Comparison of MR Imaging Techniques to Estimate the Iron Concentration in the Brain

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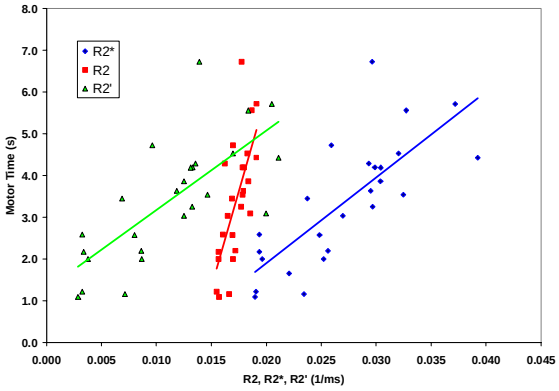
Introduction Ferrous iron is known to catalyze the oxidation of membranes and lead to the destruction of mitochondria and hence premature cell death. Excess concentrations of iron have been demonstrated in various neurodegenerative diseases including Parkinson's, Huntington's and Alzheimer's. However, the best imaging method to measure the tissue iron concentration is unknown. We have imaged a population of rhesus monkeys and measured R2, R2* and calculated R2'=R2*-R2, each of which are hypothesized to increase proportionately to the concentration of iron. We compared these measurements with independent measurements of the animal's motor function as determined by an automated movement analysis system. The results demonstrate a correlation between the motor performance times and these relaxation rates for several gray matter regions of the brain. The R2* relaxation rate showed the highest correlation for the striatum, globus pallidus (GP) and substantia nigra (SN). The correlation of motor speed with R2* was greater than with age alone implying that increased burden of iron leads to greater neural degeneration manifested as motor slowing.

Methods Twenty three female rhesus monkeys spanning the age range of 6-32 were included in this study. The animals were anesthetized and imaged on a 1.5T Siemens Vision system using the extremity coil. Images were acquired in the coronal plane with an in-plane resolution of 1×1 mm^2 and a slice thickness of 2 mm. Double echo spin echo images were acquired to measure T2. Multiple echo gradient recalled echo images were acquired to estimate T2*. These parameters were calculated from least squares techniques performed in custom-written programs developed in IDL. Data were extracted from hand-drawn regions of interest by a rater blind to the animal's age. Measurements were taken from the striatum, globus pallidus (GP), and substantia nigra (SN). Measurements taken on the left and right sides of the brain were averaged before analysis. The motor performance of each animal was assessed using an automated movement analysis panel which measured the time each animal took to retrieve food (a Lifesaver ®) from a rod bent into a "?" shape (1). This task measures the time for fine motor performance.

Results The reproducibility of the hand-drawn measurements was assessed by repeating the drawing of the GP, striatum and the SN for ten animals representative of the age range. The average R2 was highly reproducible with the maximum deviation of the mean ROI value between approximately 15 – 30% of the standard deviation of the values in a given ROI. Regression analysis of the motor performance time against R2, R2* and R2' showed the two were correlated for, GP, SN and highly correlated for the striatum which had a Pearson correlation coefficient of r=0.767. Multiple regression analysis was used to search for the significance of the correlation between motor performance time and R2* with age as a possible predictor. This analysis demonstrated that R2* predicted the majority of the variation in motor performance time. The correlation between R2* and R2' for the three tissues were always very high (r~0.97) indicating that the two were not independent measurements and the majority of the variation in R2' arose from R2*.



Conclusions These result are in agreement with the work of Hikata *et al* who demonstrated a higher correlation between R2* and the predicted iron concentration in the brains of humans than for either R2' or R2 (2). These results contradict those of Ordidge, and Gelman (3) who argued that R2' was a superior estimate of iron content than R2*. However, these results must be viewed tentatively as independent measurements of the tissue iron concentration in the brains of these animals were not available. This work supports the importance of developing a reliable and accurate MR imaging method to measure iron concentration. It also emphasizes the importance of iron as a biomarker of the aging process and potentially its role in causing neurodegeneration.

Figure 1. Motor performance time versus R2* (◊), R2 (■) and R2' (Δ) for striatum.

Reference:

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(2) T. Hikita, K. Abe, et al, *Comparison between R2 and R2' in estimating the iron deposits in the ganglia*. ISMRM 2004, #2309.

(3) Ordidge, R.J., Gorell, J.M. Assessment of relative brain iron concentrations using T2-weighted and T2*-weighted MRI at 3 Tesla. Mag. Reson. Med 1994.