Iron and myelin induced contrast variations in the corpus callosum

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Target audience

Researchers in the fields of iron deposition, phase and quantitative susceptibility mapping (QSM), relaxometry, and susceptibility induced contrast mechanisms in white matter.

Purpose

Brain iron levels were shown increased in inflammatory and neurodegenerative disorders including Alzheimer's disease and multiple sclerosis. While iron can by assessed reliably by MRI in gray matter, white matter susceptibility is strongly affected by the diagmagnetism of myelin but also by the orientation of white matter tracts which has hindered a reliable estimation of the iron content in white matter so far.[1,2]

The corpus callosum (CC) is suited ideally to study effects only originated from iron and myelin because all its fibers are perpendicular to the main magnetic field (B_0), thus, minimizing orientational variations in this structure.

The aim of this study was to investigate the iron distribution along the CC and to relate it to myelin content and susceptibility induced R2 contrast.*

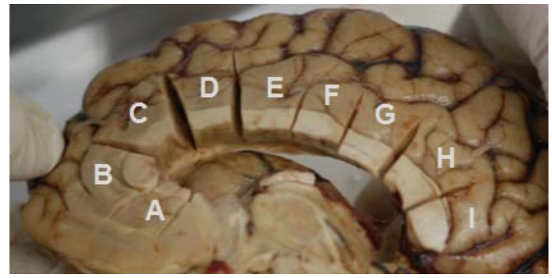

Figure 1: Sagittal 10mm-thick brain slice with the CC dissected in 9 substructures.

Methods

Four deceased subjects (age at death: 56-92 years) underwent quantitative MRI at 3T (TimTrio, Siemens) in situ including a multi-echo gradient echo sequence (TR/TE/ΔTE=68ms/5ms/5ms, resolution=1x1x4mm³) for the calculation of R2* relaxation rates and an additional gradient echo sequence (TR/TE=40ms/7ms, resolution=1x1x4mm³) with and without saturation pre-pulses to obtain the magnetization transfer ratio (MTR).

After MRI, brains were extracted and fixed in 4% neutral buffered formalin. Tissue specimens were taken from the genu (Figure 1: B), body (E-F) and splenium (I) of the CC and iron concentrations were determined with an inductively coupled plasma mass spectrometer at m/z 56 in He-mode.

In one subject (age at death: 74 years), the iron profile was assessed with a higher resolution by dissecting the CC into 9 substructures (Figure 1).

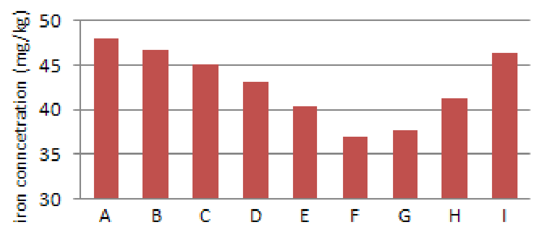

Figure 2: Iron levels along the CC determined by inductively coupled plasma mass spectrometry. Regions (letters) are corresponding to Figure 1.

Results

The mean iron concentrations showed a consistent pattern with substantially higher iron concentrations in the genu and splenium than in the body of the CC (Table 1). A detailed analysis of the 9 substructures confirmed this distribution along the CC (Figure 2). Effective transverse relaxation rate R2* and the MTR were higher in the splenium than in the genu and body (Table 1).

	Iron	MTR (%)	R2* (1/s)
Genu	43.2 ± 6	34.5 ± 0.04	21.2 ± 4
Body	38.1 ± 5	35.5 ± 0.04	21.4 ± 3
Splenium	46.9 ± 5	36.9 ± 0.03	24.8 ± 3

Table 1: Iron concentrations (mg/kg wet tissue) and MR measures along the CC.

Discussion and Conclusion

Disentangling contributions from iron, myelin and fiber orientation to susceptibility induced contrasts (R2*, phase, QSM) is currently a very active area of MR research.[1-3] This work provides direct experimental evidence that the contributions of iron and myelin (as assessed by the MTR) are impacting the effective transverse relaxation rate R2* additively.[2] A lower MTR along with a higher iron content in the genu yielded comparable R2* rates to the body of the CC, where this relation was reversed.

In conclusion, this study provides regional reference values for iron in the CC and demonstrates a heterogeneous distribution along the CC. Although the differences in iron concentration are relatively moderate (ca. 9 mg/kg), they substantially impact R2* and, thus, will consequently also alter phase and bulk susceptibility.[3] These findings have to be accounted for the development of techniques separating contributions of myelin and iron as well as enable their accurate determination in white matter.

References

1. Wharton S, Bowtell R. Fiber orientation-dependent white matter contrast in gradient echo MRI. *Proceedings of the National Academy of Sciences of the USA*. 2012 (ePub). 2. Langkammer C, Krebs N, Goessler W, et al. Susceptibility induced gray-white matter MRI contrast in the human brain. *NeuroImage.* 2012;59(2):1413-1419. 3. Deistung A, Schäfer A, Schweser F, et al. Toward in vivo histology: A comparison of Quantitative Susceptibility Mapping (QSM) with Magnitude-, Phase-, and R2*-Imaging at Ultra-High Magnetic Field Strength. *NeuroImage*. 2012 (ePub)