

# CSF, MRI, and PET biomarkers of neuroinflammation in Alzheimers disease

<https://www.neurodegenerationresearch.eu/survey/csf-mri-and-pet-biomarkers-of-neuroinflammation-in-alzheimers-disease/>

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### Country

USA

## Title of project or programme

CSF, MRI, and PET biomarkers of neuroinflammation in Alzheimers disease

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

€ 3,417,155.05

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15/08/2016

## Total duration of award in years

1

## The project/programme is most relevant to:

Alzheimer's disease & other dementias

## Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Immune System... Neurodegenerative... Neurosciences

## Research Abstract

**ABSTRACT** Alzheimer's disease (AD) is the most common form of neurodegenerative disorder. Inflammatory changes in the brain are thought to represent key processes in the onset and progression of AD, but it remains unclear whether neuroinflammation confers neuroprotection, accelerated degeneration, or possibly both. Such an understanding in living humans is critical if we are to begin clinical trials using the array of FDA-approved immunomodulatory drugs in the future. We propose that complement-mediated neuroinflammation is protective in the early AD stages, while suppression of complement activities is accompanied by the development of greater cognitive deficits and faster cognitive decline. Our preliminary data from multiple cohorts support this hypothesis by showing 1) reduced levels of cerebrospinal fluid (CSF) complement-related markers occur in the dementia stage but not mild cognitive impairment (MCI) stage of AD; 2) reduced CSF complement-related markers and elevated CSF interleukin-10 (IL-10) levels are associated with faster decline in AD; and 3) CSF inflammatory protein alterations reveal networks of cellular and protein regulations. In the current application, we will build on the association between complement related proteins and rates of cognitive decline in AD to identify associated changes in soluble CSF cytokines and chemokines, differential inflammatory cell type regulation, and imaging correlates of neuroinflammation. This application takes advantage of our group's strengths in performing CSF cytokine measurements, CSF immunophenotyping, molecular imaging of neuroinflammation through positron emission tomography (PET) and iron-enhanced MRI, and network analysis through a novel biochemical-bioinformatics pipeline. We will directly identify individual and networks of soluble CSF cytokines that accompany the transition from the MCI to the dementia stage of AD, correlate the complement and other altered pathways with microglial activation through two modern PET tracers (11C-PBR28 and 18F-FEPPA), and measure changes in individual T helper cell (type 1, 2, 17) and non-T cell populations. This application represents the first attempt to correlate, at the individual level and at the group level, CSF and imaging measures of neuroinflammation. If successful, this application will advance the understanding of neuroinflammation in AD through parallel approaches, form the basis of a new biomarker panel (and algorithm) to diagnose AD through a combination of degenerative and inflammatory markers, and accelerate the target identification of future therapeutics aimed at modulating the immune system in AD.

### **Lay Summary**

Brain inflammation is a key event in the onset and progression of Alzheimer's disease, but it is not clear whether it is harmful, protective, or both. The current proposal aims to confirm our finding that a switch from the protective to harmful type of inflammation predicts more severe symptoms and faster progression in Alzheimer's disease, and we can identify people with the protective and harmful inflammation by studying the cerebrospinal fluid (circulating proteins and cells) and brain imaging (PET and MRI scans).

### **Further information available at:**

#### **Types:**

Investments > €500k

#### **Member States:**

United States of America

#### **Diseases:**

Alzheimer's disease & other dementias

**Years:**

2016

**Database Categories:**

N/A

**Database Tags:**

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