Measuring the Iron Content of Gray Matter with T2 and T2* MR Imaging

P. A. Hardy[1], Z. Zhang[2], R. Grondin[2], R. Yokel[3], A. H. Andersen[2], D. M. Gash[2]

[1]Biomedical Engineering, University of Kentucky, Lexington, Kentucky, United States, [2]Anatomy and Neurobiology, University of Kentucky, Lexington, Kentucky, United States, [3]College of Pharmacy, University of Kentucky, Lexington, Kentucky, United States

Introduction: Recent evidence supports the view that excess accumulation of iron in the basal ganglia contributes to Parkinson's disease (PD).[1] Monitoring the accumulation of iron with age and with the onset and severity of PD would be extremely valuable in further defining the link between iron accumulation, loss of dopaminergic neurons in the basal ganglia and the decline in locomotor performance which characterizes the progression of PD. One non-invasive method to estimate iron content may be to measure the tissue's T2 using MR imaging as the relaxation rate (1/T2) should be proportional to the concentration of tissue ferritin.[2] Unfortunately, 1/T2 is also proportional to other factors and so testing the accuracy of the relationship is important.

Methods: Imaging: We imaged 10 female rhesus monkeys spanning the age range of 8 to 23 years using a 1.5T system. The animals were anesthetized, their heads placed in the extremity coil and secured using a customized head holder. Images were acquired in the coronal plane using a standard double echo-spin echo sequence TR/TE1/TE2 = 2200/20/80 ms. The slices were 3 mm thick and had an in-plane resolution of 1 mm. The left and right Globus Pallidus (GP), and Substantia Nigra (SN) were identified on the TE=20 and TE=80 images and outlined independently by two observers. From these images T2 was calculated as, $T2=(TE2-TE1)/\ln[S1/S2]$. T2* was measured from a multi-echo GE sequence which produced images at 11 TE values.

Iron measurements: The animals were euthanized and their brains were perfused with saline and removed. The brains were fixed in paraformaldehyde, sectioned and tissue punches throughout the basal ganglia were taken. The samples were digested in nitric acid, dried and analysed using an atomic absorption spectrometer for total iron content.

Results: The iron content of the GP and SN increased linearly with age of the animal with no sign of a plateau in distinction to the behavior seen in humans. The concentration of iron was also higher than typically seen in human brains for an equivalent age assuming that rhesus age three times faster than humans. The relaxation rates (1/T2 & 1/T2*) for the GP and the SN showed a linear increase with total tissue iron content. The slope of the 1/T2 vs [Fe] graphs was 0.040±0.007 for the GP and 0.029±.017 $msec^{-1}$ $(\mu g\ Fe/gm\ tissue)^{-1}$ for the SN. The correlation with iron was higher for the 1/T2 than for 1/T2*.

Discussion: The accumulation with age of iron in the basal ganglia results in substantially increased deposits of ferritin in the putamen, GP and SN,[3] which results in greater relaxation of water protons in the vicinity of the ferritin.[4] We found a similar linear relationship between 1/T2 and iron content for both tissues. The correlation for the GP (R^2=0.75) was stronger than for the SN (R^2=0.27) probably because of the increased size of the GP which allowed a more consistent definition of the tissue margins. This study is one of the very few to compare T2 measurements with measured tissue iron concentrations. In previous work measuring iron levels and T2 in humans the concentration of iron was approximately one half that measured here.[5] The relaxivity (1/T2/[Fe]) measured in human caudate was, however, higher at 0.086±0.025 $msec^{-1}$/ $(\mu g\ Fe/gm\ tissue)^{-1}$. This may indicate that iron in the brain of the rhesus is packaged or distributed differently than in humans. Understanding any difference in ferritin relaxivity is important for the development of measurements of iron burden in humans.

References

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