

7 T MRI reveals an inhomogeneous cortex and changes in gray-white matter phase in Alzheimer's Disease

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Introduction

Alzheimer's disease (AD) can only be diagnosed with certainty at the autopsy stage. A histological hallmark of the disease is the presence of senile plaques which contain fibrillary amyloid- β (A β) and neurofibrillary tangles. In a previous study we demonstrated that abnormal MRI features could be visualized *post mortem* at 7 Tesla, with an acquisition time of 9 minutes, in human brain specimens containing cerebral A β deposition (1). These MRI features included distinct hypointense foci in the cerebral cortex and the presence of a so-called inhomogeneous cortex. The general aim of the present study is to reproduce our ex-vivo observations in living subjects who have been clinically diagnosed as being probable AD patients using a 7 Tesla human MRI system. If successful, our results could lead to a new tool to detect AD in living patients at an early stage.

Methods

Seven AD patients and 13 memory complainers (MC) were scanned using a high resolution transverse 2D T₂*-weighted scan including the frontal and parietal regions of the brain. Acquisition parameters were: TR/TE/flip angle 794 ms/25 ms/45°, voxel size=0.24×0.24×1 mm³, FOV=240×180 mm², 20 axial slices with a gap of 0.1 mm, total acquisition time: 10 min. (adapted from Duyn et al. (2)). To correct for f0 variations, a navigator echo was applied as previously described (3). The phase images were subsequently unwrapped by highpass filtering with a 92×92 kernel size. Susceptibility weighted images (SWI) were constructed by applying 4 phase mask multiplications (4). Magnitude, unwrapped phase and SWI images were evaluated for the presence of hypointense foci and an inhomogeneous cortex (1). Sensitivity and specificity of all MRI features to detect AD were calculated. During the evaluation, we frequently observed that on magnitude images the difference in intensity between gray and white matter was lost in AD, whereas this intensity difference on phase images seemed to be even larger in ADs than in MCs. To quantify this observation, the phase of gray and white matter was determined by measuring the phase in 16 different regions in both the grey and subcortical white matter separately in each slice. The phase values were averaged for gray and white matter per subject and the difference between gray and white matter phase was calculated. A non-parametric t-test was used to assess differences in phase values between the AD and MC groups.

Results

Figure 1 shows an example of a magnitude, unwrapped phase and SWI image of an MC (top row) and AD patient (bottom row). On the phase images, an inhomogeneous cortex was found in 7/7 AD patients and 4/13 MCs, resulting in a sensitivity and specificity of 100% (95 CI: 59%, 100%) and 69% (95 CI: 39%, 91%), respectively. On SWI, an inhomogeneous cortex was found in 6/7 AD patients and in 5/13 MCs yielding a sensitivity and specificity of 86% (95 CI: 42%, 100%) and 62% (95 CI: 32%, 86%), respectively. On the magnitude images, the presence of an inhomogeneous cortex was not detected in any of the AD or MC subjects. No hypointense foci were found on the images. On the phase images, the phase difference between gray and white matter was larger in the AD patients (Mdn = 0.853 rad) than in the MCs (Mdn = 0.609 rad), U = 2.00, p < .001, r = -.77.

Conclusion

This study showed that one of the features related to cerebral A β deposition as shown in AD brain specimens, an inhomogeneous cortex, also can be visualized in living AD patients with a human 7 T MRI. This feature is best visualized on the phase images. This pattern might be due to smaller plaques with less iron, which are not large enough to cause complete signal voids, but with enough susceptibility difference to cause a partial signal loss, resulting in an inhomogeneous patchy effect (1). Another marker of AD could be the increased phase difference between gray and white matter in AD patients, which most likely indicates a higher amount of iron deposition in the gray matter related to cerebral A β deposition as shown by Duce and coworkers (5). In summary, we have shown that phase and SWI images can be used to visualize changes in the cortex of AD patients that are not visible on magnitude T₂*-weighted images.

References

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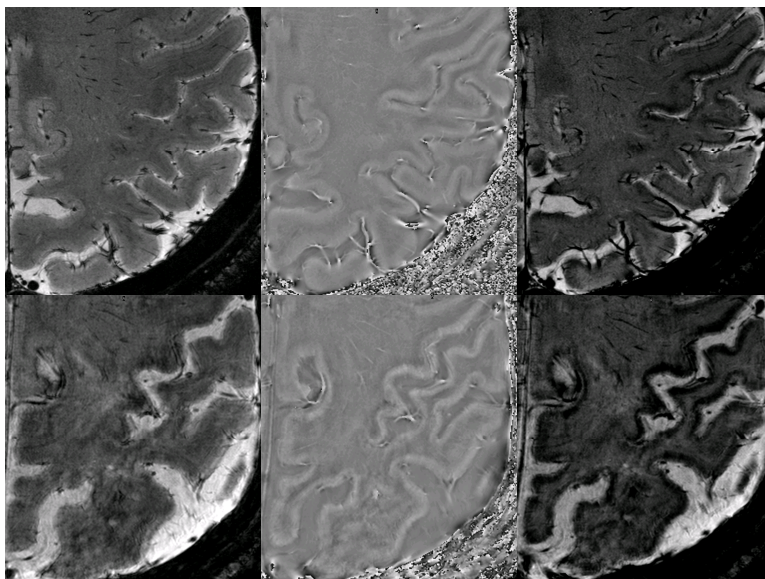


Figure 1: Images on the left show magnitude images, in the middle phase and on the right SWI. Top row shows an MC and bottom row an AD patient. An inhomogeneous cortex is shown in AD patients on the phase and SWI images. The difference between the intensity of the gray and white matter in AD is lost on magnitude images as opposed to MCs, whereas this difference is larger on the phase images in AD patients than in MCs.