In vivo detection of age-related brain iron differences with MFC

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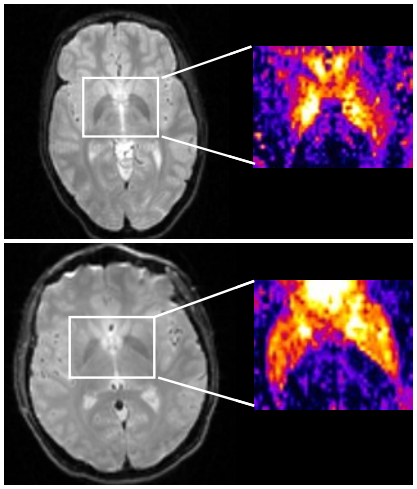
INTRODUCTION: Histochemical studies have demonstrated that the nonheme brain iron content is low at birth and dramatically increases during the first two decades of life in the globus pallidus, red nucleus and substantia nigra [1]. Only a few reports [2,3] have addressed changes in iron concentration in the developing brain through adolescence using MRI. Magnetic field correlation (MFC) imaging is a novel technique developed in our lab and is based on the quantitative characterization of the local magnetic field experienced by water protons in biological tissues. Interestingly, the MFC is strongly dependent on the spatial distribution of the microscopic magnetic field inhomogeneities, such as those generated by ferritin iron localized in oligodendrocytes, and therefore is likely to be a more specific measure of iron content than R_2 (=1/T_2). The MFC can be measured using an asymmetric spin echo sequence. The feasibility of quantitative MFC imaging in healthy adults has been previously reported *in vivo* [4], along with its high correlation with regional putative iron concentrations. In this abstract, we have assessed age-related differences in regional brain iron concentration as measured by MFC in both healthy adolescents and adults, and correlated the MFC with putative iron concentrations [1].

EXPERIMENTAL METHODS: Asymmetric spin echo images were acquired using a segmented EPI sequence from six adults (mean age 35.8 years) and 8 adolescents (mean age 15 years) on a 3.0 T MRI scanner (Trio, Siemens Medical Solutions). 20 slices (1.8 mm thick) were acquired using a 128 x128 matrix, 25 averages, FOV 230 mm, TR/TE = 2000/32ms with five refocusing pulse shifts (0.0, -3, -6, -9, and -12 ms). Additional zero shift images were acquired at TE=50ms for the estimation of R_2.Signal intensities were measured from brain regions including putamen, globus pallidus (GP), putamen (PUT), red nucleus (RN), substantia nigra (SN), corpus callosum (CC), thalamus (THL), head-of-caudate (HOC), frontal white matter (FWM) and cortical gray matter (CGM). MFC maps were calculated by fitting the signal intensity as a function of the pulse shifts, to a Gaussian function, on a pixel-by-pixel basis.

RESULTS: Figure 1 shows representative spin echo EPI images (shown on left) with an enlargement of the MFC map from basal ganglia region (shown on right) obtained from a 14 year old (a) and a gender-matched adult (b). Both maps were created from slices in similar anatomical regions. MFC values from several brain regions were correlated with established brain iron concentrations (2), suggesting that MFC imaging is highly sensitive to iron-induced differences in brain-tissue susceptibility. Figure. 2 shows scatter plots of MFC and R_2 versus age for two regions (GP and PUT). The curves are taken from the landmark paper of Hallgren and Sourander [1] based on post-mortem studies of iron concentration. The overall normalization of the curves is based on a global fit to the adult MFC data [4].

Figure 1. MFC Map of an adolescent (top) and a gender-matched adult (bottom)



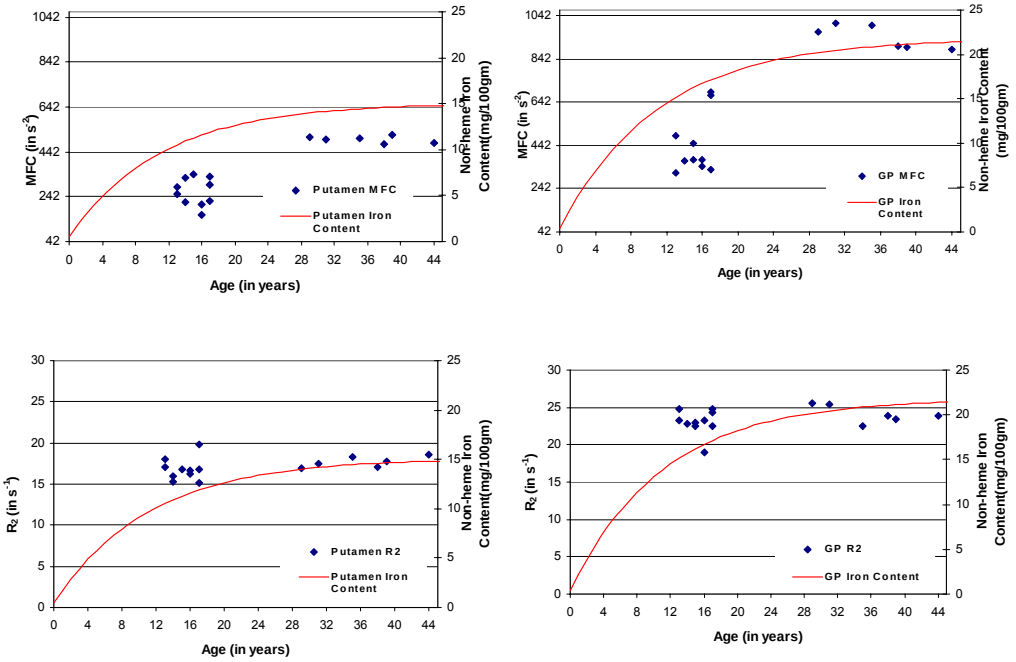


Figure 2. Scatterplots of MFC and R2 with age (in GP and PUT)

DISCUSSION: The differences in the MFC values between adolescents and adults were found to be significant in several brain regions, in particular the average MFC in the GP was 484.4± 144 s^{-2} for the adolescents and 941.4±54.2 s^{-2} in adults (p=0.0006). In contrast, differences in R_2 values were not significant in any region studied, with the exception of corpus callosum and frontal white matter. The usefulness of R_2 as a measure of tissue iron content is limited due its lack of specificity, since its is affected by other factors such as tissue density and water content, in addition to the presence of iron making the interpretation difficult. We have shown that MFC imaging is a sensitive technique capable of quantifying age-related differences in brain iron and is of potential use in the assessment of iron-related abnormalities in adolescents such as Hallervorden-Spatz syndrome, beta-thalessemia major and ADHD.

Region	MFC (in s^{-2})			R_2 (in s^{-1})		
	Adolescents	Adults	p-value	Adolescents	Adults	p-value
GP	441.03 ± 104.1	941.13 ± 94.1	< 0.001	22.05 ± 2.9	24.45 ± 0.8	0.06
PUT	264.39 ± 60.1	497.76 ± 49.7	< 0.001	16.34 ± 0.6	18.75 ± 1.0	0.08
RN	263.91 ± 100.0	763.87 ± 76.3	< 0.001	19.02 ± 2.5	22.14 ± 1.5	0.06
SN	333.61 ± 83.8	905.91 ± 90.6	< 0.001	20.05 ± 2.3	18.91 ± 1.9	0.07
HOC	271.96 ± 73.6	461.81 ± 46.2	0.005	15.54 ± 0.9	17.18 ± 0.3	0.08
CC	297.34 ± 94.6	289.22 ± 40.3	0.04	19.11 ± 3.0	15.76 ± 0.9	0.05
CGM	217.29 ± 80.2	227.80 ± 22.8	0.14	13.14 ± 2.3	13.17 ± 0.6	0.18
FWM	229.67 ± 94.1	154.91 ± 15.4	0.078	16.72 ± 1.1	9.67 ± 0.6	< 0.001
THL	155.04 ± 47.3	298.88 ± 29.8	< 0.001	15.79 ± 1.0	18.06 ± 0.1	0.06

Table 1. Regional estimates of MFC and R2

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