Inflammation and delayed cognitive dysfunction after stroke

https://neurodegenerationresearch.eu/survey/inflammation-and-delayed-cognitive-dysfunction-after-stroke/

Principal Investigators

DOYLE, KRISTIAN PAUL

Institution

UNIVERSITY OF ARIZONA

Contact information of lead PI
Country

USA

Title of project or programme

Inflammation and delayed cognitive dysfunction after stroke

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 785,420.18

Start date of award

25/03/2014

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Impaired cognition, Vascular Dementia, stroke, Inflammation, Wallerian Degeneration

Research Abstract

Project Summary/Abstract. Up to 30% of stroke patients experience cognitive decline in the months and years after stroke. This dementia is commonly referred to as vascular dementia and its etiology is unknown. Our goal has been to develop the first model of post stroke dementia to

improve its classification, determine the cause(s) and develop treatments. We developed a new model of stroke that creates a highly consistent cortical lesion. In the first week after stroke mice have a motor and sensory deficit but no cognitive deficit. In the weeks that follow they recover from their sensory and motor deficit, however they experience cognitive decline, recapitulating one type of vascular dementia in humans. We have found that the development of the cognitive deficit correlates with the appearance of a delayed inflammatory response in the striatum and internal capsule of stroked mice, characterized by activated macrophages/microglia and infiltration of T cells. We hypothesize that this inflammatory response is in response to Wallerian degeneration of the axons that project from the stroke lesion. Furthermore we hypothesize that because Wallerian degeneration in the CNS is very slow, taking months to years to resolve, this inflammation may cause T cell mediated autoimmunity, and that this may be the cause of dementia in a large number of stroke patients. To test this hypothesis we propose to determine the structural basis of the cognitive impairment in our mouse model, determine if cognitive impairment correlates with autoimmunity, and determine if T cells are necessary for cognitive dysfunction to occur. We will also determine if multiple strokes accelerate and amplify the immune response to stroke, and if tolerization to brain antigens can prevent cognitive dysfunction. To help me accomplish these aims I have sought help from expert mentors and consultants to provide instruction in each of the areas that I require further training. With the help of my mentor Dr Buckwalter, co-mentor Dr Wyss-Coray, and in conjunction with my consultants Dr Longo, Dr Steinman and Dr Shamloo I will gain expertise in a wide range of experimental techniques and methods of analyses. I have also put together a training plan to facilitate my transition to a tenure-track academic position that incorporates learning management, mentoring and job search skills. My long-term goal is to develop treatments for vascular dementia to improve the lives of patients and their caregivers. The proposed research and training plan will contribute enormously to the accomplishment of this goal.

Lay Summary
Project Narrative: Vascular dementia is the second leading cause of dementia representing approximately 15-20% of diagnosed cases of dementia throughout the world. The etiology of vascular dementia is unknown and there are no animal models. The goal of this proposal is to develop a model of vascular dementia and identify its causes.

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