Iron deposition influences measurement of water diffusion tensor in the human brain: a combined analysis of diffusion and iron-induced phase changes.

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Purpose

It is well established that aging has a significant effect on water diffusion in the human brain. Typically, FA decreases while MD increases with advancing age in the white matter, commonly observed in regions such as the prefrontal lobe. By contrast, many authors reported increased FA and reduced MD in the deep grey matter during aging, especially in the putamen. Such changes were usually considered as a reflection of changes of underlying tissue microarchitecture during aging. However, previous studies suggested that iron deposits in the brain influence local signal intensity of diffusion weighted imaging, which may affect the estimation of water diffusion. Therefore, the change of water diffusion in the brain may be influenced by local iron accumulation during aging. In this study, we reviewed DTI metrics with susceptibility weighted phase imaging (SWPI) data collected in a life-span sample of healthy adults. The SWPI was used to estimate the brain iron concentration. The purpose of this study was to evaluate the impact of iron deposition on the measurement of water diffusion in the brain.

Methods

DTI and SWPI collected from 65 healthy adults (23-72 years old) were retrospectively analyzed. All the MR data were obtained using a 1.5 T MR scanner. A 3D GRE sequence (TR/TE = 51/38 ms, flip angle = 20, slice thickness = 2 mm with no gap, slice number = 28, FOV = 24 cm, matrix size = 256 × 256) was used for SWPI acquisition. A single-shot SE EPI sequence (TR/TE = 10000/86 ms, slice thickness = 3 mm with no gap, slice number = 32, FOV = 24 cm, matrix size = 128 × 128, NEX = 2, b value = 1000 s/mm^2 and diffusion direction =15) was used for DTI acquisition.

The original SWPI images were filtered with a high-pass filter to create the corrected phase image. After filtering, the phase values measured on the corrected phase image are mainly induced by local iron deposition. The greater the negative phase value indicates higher brain iron concentration.

The original DTI images were first corrected to remove EPI distortions due to eddy currents, susceptibility and motions by scaling, de-skewing, and translating methods. Two DTI metrics, MD and FA, were calculated on a voxel-by-voxel basis.

We chose the frontal white matter (FWM) and the putamen as the region of interest (ROI) to access the relationship of iron deposition and water diffusion. Regional phase value, MD and FA were recorded for further analysis.

Pearson correlation analysis was used first to test the age dependence of DTI metrics and iron concentration in these two regions. Multiple linear regression models were then built to examine the independent effect of age and iron deposition on DTI metrics. Age and iron concentration were used as the explanatory variables, with DTI metrics as outcome variables.

Result

Consistent with previous reports, FA decreased linearly ($r = -0.342$, $P = 0.006$) with aging in the FWM, and MD tended to increase with advancing age ($r = 0.240$, $P = 0.055$). Meanwhile, FA increased ($r = 0.463$, $P < 0.001$) and MD decreased ($r = -0.371$, $P = 0.002$) linearly with aging in the putamen. Furthermore, age related iron deposition occurred in the putamen ($r = 0.680$, $P < 0.001$) and FWM ($r = 0.333$, $P = 0.007$).

Multiple linear regression analysis showed that in the putamen, local iron accumulation and aging were both associated with an increase of FA and a decrease of MD. The statistically significant finding was that excluding the effect of age, FA increased ($P = 0.042$) and MD decreased with marginal statistical significance ($P = 0.067$) with elevated iron concentration. Above results indicated that iron deposition during aging may be the cause of increased FA and reduced MD observed in the putamen.

In the FWM, increase in iron level was also associated with an increase in FA and a decrease in MD. Whereas, advanced age was associated with a decrease of FA and an increase of water diffusivity. Above results suggests that iron deposition in FWM may counteract the changes of water diffusivity induced by aging.

Conclusion

Our study suggested that increased iron deposition would cause a decrease in the estimated diffusivity and an increase in the estimated anisotropy. This finding indicates that iron deposition influences significantly the measurement of water diffusion tensor in the human brain. Caution is needed when using DTI metrics for diagnosis of various neurological diseases involving abnormal iron deposition.