Understanding transverse relaxation in human brain through its field dependence from 1.5 to 7T

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Introduction

Recently, the ability to perform accurate bioiron quantification based on relaxation phenomena, such as T_2, T_2^*, or the phase component of T_2^*-weighted images, has emerged as an important capability of MRI. However, most of the methods used to quantify iron have relied on having a linear relationship between the relaxation parameter and the regional iron concentration [Fe]. We have recently found that the apparent transverse relaxation rate ($R_2^\dagger$) of tissue water in human brain has a considerable contribution from the regional macromolecular fraction f_M defined by 1 – water fraction, and is described as a linear combination of [Fe], f_M, and a region independent term, thus, $R_2^\dagger = \alpha[Fe] + \beta fM + \gamma$ (1). In the present work, we obtained the coefficients α, β, and γ at five different magnetic fields (1.5, 1.9, 3.0, 4.7, and 7T), and attempted to elucidate transverse relaxation mechanisms from the field dependence.

Materials and Methods

$T_2^\dagger$ maps in human brain were obtained from a transaxial plane at the level of the basal ganglia region using a MASE sequence with parameters reported previously (1). Altogether, 71 measurements were conducted at 1.5, 1.9, 3.0, 4.7, and 7.0T using Agilent and Siemens systems. To determine coefficients α, β, and γ we performed a multiple regression analysis using the regional [Fe] and f_M as two variables on $R_2^\dagger$ values from six brain regions in frontal gray matter (fr. GM), caudate, putamen, thalamus, globus pallidus, and frontal white matter (fr. WM). To simulate the relaxation of the tissue water due to f_M, we considered the net rate constant to be the sum of isochronous exchange (IE) and anisochronous exchange (AE) of the bulk water protons with protons in macromolecules (MM) in the tissues. The IE component due the interaction with protons of macromolecules via dipolar interactions is described as

$$R_{2s} = 0.5\,[R_{2f0} + R_{2s0} + k_f + k_s - \{(R_{2f0} - R_{2s0} + k_f - k_s)^2 + 4k_fk_s\}^{1/2}], \quad [1]$$

where R_{2s0} and R_{2f0} are the intrinsic R_2 values due to dipolar interactions at the slow (bulk) and fast (MM) relaxing sites (2), and k_f and k_s are the exchange rate constants from the fast to the slow relaxing site and vice versa, respectively. The AE component originating from the exchange with OH, NH_2, and NH protons located on the surface of macromolecules is described as

$$R_{ex} = P_s P_f \delta\omega^2 k_{ex} / [k_{ex}^2 + \{(2\sqrt{3} / \tau_{es})^4 + P_s^2\delta\omega^4\}^{1/2}], \quad [2]$$

where P_s and P_f are populations of protons in slow and fast relaxing sites, respectively. τ_{es} is the period of the echo spacing, and $\delta\omega$ is the average chemical shift difference between the bulk water protons and those at exchangeable sites (3,4). Then, the macromolecular contribution to R_2 was calculated as the fractional sum of R_{2s} and R_{ex} with the fraction determined experimentally.

Results and Discussion

The coefficient α manifested a linear dependence on B_0 (Fig. 1a), whereas β increased quadratically on top of a field independent component (Fig. 1b). γ was mostly independent of B_0 (data not shown). The linear dependence of α on B_0 in the present study is similar to what was reported for ferritin solutions (5), indicating similar relaxation mechanisms in ferritin solutions are working for iron-related relaxation in vivo. In terms of macromolecular contribution, βf_M in brain six regions were well simulated with the model described in Materials and Methods as shown in Fig. 2 (only fr. GM and thalamus are shown). Parameters employed for the simulation were; k_s = 1 Hz, τ_c for the fast and slow relaxing site = 5 x 10^{-5}s and 10^{-10} s, respectively for IE, and k_{ex} = 5000Hz, P_f = 0.02f_M, and $\delta\omega$ = 2.2 ppm for AE, and the fraction of IE was 0.5. These parameters were within the range of previously reported values. Therefore, contribution of macromolecular fraction to the transverse relaxation was well explained by the exchange model.

Conclusions

The apparent transverse relaxation of tissue water in human brain was described as a linear combination of the regional iron and macromolecular content for a wide B_0 range of 1.5 to 7T. Linear dependence of the iron contribution on B_0 was similar to that observed in the ferritin solution. Quadratic dependence of the macromolecular contribution was accounted for by equally contributing iso- and anisochronous proton exchange mechanisms.

References

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Acknowledgments

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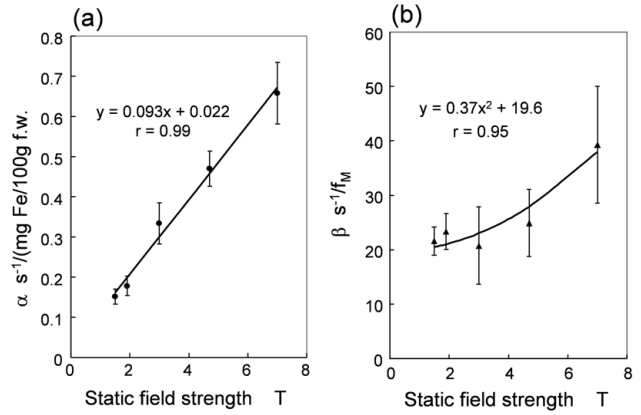

Fig.1. B_0 dependence of α and β

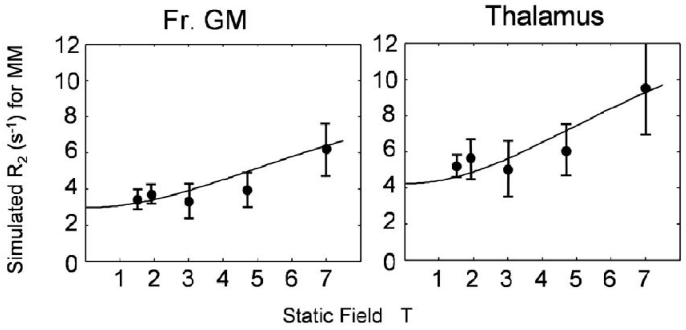

Fig.2. Simulated transverse relaxation rates for fr. GM and thalamus (solid lines) with observed $R_2^\dagger$ (circles)