Non Invasive Detection of Glucose in the Brain of a Patient with Type 1 Diabetes by Means of 1H MRS at 3 Tesla

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Introduction

While "high–energy" phosphates (ATP, PCr) can be monitored non–invasively in living tissue by means of ^{31}P magnetic resonance spectroscopy (MRS), the *in vivo* detection of glucose (Glc), another important compound of energy metabolism, with ^{1}H MRS is difficult. Not only is the Glc concentration critically low (~ 1 µmol/[g wet weight]), but also the ^{1}H MR spectrum is complex due to *J*–couplings which split the available information into multiplet structures thus reducing the intensity of individual lines. As a consequence basal Glc levels can presently not be detected with standard clinical MRI equipment.

In experimental MR systems at B_0 = 4 T several ^{1}H MRS studies with patients employed the glucose/insulin clamp technique with blood glucose levels up to 16.7 m*M* successfully to obtain a quantifiable glucose signal in the spectra [1,2]. The purpose of our study was the introduction of a single–voxel ^{1}H MRS technique to a clinical 3–T tomograph for detection of slightly elevated blood glucose concentrations in the human brain.

Materials and Methods

To evaluate the feasibility of direct detection of Glc ^{1}H MR signals at B_0 = 3 T and suppression of unwanted coherences, experiments were first performed on model solutions of Glc (10 and 100 m*M*) and suspensions of Glc and *myo*–inositole (mI) (50 m*M* each in 0.1 *M* phosphate buffer, pH 7.1). Then volunteers were examined after giving their informed consent according to procedures approved by the institutional ethical review board. Blood samples for the determination of plasma glucose levels were obtained from the fingertips using an ACCU–CHEK® Comfort measuring device (Roche, Mannheim, Germany).

All examinations were performed on a commercial 3–T scanner (Magnetom Trio™; Siemens Medical Solutions, Erlangen, Germany) using the standard matrix head coil. Based on T_{2w} MRI data, VOIs (2×2×2 cm^3) were placed in the parietooccipital cortex. Shimming was performed using an automated procedure for all first– and second–order terms followed by manual fine tuning of first–order shims which resulted in water proton linewidths of 12–14 Hz. The 3,1–DRYSTEAM technique from Ref. [3] was modified by implementing variable frequency offset (1–25 Hz) of water–suppression pulses (WET [4], bandwidth 40 Hz) in order to minimize the effect of selective suppression on the Glc–αH1 proton which resonates at chemical shift δ = 5.24 ppm.

Data from the VOI was acquired in blocks of 8 min (nex = 256, TR = 2 s, TE = 20 ms); plasma glucose was determined afterwards. Spectral information obtained from healthy volunteers was compared to those of a patient with type–1 diabetes considering the intensity ratio of Cr–methyl protons (δ = 3.03 ppm) and Glc–H1.

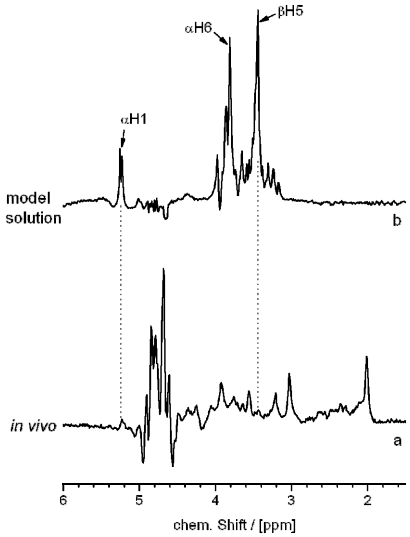

Fig. 1: Localized ^{1}H MR spectra from the parietooccipital cortex of a patient with diabetes (a) and a model solution with 100 m*M* glucose (b). 3,1–DRYSTEAM with TR = 2 s, TE = 20 ms, nex = 256, measurement time = 8 min, voxel = 2×2×2 cm^3, B_0 = 3 T. Dotted lines: Glc peaks at δ = 3.44 ppm and 5.24 ppm.

Results and Discussion

The experiments demonstrated effective water signal suppression without affecting the αH1 peak (δ = 5.24 ppm), which is of interest for Glc detection [5]. There is only one other potential candidate for that purpose: the βH5 resonance at δ = 3.44 ppm. In model–solution spectra, this peak could be clearly separated from mI signals.

MRS examinations of five healthy volunteers did not show signals, which could be assigned to spectral data of glucose. In contrast, spectra (Figs. 1, 2) from the brain of a 25–year–old volunteer with type–1 diabetes, who was cut off from his permanent insuline supply during the examination, displayed resolved peaks at 3.44 ppm and 5.24 ppm (in all 4 spectra of the examination), which is explained by increased cerebral glucose levels owing to the lack of insuline and manifest hypoglycemia unawareness. The plasma glucose level in this patient was 0.66 m*M* at the beginning of the examination and 1.31 m*M* 60 min later (end of the examination).

For quantification of brain–Glc levels the peak at 5.24 ppm is more appropriate than that at 3.44 ppm which resonates with lower SNR in a chemical range where different metabolite resonances superimpose.

The 3,1–DRYSTEAM technique does not require specific equipment and is therefore easily included in clinical routine MR examinations at B_0 = 3.0 T. High–resolution spectra allow to detect and estimate enhanced glucose levels in the human brain. Its potential application to non–invasive diagnosis of diabetes is presently explored in an ongoing clinical study in our institution.

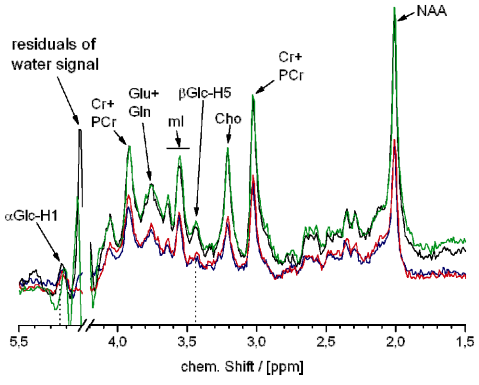

Fig. 2: Stability of glucose signal detection in localized *in vivo* ^{1}H MR spectra from the brain of a patient with type–1 diabetes (measurement parameters: Fig. 1).

References

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