High field quantification of brain iron with R_2 mapping at multiple interecho spacings

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Introduction

Abnormal iron regulation in neural tissues is implicated in numerous neurodegenerative conditions [1]. Visualization and quantification of brain iron could enable clinical exploitation of this biomarker.

The transverse relaxation rate (R_2) is correlated with iron concentration and increases linearly with field strength as a result of iron [2, 3]. Direct R_2 measurements are confounded by water content while high field specific acquisition and processing challenges preclude widespread implementation.

We revisit the variable interecho spacing (ESP) method for iron detection [4, 5] at high field using recent methodological advances. We investigate the relationships between relaxation rates, their interecho dependence, and non-heme brain iron at 4.7 T to elucidate the merits of transverse relaxometry with single or multiple ESP for iron detection.

Methods

We employed the B_1 insensitive multiecho spin echo R_2 mapping method [6] to image a single slice ($1.5 \times 1.5 \times 4.5$ mm^3) through the basal ganglia of seven healthy volunteers (40±9.6 years old; 6 m, 1 f) at 4.7 T.

R_2 maps were obtained with ESPs of 6.0, 10, 15, 20, 30, and 45 ms; echo trains were 180 ms long, except ESP=6 ms, which was 120 ms. TR was 2.8 s; all other parameters were held constant.

Region-of-interest (ROI) analysis was performed on frontal white matter (WM), frontal gray matter (GM), occipital GM, caudate nucleus, putamen, globus pallidus, and thalamus to obtain average R_2 values. Two analyses were performed:

i) R_2 values measured with ESP=6 ms were correlated with non-heme iron levels, estimated from a post-mortem study accounting for brain region and subject age [7].

ii) Regression of R_2 versus log(ESP) was performed to obtain a slope; these slopes were then correlated to estimated non-heme iron levels.

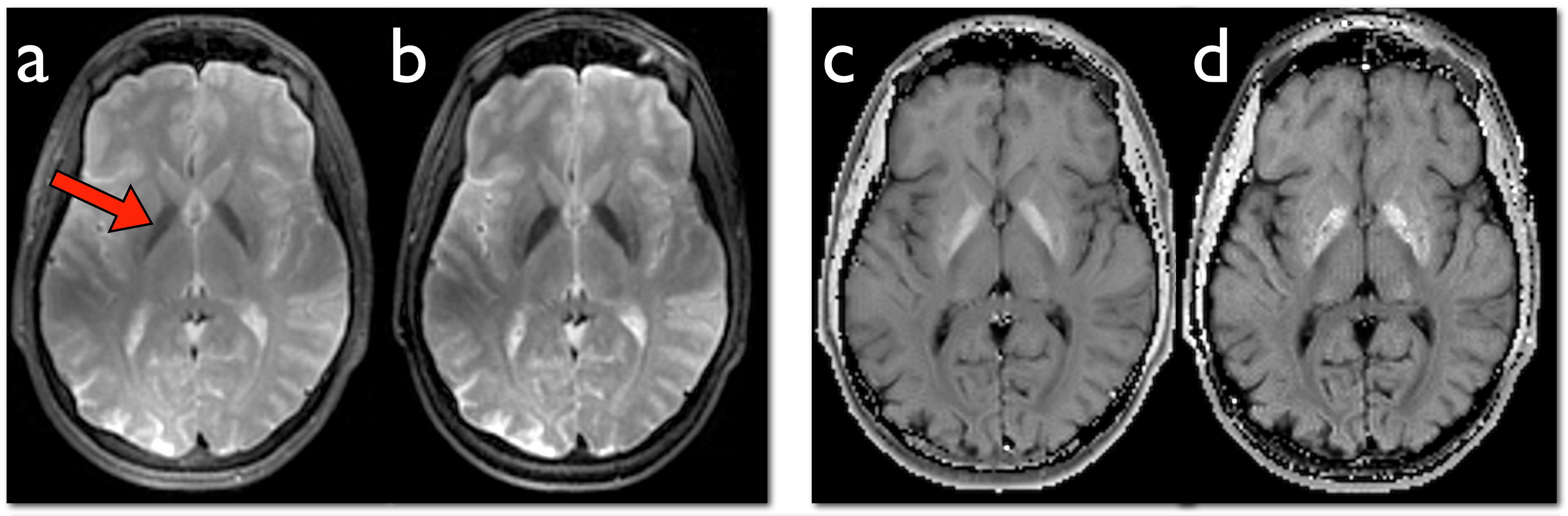

Figure 1: T2-w images (a, b) and R2 maps (c, d; scaled 0 to 40 s^{-1}). ESP is 6.0 (a, c) and 30 (b, d) ms. Contrast and R_2 differences between 6.0 and 30 ms are visible in the globus pallidus (red arrow) and other basal ganglia structures.

Results

T_2-weighted images and R_2 maps obtained with ESP=6 and 30 ms are shown in Fig 1. Hypo-intensity in the globus pallidus (red arrow) is visible at ESP=6 ms and obvious at 30 ms; quantitative ROI analysis reveals a near linear increase in R_2 as a function of log(ESP) in all regions measured, Fig 2. Regression of R_2 vs. non-heme iron provides a high correlation coefficient (R^2=0.77), but yields a non-zero intercept and three regions (FWM, OGM, Thalamus) are offset from a stronger linear trend through the remaining regions, Fig 3a.

Results (continued)

With variable ESP, a linear increase in slope is observed with non-heme iron, Fig 3b. A lower correlation coefficient (R^2=0.42) is measured than with R_2 vs. iron, but systematic regional bias is reduced and an insignificant baseline is observed.

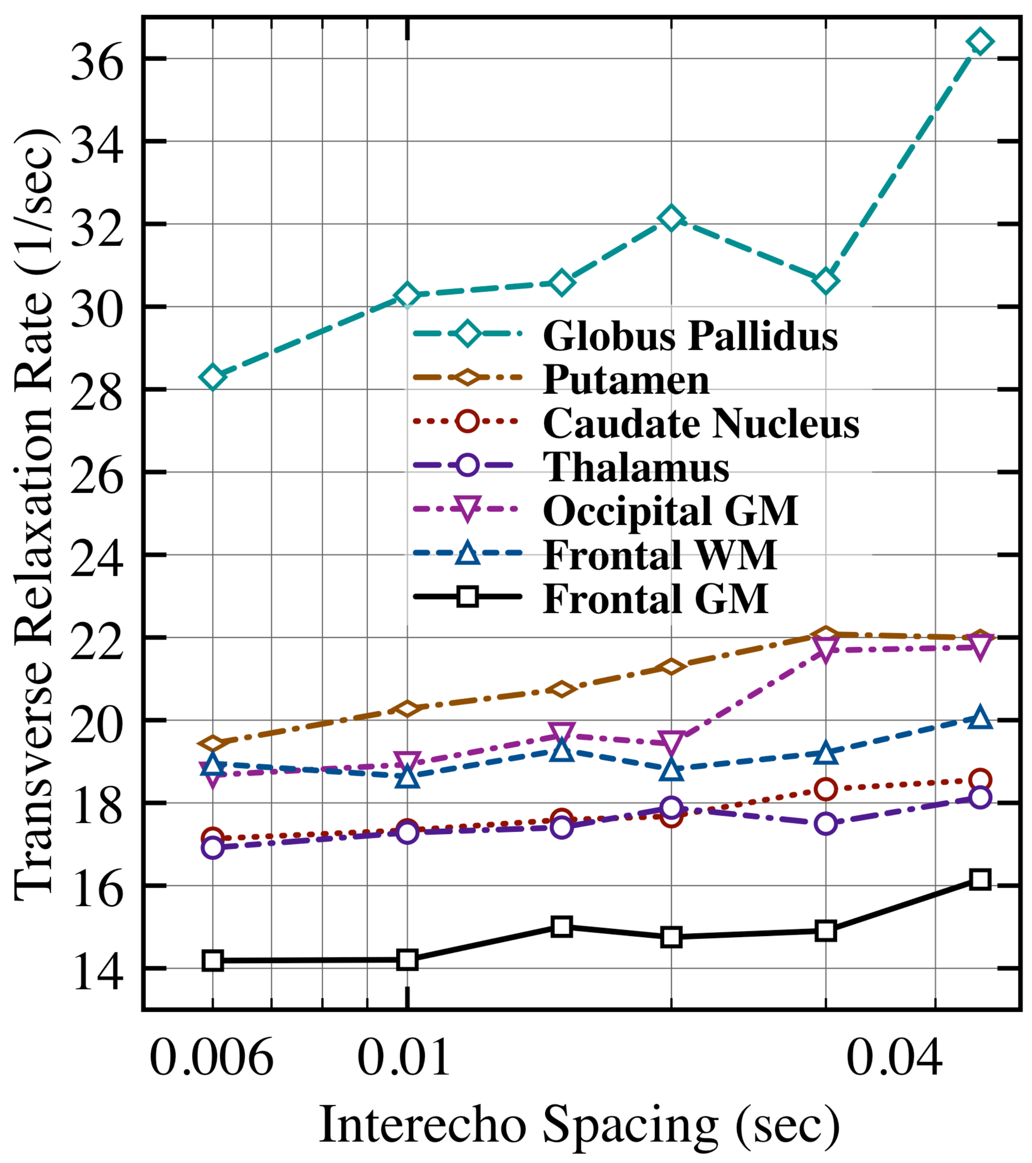

Figure 2: R_2 versus ESP for seven brain regions, as labeled, for a healthy 35 year old subject.

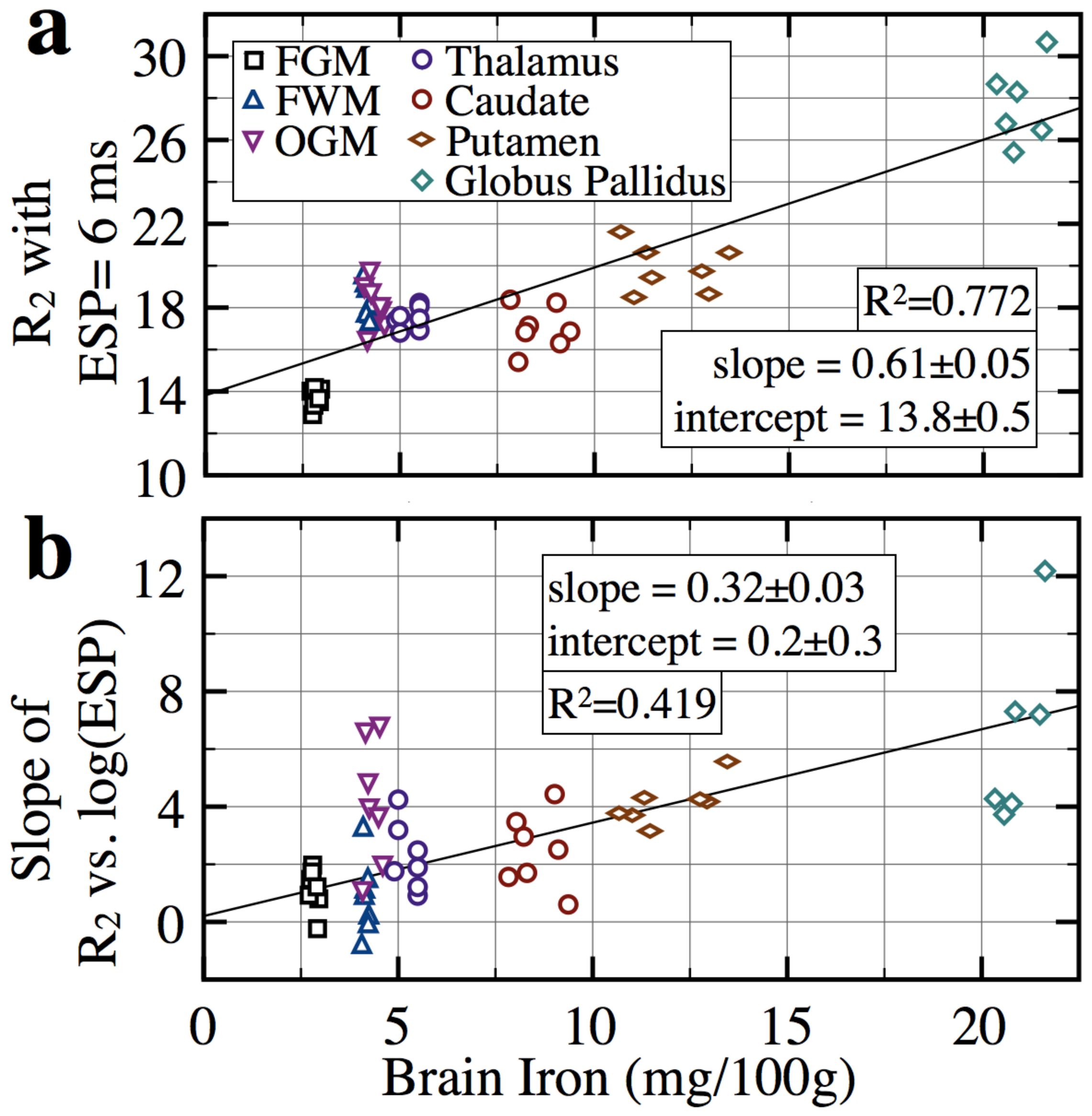

Figure 3: Fig. 3: (a) R2 with ESP=6 ms (first points on Fig. 2) and (b) Slope of R2 vs. ESP against brain iron.

Discussion and Conclusion

Direct R_2 measurements correlate well with non-heme iron and are very sensitive (iron induced relaxation is equal to spin-spin relaxation at 4.7 T, Fig 3a), but lack specificity due to a confound with the water content/macromolecular fraction [3].

Multiple ESPs reduce the water content confound by measuring changes in the relaxation rate. In this case, the rate of change of R_2 with ESP is linearly dependent on non-heme iron for all regions investigated. The current study excludes the heme iron contribution to brain iron; this may account for some variation observed in Fig 3.

The mulitple ESP method is limited by sensitivity and acquisition challenges. Sensitivity increases with field strength, making ultra-high field systems ideal for iron detection with single or multiple ESPs (inherent spin-spin relaxation is largely field-independent while iron induced relaxation increases with main magnetic field strength). High field specific acquisition challenges – notably B_1 heterogeneity and SAR – can be overcome with novel data processing and new acquisition methods.

In conclusion, transverse relaxometry at high field is possible. A strong correlation is observed between non-heme iron and R_2; multiple ESPs reduce confounds that typically preclude iron measurments with a single ESP and may be a promissing method for iron quantification at high field.

References

[1] Schenck JF and Zimmerman EA, NMR Biomed 17(7) 2004. **[2]** Bartha R et al. MRM 47(4) 2002. **[3]** Mitsumori F et al. MRM 62(5) 2009. **[4]** Ye FQ et al. MRM 35 (3) 1996. **[5]** Vymazal J et al. MRM 35(1) 1996. **[6]** Lebel RM and Wilman AH, MRM 64(4) 2010. **[7]** Hallgren B and Sourander P. J Neurochem, 3(1) 1958.

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