Automatic detection of amyloid plaques on ex vivo APP/PS1 mouse brain using a zoom T2-weighted spin echo sequence

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Introduction

Amyloid plaques are known as a marker of Alzheimer's disease. They are traditionally detected as hypointense spots on T_2^*-weighted images taking advantage of the susceptibility effect due to iron embedded inside them. However it has been recently reported that T_2 contrast might be more efficient to detect cortical amyloid plaques [1]. In this context, the goal of the present study was to compare two different strategies: (i) a conventional T_2^* gradient echo sequence with volume coil [2], and (ii) a zoom adiabatic T_2 spin echo sequence with surface coil [1]. The images of an *ex vivo* APP/PS1 mouse brain acquired with both approaches were compared based on their ability to allow successful plaques detection using a home-made automatic procedure.

Materials and Methods

Animal protocol. A transgenic APP/PS1 mouse was sacrificed and its brain was immersed during 4 days in a solution containing 4% formalin and 2,5mM of a gadolinium-based contrast agent (Dotarem©, Guerbet, Roissy Charles de Gaulle, France), according to a 'passive staining' protocol previously established [2].

MRI acquisitions. The mouse brain was removed from the solution and placed in a container filled with Fluorinert© (3M, USA). MRI experiments were performed on a 7T small animal MRI scanner (Bruker, Ettlingen, Germany). T_2-weighted images were obtained with a 3D adiabatic zoom multi-spin echo sequence (Fig.1) (TR/TE=500/40ms, resolution=50µm^3, acquisition time=11hrs) using a home-made quadrature surface coil (two 12mm-diameter loops, loaded quality factor=110). For comparison, T_2^*-weighted images were acquired using a 3D multi-gradient echo sequence (TR/TE=100/16ms, resolution=50µm^3, acquisition time=11h30) using a home-made quadrature birdcage coil (inside diameter=28mm, loaded quality factor=120).

Data processing. An automatic procedure written in Matlab (The MathWorks Inc, Natick, USA) computes local intensity gradients to detect hypointense signals in MR images and segment amyloid plaques.

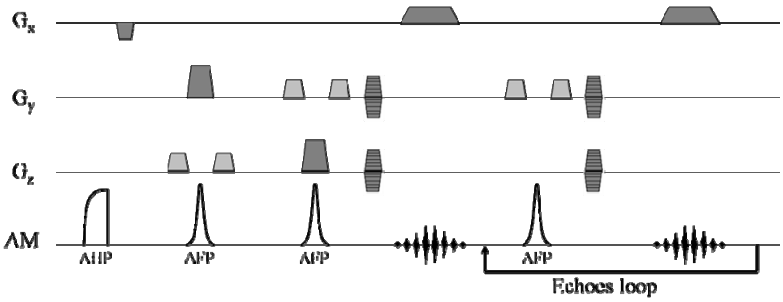

Fig.1 3D adiabatic zoom multi-spin echo sequence. The magnetization is excited by an adiabatic half-passage pulse (AHP), the field-of-view is then selected by two slice-selective adiabatic full-passage pulses (AFP20) [3] in the phase encoded directions (zoom). Finally a series of echoes is acquired using non-selective AFP20 pulses in order to limit signal loss.

Results and Discussion

Thanks to the high resolution zoom sequence combined to the increased sensitivity of surface coil, the T_2 strategy allows resolving individual amyloid plaques *ex vivo* (Fig. 2a, 2c and 3a) in a reasonable acquisition time, including in deep regions of the brain far from the coil.

On the T_2^*-weighted image, cortical blood vessels also appear as hypointense signal and can disturb the detection of amyloid plaques in this area (Fig. 2b, 2d and 3b). This might explain why a better specificity to amyloid plaques is achieved when applying the segmentation algorithm on the T_2-weighted image (Fig.3).

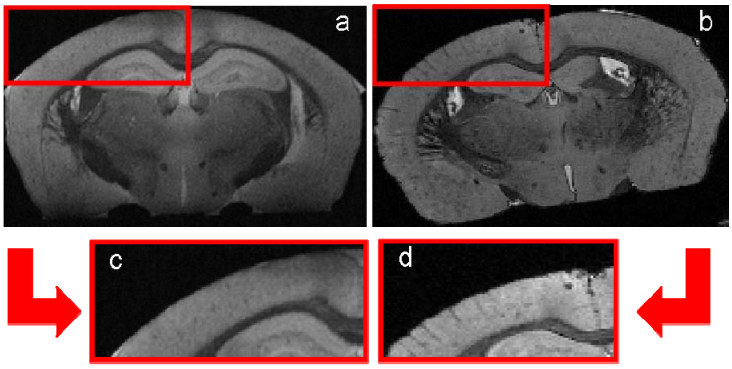

Fig.2 Coronal slices of the APP/PS1 mouse brain revealing amyloid plaques. a) T_2-weighted image, b) T_2^*-weighted image with respective zooms in one cortex area (c and d)

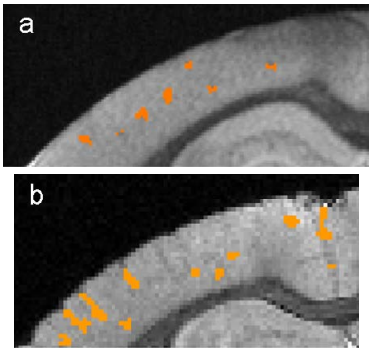

Fig.3 Automatic segmentation of individual amyloid plaques in one cortex area (same as Fig.2). a) T_2-weighted image, b) T_2^*-weighted image

Conclusion

In this study, we have shown that we are able to automatically localize individual amyloid plaques *ex vivo* on APP/PS1 mouse brain combining the zoom spin echo sequence and a dedicated segmentation procedure. The comparison with a standard gradient echo sequence reveals that T_2 contrast allows resolving amyloid plaques with a better specificity than T_2^* contrast, which is disturbed by the hypointense signals coming from blood vessels.

A histological study will be done to correlate amyloid plaques with MR images and confirm the present work. The next step will be to be able to detect the amyloid plaques *in vivo*.

References

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