Transverse relaxation of tissue water in human brain: relative contributions of iron and macromolecules

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Introduction

T_2 contrast generated by transverse relaxation is routinely used for diagnosis for various diseases and for uncovering living processes like brain activations. Another interesting aspect of T_2 contrast in human brain is its close relationship with regional iron concentration. Since Drayer pointed out the correlation [1], a number of works have been done to clarify the relationship. Vymazal reported that linear correlation is seen between T_2 and non-hemin iron concentration [Fe] in the postmortem brain tissue [2]. However, the correlation obtained with living brain is not necessarily good, partly because difficulty in measurements of accurate T_2 in a slice-selective manner, and partly because presence of confounding factors to T_2 in addition to [Fe]. We developed a multiecho adiabatic spin-echo (MASE) sequence to overcome the first difficulty [3]. On the second difficulty, we recently reported that the observed apparent transverse relaxation rate in living brain is better explained by considering macromolecular mass fraction (f_M) defined as 1 – water fraction as an additional relaxation source [4]. In the present work, we conducted T_2 measurement using MASE at four different fields of 1.9, 3, 4.7, and 7T to confirm whether the observed T_2 in human brain is explained in the same way at different fields.

Materials and Methods

Human brain T_2 measurements were conducted on healthy volunteers using a MASE sequence at four different fields. Obtained transverse relaxation time constant with this sequence is expressed as $T_2^\dagger$ because it is affected by T_{2rho} during the RF pulse. Measurement at 4.7T was performed with a Varian Inova spectrometer and those at 1.9T with the same system after the field strength was ramped down to 1.9T. Measurements at 3T and 7T were performed with Siemens Magnetom Trio systems. Number of subjects examined was 10, 54, 5, and 6, respectively. A single 2.5 mm slice plane was positioned across the basal ganglia region in the transaxial orientation. Six echoes were obtained with TR/TE of 4000/26, 52, 78, 104, 130, and 156ms except for the case of 7T, where four echoes were collected with TR of 5s. Data matrix of 256 x 128 was collected in the FOV of 25.6 x 25.6cm with an echo spacing of 13ms. $T_2^\dagger$ values were extracted at five GM regions of frontal cortex, caudate, putamen, thalamus, and globus pallidus, as well as at frontal WM region. $R_2^\dagger$ (= 1/ $T_2^\dagger$) values were fitted with a linear combination of regional [Fe] and f_M, thus $R_2^\dagger = \alpha[Fe] + \beta f_M + \gamma$ [R2] (equation 1).

Results and Discussion

Figure 1 shows $T_2^\dagger$ maps obtained at four different fields. It is obvious that $T_2^\dagger$ in the brain is shortened with B_0. When $R_2^\dagger$ values in six brain regions were plotted against regional [Fe], the dependence on [Fe] is similar at each field (Fig. 2). Furthermore, the observed $R_2^\dagger$ are well fitted with equation 1 at each field. This result indicates that transverse relaxation of the tissue water in human brain is dissected to contributions from regional nonhemin iron and macromolecules in a wide range of B_0 between 1.9 and 7T. Coefficients α, β, and γ showed B_0 dependencies in different ways. Coefficient α due to iron showed a linear increase with B_0 as previously observed for water relaxation in ferritin solution, suggesting the same mechanism is working for the relaxation due to iron in human brain [5]. In contrast, the coefficient β appears to increase quadratically with B_0, suggesting a mechanism of diffusion-mediated dynamic dephasing and/or exchange for the macromolecular term. The coefficient γ is nearly constant independent of B_0, thus the classical dipole-dipole mechanism is likely to account for this term.

Conclusions

Apparent transverse relaxation of the tissue water in human brain is dissected to contributions from regional nonhemin iron and macromolecules at a B_0 range of 1.9 to 7T. B_0 dependence of each contribution suggests that different relaxation mechanisms are working for iron and macromolecules, and constant part.

References

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Acknowledgments

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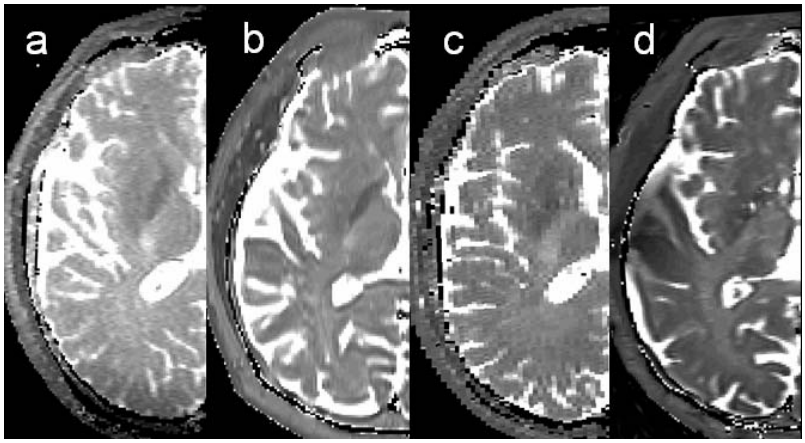

Fig.1. $T_2^\dagger$ maps of human brain obtained at (a) 1.9T, (b) 3T, (c) 4.7T, and (d) 7T.

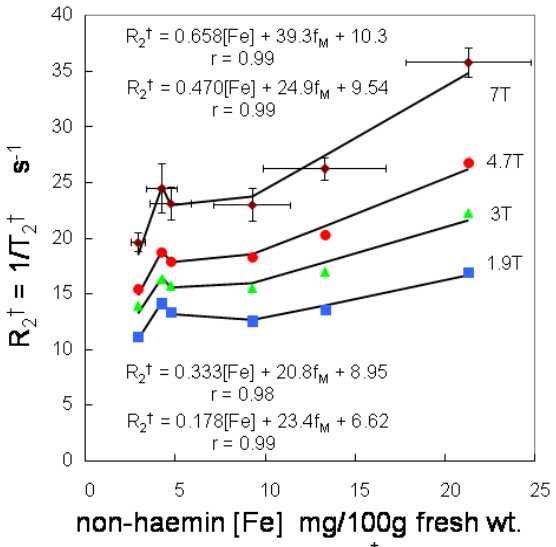

Fig.2. Correlation between $R_2^\dagger$ and [Fe] at various B_0. Solid lines show the fitted result using a linear combination of regional [Fe] and f_M