Tau-induced axonal degeneration in Alzheimers disease and tauopathies

https://neurodegenerationresearch.eu/survey/tau-induced-axonal-degeneration-in-alzheimers-disease-and-tauopathies/

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Country

USA

Title of project or programme

Tau-induced axonal degeneration in Alzheimers disease and tauopathies

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,711,848.62

Start date of award

30/09/2014

Total duration of award in years

3

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... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease and other tauopathies are aging-related neurodegenerative diseases that are representative of a significant impending economic and treatment burden for the US healthcare system that will only increase as the population shifts to a more aged demographic. These diseases are characterized by the pathological accumulation of abnormally modified tau proteins, which is closely linked to their observed cognitive deficits. Since the underlying causes of tauopathies remain unknown, it is accordingly difficult to develop effective therapeutic interventions. Some of the earliest pathological changes, especially in AD, follow a “”dying-back”” pattern in which axons are the first to exhibit abnormal structural changes. A likely pathogenic factor contributing to axonal degeneration is the protein tau, as it is critical in maintaining axonal function. Indeed, studies using human tissue and animal model systems suggest that tau abnormalities and axonal degeneration are interconnected components of the early degenerative sequelae of AD. Our preliminary data indicate that disease-related modifications of tau that expose the amino terminus of the protein cause axonal dysfunction and degeneration in cultured neurons and in vivo. The primary goal of this proposal is to test whether disease-associated abnormalities in tau can induce axonal degeneration. Three independent specific aims are proposed to take a multifaceted approach aimed at addressing this hypothesis. Aim 1 will establish the relative contribution of tau modifications and the molecular events associated with tau-induced axon degeneration in primary cultured hippocampal neurons as well as a novel, viral vector-based rat model. Aim 2 will define the functional relationship between tau protein and enzymes linked to tau-induced axonal dysfunction (i.e. protein phosphatase 1 and glycogen synthase kinase 3?). Lastly, Aim 3 will define the relationship between abnormal forms of tau protein and axonal degeneration in the progression of human AD using post-mortem tissue from cases ranging between non-demented controls to severely demented AD. If successful, these studies will identify a molecular mechanism for tau-induced axon dysfunction/degeneration that could be targeted for disease-modifying therapeutic interventions in AD patients, as well as those suffering from other tauopathies.

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer’s disease and other tauopathies are aging-related neurodegenerative diseases that represent a significant problem for the healthcare system and economy of the US that will only increase as the aging population continues to grow. This project is aimed at addressing the hypothesis that the protein tau, which accumulates in neurons, directly participates in the degenerative events that underlie these diseases. Together, these proposed studies will provide significant insight into tau’s role in disease pathogenesis and identify new potential targets for therapeutic interventions aimed at mitigating the deleterious effects of tau on axon function and survival.

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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