Decoding the role of diverse astrocyte populations in aging and AD

https://www.neurodegenerationresearch.eu/survey/decoding-the-role-of-diverse-astrocyte-populations-in-aging-and-ad/

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Contact information of lead PI
Country

USA

Title of project or programme

Decoding the role of diverse astrocyte populations in aging and AD

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,886,190.83

Start date of award

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)... Brain Disorders... Dementia... Genetics... Neurodegenerative... Neurosciences

Research Abstract

Astrocytes are the most abundant cell type in the CNS that play vital roles in all facets of brain physiology. Activation of astrocytes, or reactive astrogliosis, is associated with morphological, gene expression, and functional alterations. Although changes in astrocyte dynamics a common feature in Alzheimer’s disease (AD), its underlying mechanisms and functional consequences remains poorly understood. Our recent studies identified five astrocyte subpopulations that display diverse molecular and functional characteristics in the brain. Significantly, one of the subpopulations, the synaptogenic astrocytes, strongly correlated with human AD expression datasets. This is exciting because synaptic dysfunction is widely accepted as an early and causal event in AD pathogenesis. Our long term goal is to decode the astrocyte types and determine the impact of the diverse astrocyte populations in aging and AD. The objectives of this proposal are to define the cellular and molecular heterogeneity of astrocytes in the cortex and hippocampus and to ascertain the functional role of synaptogenic astrocytes during aging and in AD mouse models. We hypothesize that diverse astrocyte subpopulations in the adult brain differentially contribute to AD pathogenesis and that reduced function of synaptogenic astrocytes plays a crucial role in driving synaptic dysfunction in early AD. To test the hypotheses we will profile changes of astrocyte subpopulations and define their molecular signatures in wild-type mice and AD mouse models as a function of age and AD pathology and cross-validate these results in postmortem human samples and associated expression datasets. We will decipher the role of synaptogenic astrocytes in AD pathogenesis by genetic targeting and functional testing of selected candidates. These studies will be led by two investigators with exceptional track-record in astrocyte biology (Deneen) and AD pathophysiology (Zheng) and assisted by outstanding bioinformatics support. Overall the proposal will significantly advance our understanding of astrocyte heterogeneity in brain regions critical to AD and how early and late astrocyte dysfunction contributes to AD pathogenesis. It will also lead to the identification of novel biomarkers and therapeutic targets.

Lay Summary
Project Narrative The proposed research is relevant to public health because it will provide fundamental knowledge about the nature of aging and the consequential impacts on the progression of Alzheimer’s disease via changes in diverse astrocyte populations. In this proposal, we will investigate the alteration and functional contribution of our newly identified astrocyte subpopulations in aging and AD using cutting-edge technology and innovative research strategies. These studies are expected to identify novel biomarkers and therapeutic targets for AD.

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:
N/A