MR Visibility of Vascular Metabolites in Dynamic Uptake Studies using MR Spectroscopy

R. Kreis[1], C. Salvisberg[1], T. Lutz[2], C. Boesch[1], J. Pietz[2]

[1]Dept. Clinical Research, University & Inselspital Berne, Berne, Switzerland, [2]Dept. Pediatric Neurology, University Heidelberg, Heidelberg, Germany

Introduction

In general, vascular contributions to the *in vivo* MR spectrum are negligible. However, if the vascular metabolite concentrations are considerably higher than the cerebral levels, potential contributions of blood metabolites have to be taken into account in quantitative brain MRS. This correction is of particular importance for dynamic studies, e.g. in investigations of cerebral glucose, ethanol, or phenylalanine (Phe) uptake. Corrections are only necessary if the MR signals of the vascular metabolites are MR visible with the applied methodology. While blood glucose is generally believed to be detectable, blood Phe has been assumed not to contribute to the brain spectrum [1]. Phe is reported to bind to plasma albumin and is known to feature very broad peaks in high field NMR [2-3]. This study aimed at recording MR spectra of whole blood *ex vivo* in a clinical MR scanner at 1.5 T and to quantify blood Phe, if detectable.

Methods

All spectra were recorded on a clinical 1.5T MR scanner (Signa, GE) using a 3" surface receive coil. Data acquisition was performed with the same localization sequence as for *in vivo* brain scans (PRESS, 20ms TE, 2-3s TR, 256 acquisitions, 3 spectra per specimen). Quantitation was based on the unsuppressed water signal. Spectral fitting was performed using prior knowledge of the Phe spectrum, a parameterized background signal, and the lineshape obtained from the water spectrum [4]. The model for the background was obtained by parameterization of the control spectra, which have minimal Phe content. To prevent separation of plasma and erytrocytes [5] and hence to obtain well resolved spectra from full blood, an air-driven rotor system was constructed that enabled recording of spectra from a blood-filled glass vial rotating at about 100 rpm in an incubator at 37° C. 15 cm^3 fresh whole blood was drawn by venipuncture from human volunteers (4 healthy controls, 6 phenylketonuria (PKU) patients). Lithium heparin was added for anticoagulation. Before transfer to the glass tube, blood was fully saturated with oxygen in an Erlenmeyer flask under O_2. Tubes were sealed with rubber septa with minimal inclusion of air bubbles. Blood spectra were measured within 2 hours, while the vial was continually agitated or rotated. A SaO_2 of nearly 100% persisted for this time period. 2 ml of blood was treated separately to prepare plasma samples for standard analysis of plasma Phe content by ion exchange column chromatography of deproteinized plasma. *In vivo* brain spectra from a healthy subject under a Phe load were recorded as described previously [6].

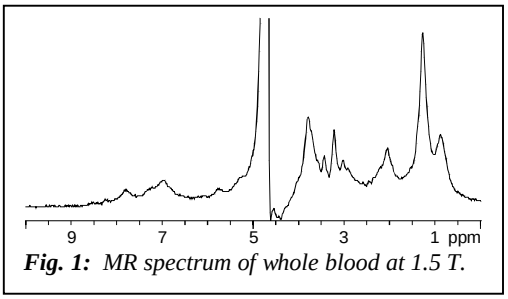

Fig. 1: *MR spectrum of whole blood at 1.5 T.*

Results

The presented setup, similar as in Ref [5], allowed recording of well-resolved spectra from fully oxygenated whole blood at body temperature on a clinical MR scanner. The average of all 12 spectra obtained from healthy controls is shown in Fig. 1. A well-resolved signal from Phe was clearly observable in all blood specimens from PKU patients (Phe by chromatography: 1.64±0.31 mM). Average spectra from patients and controls, as well as their difference are displayed in Fig. 2. Blood Phe levels determined by MRS in whole blood and by column chromatography showed excellent correlation (R^2 =0.99, one obvious outlier disregarded). If MRS results are expressed in molal units (mM/kg solvent), MRS underestimated the chromatographic results by 11%.

Discussion & Conclusion

It is demonstrated that vascular Phe is detected *in vivo* at 1.5 T in spite of the fact that it is severely broadened at higher fields. Brain levels of cerebral metabolites have to be corrected for vascular contributions whenever blood levels are substantially higher than cerebral levels. Potential signal suppression because of flow has to be considered separately, in particular for long TE scans and if spatial presaturation is used. For the current method this effect is calculated to have minimal influence. The relevance of the vascular correction of brain Phe values is demonstrated in Fig. 3, where the time courses of brain and blood Phe are plotted in a dynamic study, where a healthy person is subjected to a continued oral Phe load for 4 h. Without the appropriate correction, the brain influx is apparently faster and leads to higher levels (50% effect at earliest time point, 15% at maximum level).

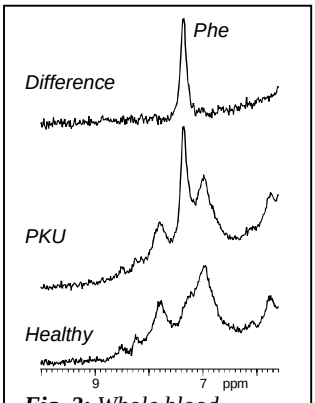

Fig. 2: *Whole blood spectra from controls, PKU patients and the difference.*

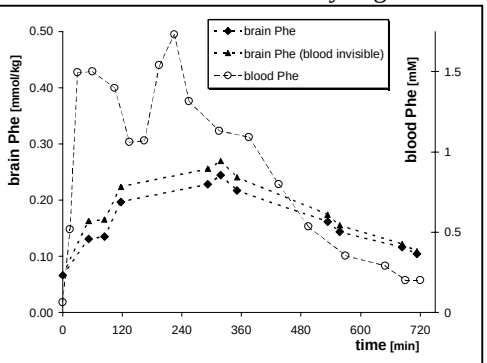

Fig. 3: *Effect of correcting for vascular Phe signals in a dynamic cerebral uptake study*

References

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