Hepatic Glycogen Alteration in Response to Hypoglycemia: A 13C Spectroscopic Imaging Study

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Introduction

Advances in magnetic resonance spectroscopy have made it possible to measure hepatic glycogen non-invasively in humans. Previously Rothman et al utilized 1-dimensional ISIS to measure hepatic glycogen, and studied the dynamics of hepatic glycogen metabolism [1,2]. Hepatic glycogen is known to be a major source for glucose production during hypoglycemia. However, it is unclear how rapidly hepatic glycogen store is altered in response to hypoglycemia in humans. Therefore, the goals of the study were: 1) to implement a 1-dimensional Gaussian weighted *k*-space encoding SI sequence to improve signal-to-noise ratios (SNR) for glycogen detection without sacrificing localization efficiency; and 2) to monitor the time course of hepatic glycogen stores in response to modest hypoglycemia.

Methods

Experiments

Scanner: a 4T Varian whole body system. *RF coil*: An 11 cm circular ^{13}C and a 13.5 cm coplanar butterfly coil for ^{1}H.

SI Acquisition Parameters: a repetition time of 0.3 sec; 500 μsec non-selective excitation pulse, 15K Hz sweep width and 2048 complex points. FOV of 60.0 cm with 32 phase encoding providing a 1D nominal voxel resolution of 1.875 cm (equivalent to slice thickness), oriented perpendicular to the C13 coil surface.

RF power calibration reference: A microsphere filled with 99% enriched ^{13}C formate at the center of the coil.

Phase encoding scheme: Gaussian weighted sampling scheme with a total of 505 phase encoding steps over 32 *k*-space values.

Human studies:

Eight overnight-fasted healthy subjects were studied (three of them under both euglycemic and hypoglycemic clamps) [hypoglycemic clamps: N=7, 29.6±7.6 yrs old, BMI=21.0±1.6 kg/m^2; euglycemic clamps: N=4, 30.5±9.2 yrs old, BMI=22.5±1.0 kg/m^2]. Using the ^{13}C SI, the hepatic glycogen was continuously measured during baseline and two hours of hypoglycemia (or euglycemia) with a time resolution of 15 minutes.

Protocol: The effect of hypoglycemic-hyperinsulinemic clamps [glucose:~60 mg/dl; insulin ~35 μU/ml] were compared to euglycemic-hyperinsulinemic [glucose: ~90 mg/dl; insulin ~35 μU/ml] clamps for 2 hours. The two clamps were done on separate days.

Results and Discussion

Comparison of Gaussian weighted vs. Conventional Encodings in Glycogen Phantom

The point spread function (PSF) of the Gaussian encoding is shown in Fig 1 without additional apodization. The PSF shows minimal ripples (FWHM: 3.52 cm/FOV=60.0 cm). The calculated SNR of C-1 glycogen signal from a phantom using the Gaussian encoding scheme was ~30% higher than that from a conventional encoding scheme using post-acquisition filtering to provide equivalent PSF. The result is consistent with a previous report [3]. Moreover, the Gaussian method showed less contamination from the adjacent voxels as evaluated by the formate resonance.

Hepatic glycogen changes in response to hypoglycemia in human subjects

Fig 2 shows a 1-D SI stack plot of proton-coupled C-1 glycogen peaks from a subject. A spectral expansion of glycogen at 100 ppm region is shown in Fig3. By the end of the two-hour hypoglycemic-hyperinsulinemic clamps, hepatic glycogen decreased progressively by 17.9±3.1 % from the basal glycogen level. Conversely, the euglycemic-hyperinsulinemic studies showed a 13.9±11.0% increase in hepatic glycogen. Thus, the net difference in hepatic glycogen between the hypoglycemia and euglycemia was ~32% of basal glycogen content. Therefore, we conclude that modest hypoglycemia induces a progressive decrease of the hepatic glycogen during initial two hours, presumably reflecting glycogen breakdown induced by counterregulation exceeding glycogen storage secondary to mild hyperinsulinemia.

References
1. Roden M et al, Recent Prog Horm Res.56:219-37, 2001. **2**. Rothman DL, et al, *Science*, 254 573,1991. **3**.Brooker HR et al, *Magn Reson Med*, 5, 417-433, 1987.

Fig 1

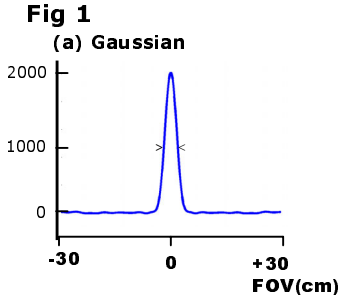


Fig 2

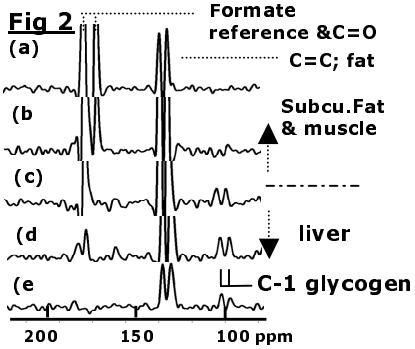
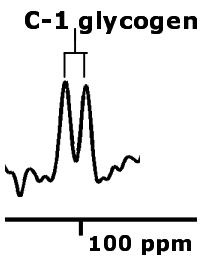


Fig 3



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