Diffuse iron deposition in the putamen and caudate nucleus in CADASIL: comparing phase and magnitude images at 7 Tesla

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Introduction

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary form of small vessel disease, caused by mutations in the NOTCH3 gene.[1] Focal areas of T2* hypointensity can be visualized in up to 40% of CADASIL patients and are caused by cerebral microbleeds.[2] Diffuse areas of T2* hypointensity, most commonly caused by diffuse iron deposition, has been described in neurodegenerative diseases such as Alzheimer disease, but also in normal aging.[3] It is unsure whether iron deposition is an exclusively neurodegenerative process, or if it can also be caused by vascular mechanisms. Last year we have shown decreased signal intensity on magnitude images of a T_2*-weighted sequence[4]. However the phase of the complex MRI signal might provide a more sensitive measure for iron quantification. The aim of this study is to use the phase to quantify diffuse iron deposition in the primarily vascular disease CADASIL and compare it to the magnitude based quantifications.

Methods

Twenty-five NOTCH3 mutation carriers and 15 healthy controls were examined using high resolution susceptibility-weighted imaging on a 7 Tesla whole body MRI scanner. A high-resolution multi-slice T2*-weighted scan over a limited field-of-view was performed (TR/TE/FA = 720ms / 21 ms / 45°, slice thickness 1.0 mm with a 0.1 mm interslice gap, 20 slices, 240 x 180 mm field of view, 1000 x 750 matrix size - resulting in a nominal resolution of 0.24 x 0.24 x 1 mm). The phase images were subsequently unwrapped by highpass filtering with a 92x92 kernel size.[5] Unwrapped phase images were evaluated for the presence of areas of increased phase shift, representative of increased iron levels. Regions of interest (ROIs) were drawn in the caudate nucleus, globus pallidus, putamen, thalamus and in the cortex and subcortical white matter of the frontal, parietal, occipital and temporal lobe. In these ROIs, mean phase shift and mean signal intensity was calculated and compared between mutation carriers and controls.

Results and Discussion

Phase shift measurements confirmed that mutation carriers had a significantly increased phase shift in the putamen (mean = 0.422 rad, p = 0.00008) and caudate nucleus (mean = 0.162 rad, p = 0.006) compared to controls (mean = 0.202 and 0.104 rad respectively). The amount of phase shift in the globus pallidus and thalamus, and in the cortex and subcortical white matter did not differ between mutation carriers and controls. Signal intensity measurements showed lower intensity in mutation carriers than in controls in the putamen (p = 0.005) and caudate nucleus (p = 0.0007). Both methods yielded similar results, however the significance level of the phase based method was higher. Magnitude and phase measurements in basal ganglia were inversely correlated (r = -0.77).

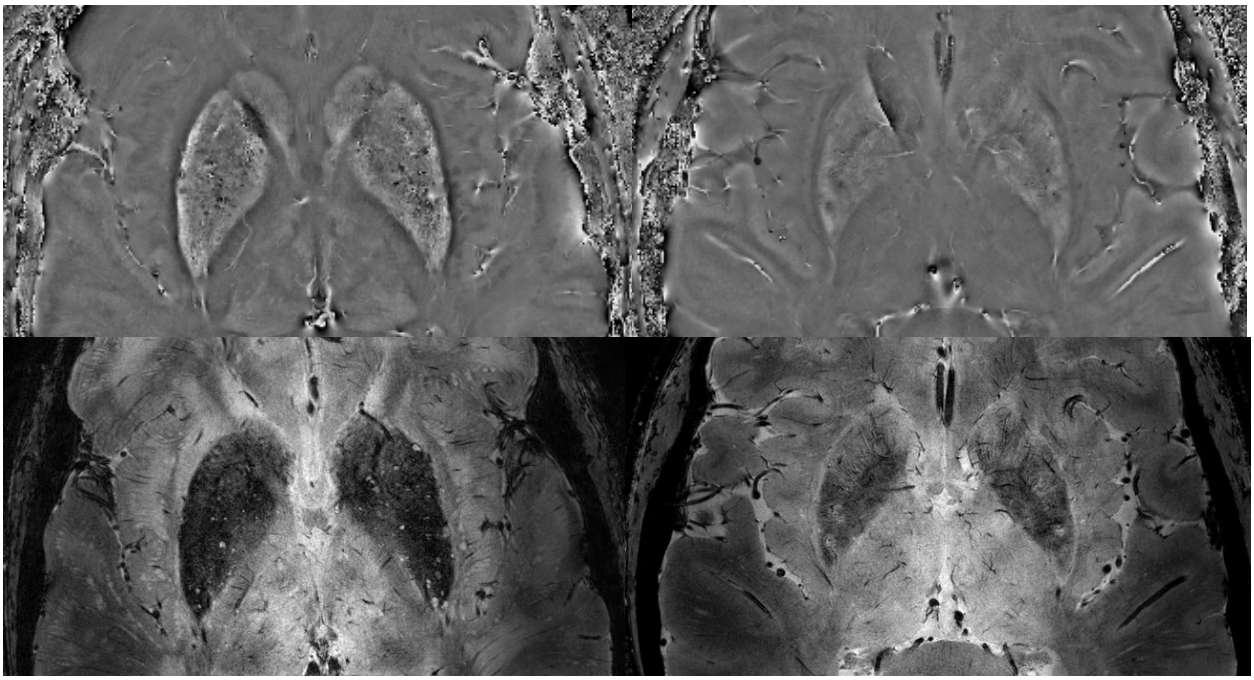

Figure 2: Unwrapped phase and magnitude images
Top row: phase images of a 60 years old CADASIL patient (left) and a 60 years old control subject (right), showing increased phase shift in the putamen and caudate nucleus of the CADASIL patient. Bottom row: corresponding magnitude images of the same subjects. Areas of decreased signal intensity are visible in the same nuclei.

Conclusion

7 Tesla MRI reveals an increased phase shift and reduced signal intensity in the putamen and caudate nucleus of CADASIL patients which is likely caused by increased diffuse iron accumulation. In the cortex and white matter no signs of increased iron accumulation were found. Phase and magnitude based analysis imaging showed similar results, with the phase based method showing slightly higher significances between patients and controls, indicating that it may be the more sensitive method to detect iron related changes.

References

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