MRI DETECTION OF Aβ-PLAQUES WITH GD-STILBEN DERIVATIVE IN ALZHEIMER TRANSGENIC MICE

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Rationale and objectives: MR protocols designed so far to assess an Alzheimer Disease (AD) in humans, such as fMRI and hippocampus volumetry still lack either the sensitivity or the specificity needed. Although distribution pattern and quantification of Aβ-plaques payload are critical for AD diagnosis, no MRI approach allows a Human application.

This study aimed at evaluating the ability of an original Aβ-targeted contrast agent, Gd-stilben derivative (P03410), in first step with icv administration, to reveal Aβ-plaques in vivo in AD transgenic mice.

Methods: Firstly, binding specificity of the P03410 was examined on Human AD slices by confocal imaging. Afterwards, six APPPS1dE9 mice were in/ex vivo imaged on a 7T MR system (Neurospin, CEA, Saclay) 6h after a 0.3 µmol Gd/ventricule P03410 [Guerbet Research] injection. Histological detection of P03410 fluorescence and staining of Aβ-plaques (4G8) were performed on mice after MRI analysis. Wild type with P03410 icv injection, APPPS1dE9 with non-specific contrast agent icv injection and non-injected APPPS1dE9 were used as controls.

Results: In contrast to control groups, number of specific susceptibility artefacts can be observed by MRI following P03410 injection in APPPS1dE9 mice, as diffused focal dots all over the mouse brain due to high local concentration of compound surrounding plaques. This colocalisation of P3410 and Aβ-deposits were confirmed by immunohistological studies.

Conclusion: We demonstrate, in the present study, that Gd-stilben derivative (P03410) could be an innovative compound to reveal by MRI, Aβ-deposits in living animals with good chance of translation to Human.