In Vivo ^{17}O Measurements of Water Rotational Correlation Time and Hydrodynamic Radius in Rat Brain

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Introduction

Water content is extremely high in a biological system. It plays essential roles in maintaining normal cellular functionalities, and is sensitive to the microscopic environment of intra- and extra-cellular spaces. This study exploits new *MR* approaches for noninvasively assessing the rotational correlation time (τ_c) and hydrodynamic radius (R_h) of the brain tissue water. *In vivo* ^{17}O MRS was used to measure the longitudinal relaxation time (T_1) of the quadrupolar ^{17}O spin of water, and the T_1 value can be used to calculate water τ_c according to a simple, field-independent relation. ^{1}H MRI was applied to image the brain translational diffusion coefficient (D_t), and the D_t/T_1 ratio can be used to determine R_h. These approaches were tested and evaluated at 9.4T using the rat brain model with varied brain temperature.

Theory

^{17}O spin has a quantum number of $I = 5/2$ and possesses an electric quadrupolar moment that can interact with local electric field gradients. The temporal fluctuation in this interaction induced by molecular motion dominates the ^{17}O relaxation process. For the water molecule with the extreme narrowing limit (*i.e.*, $\tau_c\omega << 1$, ω is the ^{17}O Larmor frequency), there is a simple relation between water T_1 (unit: ms) and τ_c (unit: picosecond) according to Eqs. [1] and [2]:

$$\frac{1}{T_1} = \frac{3\pi^2}{10}\left(\frac{2I+3}{I^2(2I-1)}\right)\left(1+\frac{\eta^2}{3}\right)\left(\frac{e^2Qq}{h}\right)^2\tau_c \quad [1]; \qquad \tau_c = \frac{13.8}{T_1}(\text{ps}) \quad [2]; \qquad \tau_c D_t = 2R_h^2/9 \quad [3]; \qquad R_h = 78.8\sqrt{D_t/T_1} \quad [4],$$

where e^2Qq/h(=-8.1 MHz) is the ^{17}O quadrupolar coupling constant, η is an asymmetry parameter and they are constant and field independent [1,2].

The relation between the translational diffusion coefficient (D_t: mm^{2}s^{-1} unit), τ_c and R_h (unit: Å) can be derived using the Stokes-Einstein and the Debye–Stokes– Einstein equations [3], leading to Eq. [3] indicating that $\tau_c D_t$ should be a constant. Solving Eqs. [2] and [3] gives Eq. [4], in which D_t can be imaged using conventional DTI with two b factors, thus, R_h can be calculated according to Eq. [4].

Methods

All NMR experiments were conducted using Male Sprague–Dawley rats on a 9.4 T animal magnet interfaced to a Varian INOVA console. A dual surface-coil probe consisting of a butterfly-shape ^{1}H coil (400 MHz) and an oval-shape ^{17}O coil (~1cm×2 cm, 54.25 MHz) was used for acquiring ^{1}H and ^{17}O data, respectively. Non-localized ^{17}O MR spectroscopy with inversion recovery pulse sequences and 8 inversion recovery times were applied for measuring T_1 values of natural abundance $H_2{}^{17}O$ in the rat brains (6 animals) with varied body temperature (T: 27-37°C, or 300-310 K). ^{1}H MR images were acquired using adiabatic spin-echo sequence with two b-values (0 and 668 s/mm^2) to measure D_t in the ROI covering a large brain region and its temperature dependence (2 animals).

Results

Figure 1A shows the relation between the ^{17}O T_1 of brain tissue water and the inverse of temperature (1/T) from different rat measurements. It indicates that the increasing temperature resulted in a longer T_1. The relation obeys a linear function (R^2=0.983). Figure 1B shows the relation between the rotational correlation time, τ_c, and the inverse of temperature (1/T), indicating a reversed linear relation (R^2=0.976), i.e., the increasing temperature shortened τ_c. Figure 2 displays the results of R_h measurements across the temperature range of 27-37°C., indicating an independent relation of R_h on temperature. Both rats had a similar trend though one animal (Rat A) showed a slightly higher R_h value compared to the other. The average R_h from two animals was 1.00±0.01Å.

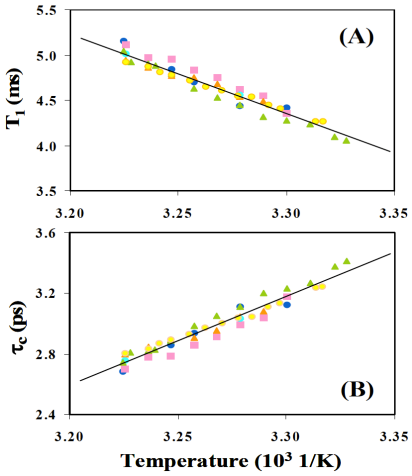

Fig. 1 Temperature dependence on (A) ^{17}O T_1 and (B) rotational correlation time τ_c of rat brain tissue water. The colors present the data from different rats and solid lines present the linear regression for all data.

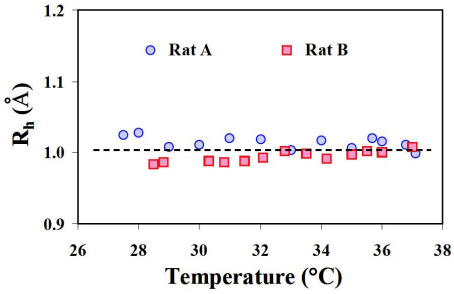

Fig. 2 Temperature independence of water hydrodynamic radius (R_h) measured in two rat brains. The solid line presents the average of R_h measurements.

Discussion and Conclusion

In this study, we tested novel MR-based approaches for *in vivo* measurements of two important parameters of rotational correlation time and hydrodynamic radius that reflect the brain tissue water dynamics at the molecular scale. It was found that the brain water τ_c was in a range of several picoseconds and is sensitive to the brain temperature change; the measured τ_c values were longer than the bulk water τ_c. For instance, based on the linear relation shown in Fig. 1B, we predicted the tissue water τ_c value of 3.5 ps at 25°C in the rat brain, which was significantly longer than that of bulk water (=2.7 ps) at the same temperature [1]. This result reveals that τ_c is sensitive to microscopic environment in the biological system as one would expect. The measured R_h values were stable across a large range of brain temperature (see Fig. 2). This result provides convincing evidence in supporting the validity of Eq. [3] and the methods proposed herein for *in vivo* measurements of brain water τ_c and R_h. The measured R_h value of ~1 Å was in line with the size of water molecular radius (~1.3 Å). This work indicates excellent utilities of *in vivo* ^{17}O MRS methods for potentially imaging the microscopic dynamics and cellular environment of brain tissue water *in vivo*.

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References [1] Glasel (1966) *Proc Natl Acad Sci U S A* 55:479-85; [2] Zhu & Chen (2011) *Prog Nucl Magn Reson Spectrosc* 59:319-35; [3] Yao et al. (2008) *Biophys Chem* 136:145-51.