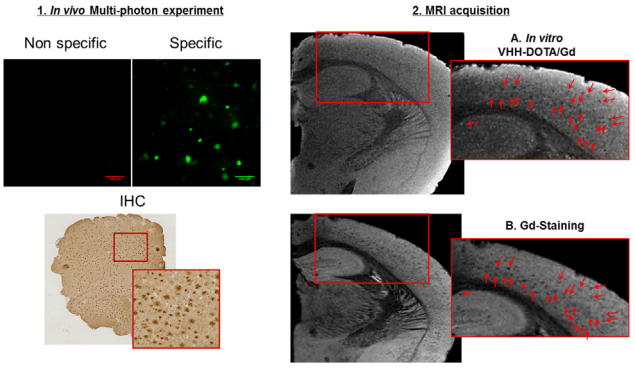
incubation with VHH-DOTA/Gd showed numerous hypointense spots in the cortex (Figure 2A). Moreover, several hypointense spots were colocalised (red arrows) with amyloid plaques revealed by the reference technique of Gd-staining (Figure 2B). **Conclusions:** This study demonstrates that VHHs cross the BBB, label amyloid plaques in vivo and can be detected by MRI following conjugation with a contrast agent. VHHs thus appear as promising tools with translational value for in vivo detection of amyloid deposits.



IC-P-016 AMYLOID PLAQUES DETECTION BY MRI: COMPARISON OF FIVE MOUSE MODELS OF AMYLOIDOSIS

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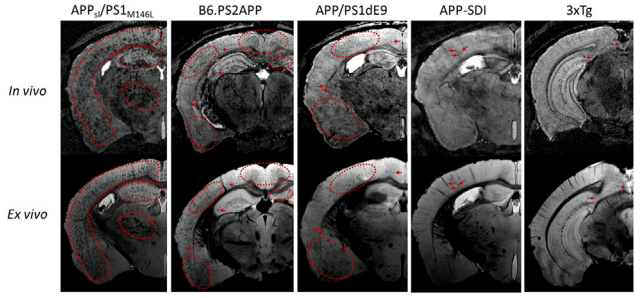
Background: Alzheimer's disease (AD) is characterized by two complementary brain lesions: amyloid plaques and neurofibrillary tangles. Amyloid plaques occur up to 20years before the first clinical signs of the disease and their detection is thus critical for an early diagnostic and to follow-up potential treatments. We developed methods of ex-vivo or in-vivo amyloid plaques detection based on the use of a non-targeted gadolinium (Gd) contrast agent for magnetic resonance imaging (MRI). Even if numerous mouse models of amyloidosis have been developed, the age of appearance, the size and the composition of the plaques in these models are different. Here, we compared the MRI detection of amyloid plaques by in-vivo and ex-vivo Gd-staining in different strains of mouse model of amyloidosis. **Methods:** Five strains of mice developing amyloid plaques before 10months were used: APP sl/PS1 M146L, APP/PS1dE9, B6.PS2APP, APP-SDI and 3xTg (APP swe/PS1 M146VKI/Tau P301L) aged of 14-15months (n=2/strain). Mice received an intracerebroventricular (ICV) injection of Gd (500mM, 1µl/side) and were imaged by in-vivo MRI one hour later. They were then sacrificed and their brains were extracted and incubated in a Gd solution (2.5mM - 48h) before ex-vivo high-resolution MRI. **Results:** Following in-vivo ICV infusion of Gd, MR images show numerous hypointense spots (upper pictures) which were previously demonstrated to be amyloid plaques (see Petiet et al., 2012 for examples). The number, size and contrast of the hypointense spots were highly variable in the different strains. This inter-strain difference was confirmed by the high signal/noise ratio ex-vivo Gd-stained MR images (lower figures). Plaques were more visible in APP sl/PS1 M146L > B6.PS2APP > APP/PS1dE9 > APP-SDI > 3xTg mice and only few plaques appeared in the two latter strains. **Conclusions:** These results demonstrate that depending on the strain, amyloid plaques display highly different aspects in MRI. These differences appear to be mainly due to the size of amyloid plaques. The contrast/noise ratio of the plaques on MR images is also critical for the detection of the plaques. This parameter can be modulated by the composition of the plaques, for example by their iron concentration or the Aβ40/42 ratio that can modulate their hydrophobicity and interaction with the contrast agent.



IC-P-017 BLINDED VISUAL EVALUATION AND QUANTITATIVE SUVR THRESHOLD CLASSIFICATION OF [18F]FLUTEMETAMOL PET IMAGES IN JAPANESE SUBJECTS

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Background: Amyloid imaging data are often quantified using a method where target region to cerebellar cortex tracer uptake ratios (SUVRcer) are computed. We investigated the agreement between blinded visual evaluations (BIE) and quantitative analysis of [18 F]f lutemetamol in a Japanese population. **Methods:** Healthy volunteers (HV; n=25, 15 elderly healthy volunteer ≥ 55 years (EHV), 10 young healthy volunteers <55 (YHV)) and patients with probable Alzheimer's Disease (pAD; n=20) and amnestic mild cognitive impairment (aMCI; n=20) each underwent a 30min dynamic PET scan, starting 90min post injection of 185MBq [18 F]flutemetamol. A 3D T 1 MRI was also obtained. Image data was processed to allow for application of a template set of regions of interest to a 30 min summation image to estimate a global cortical average SUVRcer. The optimal threshold was estimated as the midpoint between the mean of pAD and EHV cohorts in terms of standard deviation for the global SUVRcer. BIE were performed by 5 Japanese and 5 non-Japanese independent board-certified readers to obtain the majority outcomes of the ten readers. T he diagnostic capability of BIE and of global SUVRcer for differentiating AD from HV was evaluated, together with agreement between BIE and global SUVRcer. **Results:** Optimal threshold for discriminating pAD from HV was 1.391 for the global cortical SUVRcer average. Sensitivity and specificity of discriminating pAD from HV in this cohort for BIE (majority outcome) were 90% and 100%, respectively, and for SUVR cer 90% and 100%. In the efficacy evaluation, the quantitative classification categorized 18 subjects as positive (18 pAD, 0 HV), all of these were classified as positive by BIE. 27 subjects were categorized as negative quantitatively (25 HV, 2 pAD) and also by BIE, resulting in a 100% agreement between BIE and quantification using this threshold. BIE categorized 10 of 20 aMCI subjects as positive, quantitative classification added three subjects to this category. **Conclusions:** Agreement between the visual and quantitative assessment of [18 F]flutemetamol images is high. While quantitative classification should not replace visual assessment, it may be useful as a tool for detecting early stages of amyloid accumulation.