ^{13}C-^{1}H J-coupling, intensity is spread to sidebands and ^{13}C accumulation can be detected indirectly as an apparent reduction of the proton glutamate signal.*

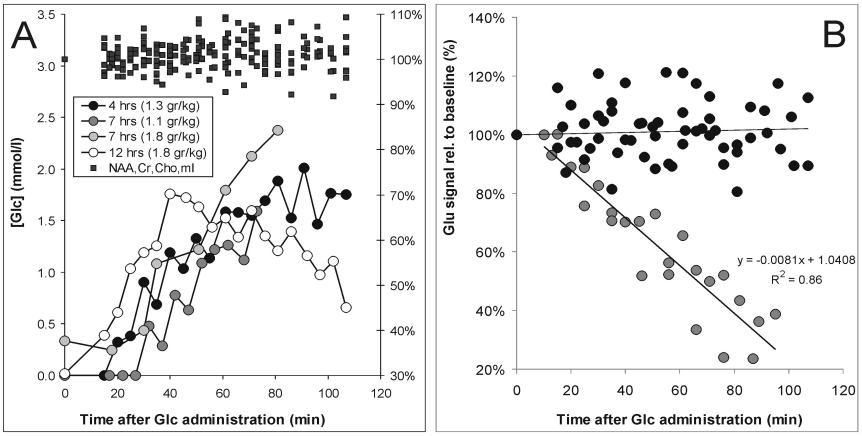

Fig. 2A: *An increase of brain Glc was observed in all four studies using regular ^{12}C Glc (circles) whereas NAA, Cr, Cho, and myo-inositol (mI) did not change significantly (102±4% of baseline values, dark squares).* ***B****: In studies using U-^{13}C Glc the glutamate signal decreased significantly (grey circles). Glu levels remained constant when ^{12}C Glc was administered (black circles). All data shown were obtained from occipital grey matter.*

Discussion:

The dramatically improved stability of MR systems allows the monitoring of glucose metabolism in the human brain using widely available and FDA approved proton MR spectroscopy methods. No additional hardware or special MR sequences are required. It is acknowledged that the simplicity of this approach comes at the cost of a vastly inferior specificity when compared with more advanced approaches such as direct ^{13}C detection, polarization transfer, and methods that employ more complex editing for indirect detection (1-4). Still, this method may be useful to answer important biological questions in clinical settings where the logistical challenges of more advanced methods cannot be overcome.

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References:

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