Comparison between R2 and R2□f in estimating the iron deposits in the ganglia

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Synopsis

To compare the volume of the iron deposits in brain, we examined 13healthy volunteers by a 1.5 Tesla MRI system using two pulse sequences and compared between three transverse relaxation rates, two R2 from both the sequences and R2' from one sequence. Both R2 have robust correlations to the iron deposits comparing to R2'. R2' is based on gradient echo and is sensitive to macroscopic field inhomogeneity around basal ganglia. R2 is insensitive to it and retains practically enough sensitivity to the iron deposits in basal ganglia.

Introduction

The relationship between iron metabolism and disease process in degenerative diseases in the central nervous system (CNS) has come to be enlightened such as oxidative stress. The recent advance of MRI enables us to estimate volume of iron deposits in tissue by measuring its transverse relaxation rate. Its principle is that local magnetic inhomogeneity is caused by iron and decreases the transverse relaxation. Generally, effective transverse relaxation rate(R2*) is represented by an phenomenalistic relationship: R2* = R2 + R2'. R2 is the irreversible contribution to 180°pulse. R2' is the reversible contribution and influenced by the local magnetic inhomogeneity. Then, it had been accepted that the local magnetic inhomogeneity caused by the iron deposits is influenced by R2' and not R2. According to this theory, Ordidge used special sequence and measured R2, R2',and R2* simultaneously and concluded that R2' correlated most to the iron deposits. However some papers proposed a new analysis that R2 also correlated to the iron deposits. In measuring the iron deposits, there has been little argument that the local inhomogeneity influences on only R2' or both R2 and R2'. To conquer the problems we have measured R2 and R2' using GE(gradient echo) and SE(spin echo) and discussed which relaxation rates are useful for estimating the iron deposits.

Methods

All MR images were performed using a 1.5T system (SIEMENS, VISION, Germany) equipped with standard head coil. Two different pulse sequences were used: GESFIDE (gradient echo sampling of free induction decay and echo) for R2* and R2 and multiple SE for R2* quantification. Ma and Wehrli proposed the GESFIDE sequence by which the reversible and irreversible contributions were obtained simultaneously. GESFIDE is basically a Hahn spin echo sequence(90°- TE/2- 180°- TE/2), and it collects a series of gradient echo every 5ms from the spin excitation to the spin echo at TE=120ms. Using the GESFIDE data, the two effective relative rates are obtained separately; R2*A(prior to the 180°pulse) and R2*B(after the 180°pulse). R2' is calculated as 1/2(R2*A - R2*B), R2'(GESFIDE), and R2 as 1/2(R2*A + R2*B), R2(GESFIDE). For multiple SE, a series of 180°pulses are used from 5 ms to 115ms every 10 ms, and signals are acquired from 10 ms to 120 ms every 10ms. For the multiple SE data, all the echoes are fitted using a single exponential curve and the relaxation rate was obtained, R2(MSE). The other parameters are common; TR =1500ms, slice thickness = 3mm, interspace gap = 1.5mm. 8 axial slices around the basal ganglia region are obtained, 128*128 matrix, FOV=200*200 and two signal averaging. 13 healthy volunteers (11 men and 2 women , mean age 35.0 ±6.9 years old, range 25-46) without neurological signs were recruited in this study. We located ROIs on these maps with drawing borderlines of anatomical structures such as the frontal lobe, the caudate nucleus, the globus pallidus, the putamen, and calculated each value of voxels in ROI. Locations of ROIs were checked by one of us (K.A) who was blind to the calculation processes. Hallgen et al. proposed the relationship between the volume of the iron deposit and the age of postmortem volunteers using a histochemical technique. In estimating the volume of iron deposit in brain, the formula of Hallgen's postmortem study was quoted. (iron deposit) = A0[1-exp{-A1×(age of volunteer)}] +A2 :A0,A1,A2 are the inherent values. Postprocessing was performed using the Matlab software.(Cybernet co.).

Results

Representative R2(MSE), R2(GESFIDE), and R2'(GESFIDE) maps are shown in **Figure 1** from left to right. In R2' map, there were high intensity lesions enclosed in rectangular A and B. These were air-bone borders, so they would be the magnetic susceptibility different artifacts. The correlations were investigated between the volume of the iron deposit and the relaxation rates. The results are presented in Figure 2. In **Figure 2**, a vertical axis stands for the presumptive volume of iron deposition based on Hallgen's postmortem study (in milligrams of iron per 100 gram fresh weight) and horizontal axis stands for values of the R2 or R2'; □ for R2(MSE),× R2 based on GESFIDE, and □ R2' based on GESFIDE sequence. Linear regression lines are described as;

R2(MSE)	y = 9.20+ 0.181× x
R2 (GESFIDE)	y = 11.56 + 0.291× x
R2' (GESFIDE)	y = 2.58+ 0.094× x (x: volume of the iron deposits per 100 gram fresh weight. y: R2(MSE),R2(GESFIDE), R2'(GESFIDE).)

R2 and R2' increases corresponding to the rise of presumptive volume of iron deposits(x axis). Therefore both R2 and R2' have enough sensitivity to the iron deposits. Correlation coefficients for each linear regression lines are 0.920 for R2 (MSE), 0.872 for R2(GESFIDE), and 0.330 for R2' (GESFIDE). R2(MSE) and R2(GESFIDE) fits better to the linear regressions than R2'(GESFIDE). The slope of linear regression of R2(GESFIDE) is higher than that of R2(MSE). Vymazal et al. studied the correlation between the volume of the iron deposit and R2 by 1.5T MRI system and their linear regression was (R2)=10.3+0.189×(iron deposit). This result is almost same to our result of R2(MSE). Gelman et al. advanced this study with 3T MRI system and compared R2 and R2' by using GESFIDE sequence. The results were R2(GESFIDE)=12.7+0.61×(iron deposit) and R2'(GESFIDE)=2.2+0.50×(iron deposit). Comparing to our results, the intercepts of regression lines are almost the same but the slopes are higher. It is for reason that R2 is inherent in iron-free tissue and independent to strength of magnetic field, and that the effect of local magnetic field inhomogeneity depends on strength of magnetic field.

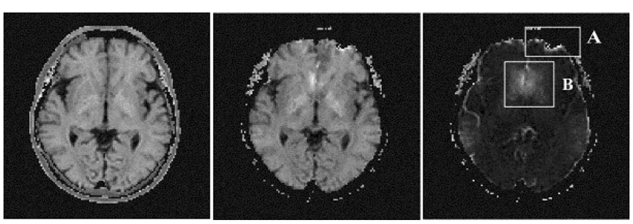

Figure 1

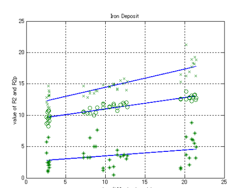

Figure 2

Discussion

In estimating the iron deposits, both R2 and R2' have enough sensitivity to iron deposits. Comparing the correlation coefficients for each linear regression lines, R2 is more fit to the iron deposits than R2'.

In comparing the correlation coefficients R2' is less useful to estimate the volume of iron. R2' suffers the influence of magnetic susceptibility difference artifact such as the rectangular B in figure 1. Ordidge et al. studied a technique of correcting local magnetic field inhomogeneity in 4T MRI system. The correlation coefficient of R2'(GESFIDE) might increases by importing this technique. However , R2 also has enough sensitivity to the iron deposits in our result and other studies concludes the same. This is because of diffusion effect of spins around magnetic perturbers. The diffusion effect prevents refocusing the spins after 180°pulse, so decreases R2(GESFIDE) and R2(MSE). This diffusion effect depends on the size of magnetic perturber, a small size like a cell would be influenced much to this effect. This diffusion effect depends also on an interval time between 180°pulses. That of R2(GESFIDE) is 60ms and of R2(MSE) is 10ms. R2(GESFIDE) has enough time to diffuse spins around magnetic perturbers compare to R2(MSE). For this reason, R2(GESFIDE) has more sensitivity to the iron deposits than R2(MSE) and the slope of the linear regression lines of R2(GESFIDE) is higher. In conclusion, R2 is the simple method for estimating the iron deposition in the basal ganglia cells and need not calibrate local magnetic inhomogeneity.

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