Monitoring of glycogen synthesis in liver of diabetic patients using ^{13}C-MR spectroscopy

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Introduction

In vivo ^{13}C MRS is potentially useful for examining human metabolic disorders[1-3], and especially for monitoring the time course changes in glucose metabolism. In this study, with a 3.0 T MR system, the signal change of [1-^{13}C] glucose vs. that of glycogen in the human liver was monitored over seven hours. In parallel, plasma sampling was performed to measure the levels of glucose and insulin. The relationships among these parameters were investigated and the availability of ^{13}C MRS for the clinical setting was discussed.

Materials & Methods

^{13}C MR spectra in the liver were obtained from five healthy volunteers (male, 39-46 years, mean 41.4) and five diabetic patients (male, 36-55 years, mean 45.4) before and after oral administration of 75 g of glucose, including 5 g of 99% [1-^{13}C] glucose. All MR experiments were performed with a 3.0 T GE Signa EXCITE equipped with a custom-made ^{13}C transmit/receive surface coil (24 ϕcm). ^{13}C MRS was performed with TR 500 ms, bandwidth 12.5 kHz, sampling points 1024 and number of acquisitions 2048. Each ^{13}C MR spectrum was obtained every hour and, in total, seven sets of data were obtained. A 1 g 99% [2-^{13}C] acetone vial was employed as an external reference. The ^{13}C signal quantification was performed using in-house software on MATLAB. In each subject, a series of nine plasma samples was taken from the antecubital vein by the same protocol.

Results

In all subjects, the time courses of [1-^{13}C] glucose signal intensity in the liver corresponded approximately to the plasma levels of glucose (Fig. 1). In the volunteers, time to the peaks of glycogen was in 3 to 4 hours after administration, and time variations of glycogen corresponded with those of the insulin. However, there were no peaks throughout the experiments in most patients (4 out of 5) even in the presence of insulin action in plasma (2 out of 5). There was a significant correlation between fasting levels of plasma glucose and increasing rate of glycogen in the liver (Spearman: r=-0.758, p<0.05, n=10) as shown in Fig. 2.

Discussion and Conclusion

It was demonstrated that in healthy volunteers, the variation of *in vivo* glycogen storage/degradation in the liver was correlated with that of insulin in plasma, although this did not apply to the patients. Less variation of glycogen spectra in the patients might reflect the dysfunction of glycogen synthesis in the liver after glucose administration. This result and the significant correlation (Fig. 2) indicate that improvement in glycogen synthesizing ability may favorably influence reduction of the blood glucose level, and in turn the treatment of diabetes. With long-term monitoring by ^{13}C MRS, it is possible to obtain information about glycogen storage/degradation *in vivo* and this could be used as a criterion of metabolic disorder. And this method will also allow widespread application for such as drug development for synthesizing glycogen in the liver. Further investigations should assist in a multilateral diagnosis and characterization of diabetes. In conclusion, ^{13}C MR spectroscopy is useful for monitoring glycogen synthesis *in vivo*.

References

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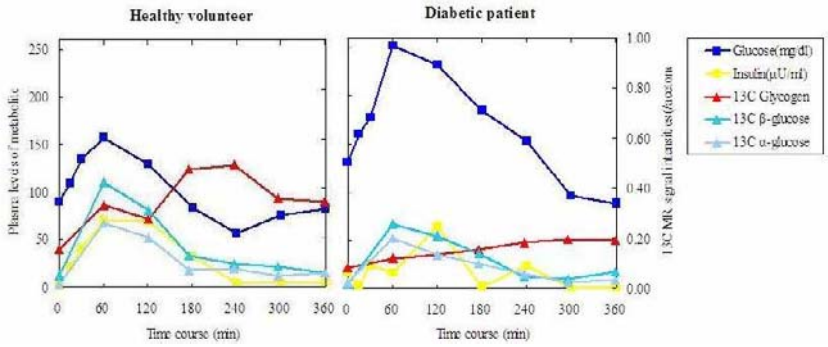

Fig. 1. Time courses of MR spectral intensities of [1-^{13}C] glucose and glycogen in the liver, and plasma levels of glucose and insulin in one volunteer and one patient.

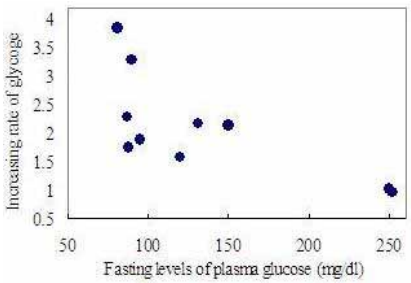

Fig. 2. Plots of fasting levels of plasma glucose against increasing rate of glycogen in the liver in each subject.
Spearman: r=-0.758, p<0.05, n=10