In vivo Iron Measurement in the Human Brain with mGESEPI

J. Wang[1], X. Sun[1], M. D. Meadowcroft[1], T. J. Mosher[1], J. R. Connor[2], M. B. Smith[1], Q. X. Yang[1]

[1]Center for NMR Research, Dept. of Radiology, Pennsylvania State College of Medicine, Hershey, PA, United States, [2]Neural and Behavioral Sciences, Pennsylvania State College of Medicine, Hershey, PA, United States

Introduction: Although abnormal iron metabolism has been implicated in several important neurodegenerative diseases such as Alzheimer's dementia and Parkinson's disease, clinical research in this field is limited by the inability to make quantitative, reproducible determinations of brain iron non-invasively. Since tissue iron directly changes tissue magnetic susceptibility, R_2* is the most sensitive MRI measurement of tissue iron status. Unfortunately, current MRI-based methods for measuring brain iron are limited by poor reproducibility and insensitivity to clinically relevant changes in iron status. Central to these limitations is the inherent difficulty in measuring tissue R_2* within a non-uniform magnetic field. The mGESEPI technique [1] is capable of measuring R_2* reliably in the images at high field. The purpose of this study is to determine the feasibility and responsiveness of mGESEPI for quantitative *in vivo* iron measurements in young normal human subjects.

Methods

Calibration Phantom: Tissue phantoms simulating the relaxation times of human brain tissues were created by adjusting agar and gadolinium concentrations. Tissue calibration samples were then generated by mixing the agar/Gd gel with iron solutions over the range of 0 to 24 mg/100g wet weight. The resulting calibration standards encompass normal tissue iron concentrations in the human brain. The R_2* vs. iron concentration calibration curves were produced with the phantoms at 37 ºC.

Human protocol: The study cohort consisted of seven normal subjects with an age range of 25 – 28 years old (average age 26.7 years), 5 males, 2 females. All subjects were right handed. MRI was performed using a Bruker MedSpec S300 3.0 T system with a TEM coil for RF transmission and receiving. An anatomic FSE scan was used to exclude subjects with focal structural or signal abnormality. A local shim was performed in the brain areas including midbrain, hippocampus, and basal ganglia. R_2* maps were obtained using mGESEPI with the following parameters: TR = 360 ms, TE = 8 ms, number of echoes = 12, echo spacing = 4.23 ms, bandwidth = 100 kHz, FOV = 25 × 25 × 1 cm^3, matrix = 256 × 192 × 16, five 10-mm-thick axial slabs, no gap between slabs, reconstructed image resolution = 0.967 × 0.967 × 0.625 mm^3.

Fe (mg/100g)	GP	Pu	RN	SN	CN
measured	19.16	10.93	15.11	17.08	6.89
predicted	19.85	10.07	19.48*	18.46*	7.46

Table 1. *Measured* tissue iron content of globus pallidus: GP, Putamen: Pu, red nucleus: RN, substantia nigra: SN, head of caudate nucleus: CN was estimated with R_2* measurement on seven 25 – 28 years old normal subjects. *Predicted* iron concentrations data were estimated from the regression formula in reference 4. * 30 – 100 years old.

Data processing and analysis

The data obtained with mGESEPI were reconstructed to twenty 2.5-mm-thick axial slices using user-developed software based on Interactive Data Language (IDL). The R_2* map was calculated on a pixel by pixel basis using linear regression. For statistical analysis, the R_2* parametric maps from all the subjects were normalized to the Montreal Neurological Institute brain template [2] using SPM2 [3]. The resulting resolution of the R_2* parameter map was 1 × 1 × 2.5 mm^3.

Results

Phantom calibration curves were used to calculate regional iron concentrations of the human subjects based on *in vivo* R_2* maps. As shown in Table 1 there is excellent agreement of measured iron concentrations with those estimated from published data. Since brain iron content is known to change with age, predicted values derived from the literature were corrected for age using a published regression formula [4]. As indicated in figure 1 there is no significant difference in iron concentration for identical structures measured in different hemispheres. However, the mGESEPI technique is able to measure statistically significant differences between different iron-rich structures (2-tailed 2-sample *t*-test, $p < 0.01$), indicating the technique is responsive to physiologically relevant differences in tissue iron concentration.

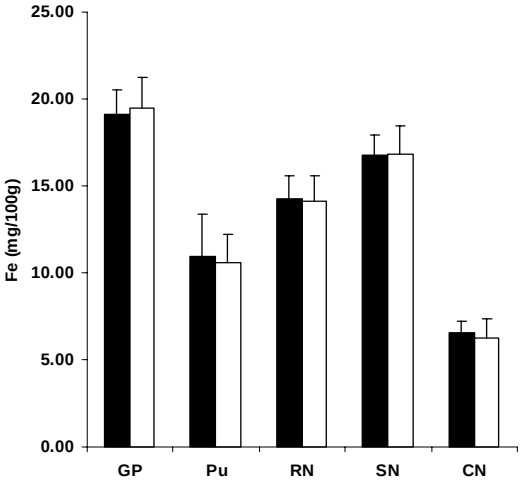

Figure 1. Right hemisphere (black) versus left hemisphere (white) comparison of measured iron concentration from 7 normal subjects. (GP: globus pallidus, Pu: Putamen, RN: red nucleus, SN: substantia nigra, CN: head of caudate nucleus.

Conclusion

Preliminary results indicate brain iron concentrations measured with mGESEPI are consistent with published values measured with invasive techniques, and are sensitive to regional differences in iron concentration within normal brain structures.

References

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