NeuroInflammation and Cognitive decline in Alzheimer’s Disease : a pilot study of PET imaging of the translocator proteine ligands (TSPO) with [18 F] DPA-714 (NICAD)

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NeuroInflammation and Cognitive decline in Alzheimer’s Disease : a pilot study of PET imaging of the translocator proteine ligands (TSPO) with [18 F] DPA-714 (NICAD)

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Research Abstract
Alzheimer Disease (AD) is the most common aetiology of dementia in the elderly. The progression of the disease widely varies among subjects, some patients having a faster cognitive decline than others. Rapid cognitive decline has been defined as at least a loss of 3

points within 6 month at MMSE global cognitive assessment. It has been demonstrated that subjects with rapid cognitive decline have poorer outcome in terms of activity of daily living and higher mortality rate. However, they could have a better response profile to symptomatic treatments (such cholinesterase Inhibitors). While demographic, clinical and genetic characteristics have been shown to be associated with a higher risk of rapid decline, there is no reliable biomarker predicting this particular outcome.
Accumulation of ß-amyloïd proteins (Aß) within senile plaques and neurofibrillary tangles (NFT) of hyper phosphorylated tau protein both associated with neuronal death are the main neuropathological hallmarks of the disease, and molecular imaging PET technique allows now assessing their brain accumulation even at early predementia stages of the disease. However, over the last decades, increasing evidence has suggested that neuroinflammation plays a crucial role in the pathogenesis of AD. Neuroinflammation is characterized by microglial activation that may be positive by increasing Aß clearance, but also be deleterious by releasing pro-inflammatory cytokines that increase Aß formation and activation.
In vivo visualization of microglial activation has become possible with the development of molecular imaging ligands (tracers) for use with positron emission tomography (PET). The translocator protein (TSPO) formerly known as the peripheral benzodiazepine receptor (PBR), a receptor located in the outer membrane of mitochondria, is upregulated during neuroinflammation. So targeting TSPO with radio labelled ligands for PET is considered as an attractive biomarker for neuroinflammation.
The new ligand [18F]DPA-714 has already allowed to quantify the microglial activation in preclinical animal studies and in healthy control subjects, but also in amyotrophic lateral sclerosis (ALS) and stroke patients. Our hypothesis is that pronounced microglial activation, that can be assessed by PET with [18F]DPA-714, might be more likely to be associated with rapid cognitive decline in AD patients.
The main aim of the present study is to assess the level of neuroinflammation in AD subject (mild to moderate) estimated with Binding Potential (BP) of [18F]DPA-714, and its relationship with the kinetics of cognitive decline over a 24-month follow-up period (as assessed by ADAS-Cog and MMSE scores).
Additional aims are: 1/ to assess the relationship between the uptake of [18F]DPA-714 and cognitive and affective/behavioural symptoms at baseline and at 24 months 2/ to assess the relationship between the uptake of [18F]DPA-714 and change in hippocampal volumetry at 24 months 3/ to evaluate the relationship between brain uptake of [18F]DPA-714 and amyloid load measured with [18F]AV-45 at baseline 4/ to evaluate the relationship between the uptake of [18F]DPA-714 and peripheral markers of neuroinflammation (IL-1ß, IL-6, TNFa, CCL2, CCL5 and CX3CL1) at baseline 5/ to evaluate the relationship between the uptake of [18F]DPA-714, and microangiopathy (WMH/leucoaraiosis and microbleeds) at baseline

Further information available at:

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