MRS thermometry of the brain using calibration results of aqueous metabolite solutions

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Introduction:

^{1}H-MRS estimation of the absolute brain temperature using the temperature independent internal reference has long been used in biomedical studies [1]. N-acetyl-aspartate (NAA) line at ~2 ppm, spectral line of creatine-phosphocreatine complex (Cr) at ~3 ppm and choline-containing compounds (Cho) at ~3.2 ppm can be used as the references due to pronounced spectral lines (TE = 80 ms) as compared to other metabolites (Fig. 1). The reliability of the estimations is however limited by accuracy of the (linear) temperature dependencies of the chemical shift differences between water and metabolite reference lines $\delta_{H2O\text{-}NAA}$, $\delta_{H2O\text{-}Cho}$, $\delta_{H2O\text{-}Cr}$ (Fig. 1) and by accuracy in estimation of spectral line positions. To our knowledge, only three research groups have performed calibration measurements in vivo [2-4]. Accuracy of those measurements was however limited by relative low signal-to-noise ratio of metabolite resonances and by narrow range of experimental brain temperatures. More accurate results of calibration measurements of aqueous metabolite solutions can be used for in vivo brain temperature estimations because the chemical shift differences $\delta_{H2O\text{-}NAA}$, $\delta_{H2O\text{-}Cho}$, $\delta_{H2O\text{-}Cr}$ are independent on magnetic susceptibility [5]. The main aim of this study was to obtain calibration data using measurements of NAA, glycerophosphocholine (GPC) and Cr aqueous solutions. A secondary goal was measurement the human brain temperature using Cho, Cr and NAA spectral references.

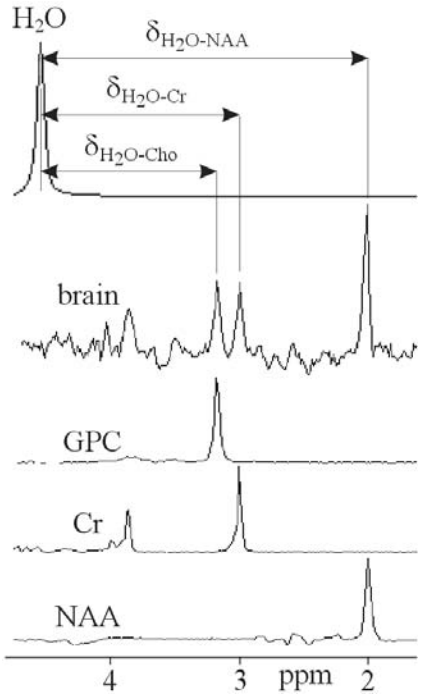

Fig. 1

Materials and Methods

All MRS experiments were performed on a 1.5 T Philips scanner using a standard quadrature head coil. Single voxel MRS of GPC, Cr and NAA aqueous solutions (Fig. 1) were performed using PRESS sequence (TR/TE 2000/80 ms, BW 1000 Hz, 1024 points, 8 cm^3 voxel size). Four dummy excitations were followed by 16 non-water-suppressed and 48 water-suppressed scans. Metabolite solutions were originally made for measurements of the LCModel's model spectra. Concentrations of GPC, Cr and NAA were 25, 50, and 50 mM, respectively. The pH factor was adjusted to 7.2. Aqueous solutions held in a 50 cm^3 Erlenmeyer glass bottles were heated/cooled in the thermally insulated basin (100x150x300 mm) containing tap water. Warming/cooling of the water bath was performed using thermostatically controlled water flowing through a glass cylinder (125 mm i.d., height 55 mm). Calibration temperature was monitored with a precision ±0.1°C using Pt-100 probe (ALMEMO 2290-8, Ahlborn Meas&Reg). A set of MRS acquisitions in thermal equilibrium were performed at the temperature range 3°C - 43°C (Fig. 2-4). Reference temperature of the phantom was measured before and after MRS. The average of these temperatures was used for calibration. Two MRS experiments were performed in each temperature level. Three consecutive MRS measurements of the brain of five healthy subjects were performed with a voxel size 4x2x2 cm^3. The voxel was placed in the parietal lobe just above corpus callosum. Body temperature was measured at the rectum. Metabolite and water resonance frequencies were estimated using the jMRUI software package [6]. The residual water signal was removed by HLSVD algorithm in a 1 ppm range around the water resonance and unsuppressed water line, GPC, Cr and NAA resonances were estimated using HLTLS algorithm. Baseline correction of the brain spectra was performed by truncation of the first two points of the FIDs. Calibration temperature T (°C) vs. chemical shift difference between water and metabolite $\delta_{H2O\text{-}M}$ (ppm) was modeled using equation $T = A(\delta_{H2O\text{-}M} - \delta_{36}) + B$, where A is the slope (°C/ppm), B (°C) is the intersection of the regression line and δ_{36} is fitted chemical shift difference between water and metabolite at 36 °C. Brain temperatures of the volunteers were measured at a room temperature (22 °C). Mean temperature was computed using chemical shift differences $\delta_{H2O\text{-}NAA}$, $\delta_{H2O\text{-}Cho}$, and $\delta_{H2O\text{-}Cr}$.

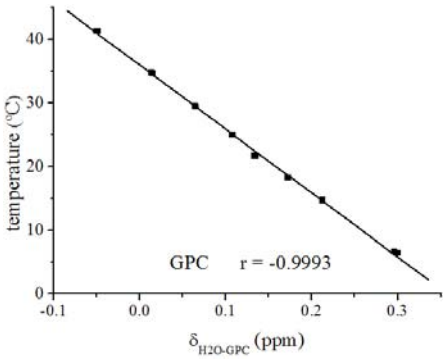

Fig. 2

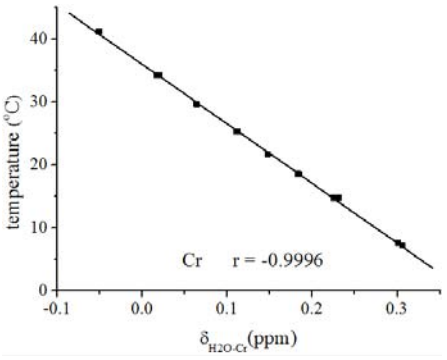

Fig. 3

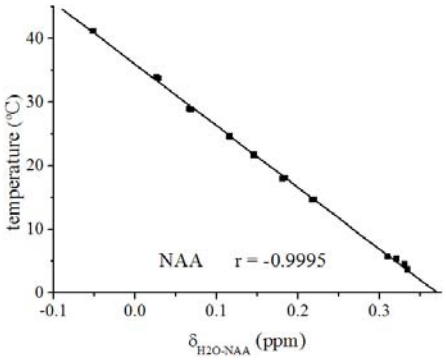

Fig. 4

Results

Figure 1 show shows representative spectrum of the brain and spectra of Cho (GPC), Cr and NAA aqueous solutions. Figures 2-4 show the temperature dependences and fitting results. Linear regressions yielded the following relationships: $T_{GPC} = -100.813(\pm0.986)(\delta_{H2O\text{-}GPC} -1.473) + 36(\pm0.156)$; $T_{Cr} = -94.768(\pm0.741)\ (\delta_{H2O\text{-}Cr} -1.66) + 36(\pm0.123)$; $T_{NAA} = -97.134(\pm0.726)(\delta_{H2O\text{-}NAA} -2.677) + 36(\pm0.138)$. Standard errors of the slopes and intercepts of the regression lines are given in brackets. Correlation coefficient r = -0.999 was achieved in all regressions. Mean brain and body (rectal) temperatures of the five volunteers were 38.1±0.3 °C and 37.6±0.2°C, respectively.

Discussion

Results of this study can be compared with previously reported in vivo MRS brain temperature calibrations [2-4]. The correlation coefficients r reported herein had a larger absolute value than previously reported and the standard errors were lower as well. These facts demonstrate improvement of calibration curves accuracy shown in Fig. 2-4. Since chemical shift differences $\delta_{H2O\text{-}NAA}$, $\delta_{H2O\text{-}GPC}$, and $\delta_{H2O\text{-}Cr}$ are independent on magnetic susceptibility, our calibration results can be used for in vivo applications [5]. Until recent times, knowledge of healthy human brain temperature was hampered by inability to make measurement inside the brain without the need for surgery. Although little is known about the temperature of the healthy human brain, mean brain temperature of our volunteers (38.1±0.3 °C) and the fact that the brain normally has a higher temperature than the body (rectum) temperature about 0.5±0.4 °C is in agreement with other studies [1].

Conclusion

Calculation of the absolute brain temperatures using Cho, Cr, and NAA spectral references simultaneously improves reliability of the temperature estimations.

References

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