Within gray and white mater R_2* variations correlate histochemical iron stain of the human brain

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Introduction

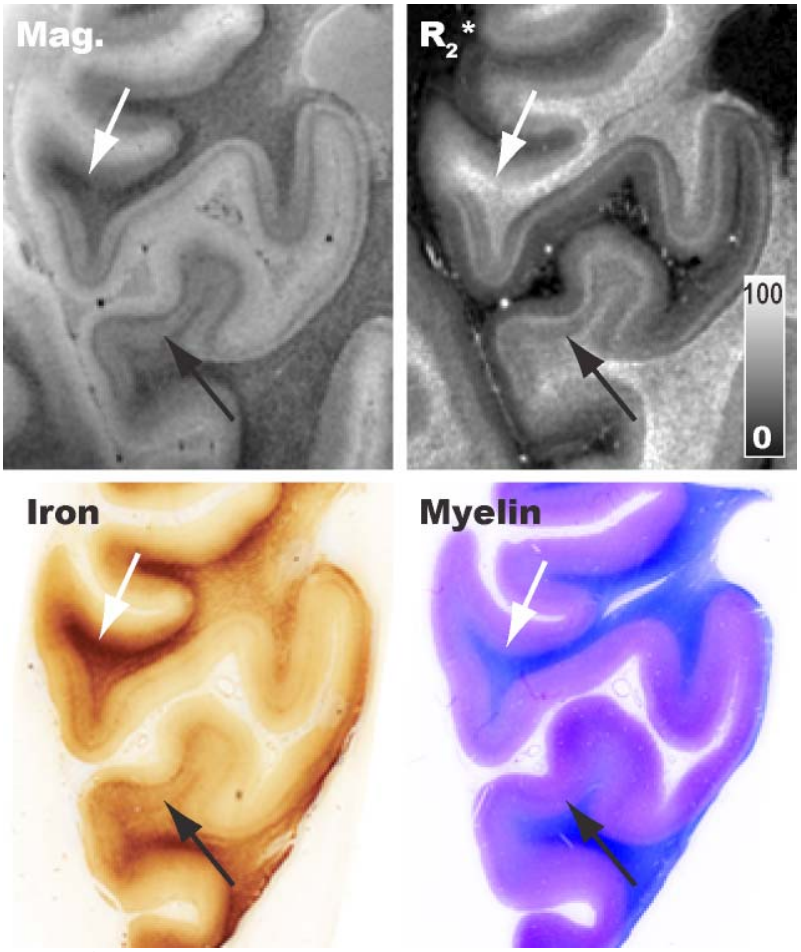
The magnitude and phase images derived from high resolution T_2* weighted MRI at high field strength have been used to reveal laminar contrast in the gray (GM) matter and fiber bundle-like structure in the white matter (WM) of the human brain [1,2]. Interestingly, this contrast is quite variable within cortical gray matter and within subcortical areas near the border between GM and white matter. This has been attributed to variations in magnetic susceptibility, possibly due to iron and myelin. A recent iron extraction study of the visual cortex suggests that non-heme iron is the primary source of cortical laminar susceptibility contrast [3]. In this study, we performed correlative R_2* mapping and histology in postmortem human visual area tissue to assess the contribution of iron and myelin in the R_2* variations within GM and WM.

Materials and Methods

MR imaging was conducted on a Signa 7.0 T whole-body MRI scanner (GE Healthcare) with volume transmit coil and a home built 8 channel receive-only detector array dedicated for imaging of tissue slabs. The formalin-fixed occipital lobe tissue slabs, which include the primary visual cortex were derived from a patient with no history of neurological diseases. High resolution 3D multi-echo gradient echo acquisition was performed with the following parameters: TR=55 ms, TE=17.5/30.9/44.2 ms, flip angle: 10 degrees, slice thickness: 0.15 mm, 200 slices, field of view: 156 x156 mm^2, matrix size: 1024 x1024 (150 µm isotropic voxel size), bandwidth: 62.5 kHz, total scan time: 3 hours 8 minutes. Data processing, including image reconstruction, calculation of magnitude image and R_2* maps was performed with IDL 6.5 (ITT Visual Information Solutions) software. Images were reconstructed using a phase-sensitive noise-weighted channel combination. After the MRI scan, Perls' non-heme ferrous (Fe^{1+}) and ferric (Fe^{2+}) iron staining with DAB enhancement and Luxol Fast Blue myelin staining were performed for 5 µm-thick serial sections from same tissue slab. The stained images were digitally scanned and nonlinearly coregistered (AIR 5.25, UCLA) to the R_2* maps, and subsequently spatial correlation of R_2* with staining intensity was calculated within and across tissue types by manually selected GM and WM ROIs.

Results and Discussion

The high resolution gradient echo images at all three echo times, but especially the longer echo times showed strong contrast variations. In GM, the MRI data showed laminar contrast suggestive of its functional subspecialization, consistent with *in-vivo* observations [2]. R_2* ranged from 20 to 55 s^{-1}. Similar laminar contrast was also seen in iron and to a lesser extent in the myelin stain images (correlation values r^2=0.80 and 0.30 respectively, Figure: black arrow). The WM R_2* varied substantially (ranging from 75 to 105 s^{-1}) and was higher than in GM. Highest values were found in subcortical WM (Figure: white arrow). Again, similar variations were seen in iron and to a lesser extent in the myelin stain data (correlation values r^2=0.56 and 0.11 respectively). Across WM and GM, a similar correspondence with histology was seen (r^2=0.82 and 0.54 for iron and myelin respectively). The results suggest that iron, and to a lesser extent myelin, contribute significantly to susceptibility contrast within and across tissue types. Further research is needed to determine their quantitative contribution by employing immuno-histochemistry.



References

[1] Li et al., Neuroimage 32:1032 (2006), [2] Duyn et al., PNAS 104:11796 (2007), [3] Li et al., ISMRM Proc. #885 2008.

Figure

Mag.: Magnitude image of 3D gradient echo at 30.9 ms echo time, R_2*: Calculated R_2* image (unit: s^{-1}), Iron: Stained image by Perls' iron staining with DAB enhancement, Myelin: Stained image by Luxol Fast Blue myelination staining.