New PET imaging agent for monitoring treatment response in Alzheimers disease

https://neurodegenerationresearch.eu/survey/new-pet-imaging-agent-for-monitoring-treatment-response-in-alzheimers-disease/

Principal Investigators

JAMES, MICHELLE LOUISE

Institution

STANFORD UNIVERSITY

Contact information of lead PI
Country

USA

Title of project or programme

New PET imaging agent for monitoring treatment response in Alzheimers disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

401063.3028

Start date of award

01/09/2015

Total duration of award in years

2

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is growing global health issue. At present, there are no drugs available to halt or reverse disease progression, and all efforts to create such therapies have failed. One reason for these failures is the lack of translatable biomarkers useful in both mouse models and humans, and the relatively small role

that appropriate biomarkers have played in the drug discovery and development process. Identification of translatable biomarkers for non-invasive assessment of therapeutic outcomes is imperative to improving the treatment of AD. Here we propose the use of a new imaging strategy for monitoring treatment response in Alzheimer's disease. The strategy involves using a specific positron emission tomography (PET) radioligand ([18F]GE-180) for the translocator protein 18 kDa (TSPO). TSPO PET radioligands are used to non-invasively detect and track microglial activation (a marker of neuroinflammation) in a living subject. Evidence suggests that neuroinflammation takes place very early in the AD, even before the formation of amyloid plaques. In addition, early anti-inflammatory intervention appears to profoundly impact the onset and progression of AD. The early involvement of neuroinflammation in AD, and the fact that it persists throughout disease and contributes to neurodegeneration, make it an ideal candidate biomarker for tracking pathology and monitoring response to early therapeutic interventions. Although there are a number of available TSPO radioligands, [18F]GE-180 has superior binding affinity and in vivo properties for imaging neuroinflammation processes in vivo. And while this tracer has undergone first in-man evaluation with favorable results, it is yet to be studied for it ability to monitor treatment response in AD. Our immediate goal is to evaluate [18F]GE-180-PET for its ability to track AD progression and monitor response to drug therapies in AD mouse models. Following this, our long- term goal is to assess the utility of [18F]-GE180-PET as a biomarker of AD treatment response in clinical trials of novel disease-modifying drugs. Our preliminary studies show that [18F]GE-180-PET can detect microglial activation in a mouse model of AD (APPL/S) at early stages of disease. In this proposal we aim to further evaluate [18F]GE-180 in AD mouse models for its use as a surrogate marker of AD neuroinflammation, and for monitoring response to novel drugs currently under evaluation for AD treatment. We will achieve our goals through the following specific aims: 1) determine whether [18F]GE-180-PET signal correlates with the extent of microglial activation and disease progression in two mouse models of AD, and 2) assess the sensitivity and accuracy of [18F]GE-180-PET for imaging response to two AD therapeutics currently in clinical trials (i.e., LM11A-31 and minocycline). The use of [18F]GE-180 could be a `game-changing' approach with potential far- reaching advantages in the whole arena of biomarker driven diagnostics and therapeutics for AD.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A