MRI DETECTION OF NEUROINFLAMMATION SURROUNDING AMYLOID PLAQUES WITH USPIO IN ALZHEIMER TRANSGENIC MICE

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Rationale and objectives: USPIO approach allows an increase of MRI sensitivity and was evaluated in animal experiments and clinical studies as MRI markers for the diagnostic of neuroinflammatory disease associated with macrophage phagocytic activity. It is known that activated microglia play a role in the pathogenesis of Alzheimer disease (AD) as they cluster around amyloid plaques. In this context, this study aimed in evaluating the ability of an USPIO (P904), to detect, via microglial phagocytic activity, amyloid plaques, in transgenic mice.

Methods: Five Tg2576 mice and 3 APPPS1dE9 mice were imaged with T2*w GE sequence in vivo on 7T MR system (Neurospin, CEA, Saclay) before and 24h after P904 [Guerbet Research] iv administration of 1000 µmol. Fe/kg and ex vivo on 2.35T MRI system (Guerbet). Histological staining of microglia (CD45), iron (Perl’s method) and amyloid plaques (Congo Red) were performed.

Results: Post USPIO injection, several susceptibility artefacts were observed as diffused focal dots all over the mouse brain whereas only limited black dots were noticed before injection probably due to the presence of endogeneous iron deposit. Microglia cells were seen in and around amyloid plaques. Iron staining was visible as small granules inside or in neighborhood of amyloid plaques and microglia cells and matched with the low signal areas in MR images.

Conclusion: These results demonstrate that P904, an USPIO, could be a sensitive tool for MRI detection of neuroinflammation surrounding amyloid plaques. This approach could be applied to AD diagnosis and therapeutic monitoring.