Understanding Amygdala Neurodegenerative Mechanisms in Alzheimer's Disease

Name of Fellow

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Institution
Funder

Alzheimer's Society

Contact information of fellow
Country

United Kingdom

Title of project/programme

Understanding Amygdala Neurodegenerative Mechanisms in Alzheimer's Disease

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Alzheimer's Society

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3.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract

Alzheimer's disease (AD) patients frequently have alterations in behaviours beyond that of memory. These include altered social conduct and anxiety traits, which are known to involve the amygdala. Classical hallmarks of AD have been noted in the amygdala, suggesting that neurodegeneration within this brain region may be causing these behaviours.

Whilst controversy surrounds the use of APP overexpressing mice in AD research, a new generation of knock-in mice that only overexpresses A? containing familial mutations have eliminated the behavioural confounds related to APP overexpression. These mice also appear to harbour A? plaques within the amygdala. Thus, they present an ideal opportunity to investigate whether A? in the amygdala is causative of changes to amygdala-related behaviours associated with AD.

This fellowship will use a multidisciplinary approach to understand the role of A? in the amygdala. Using slice electrophysiology, we will contrast oligomeric A? and the new knock-in mice to determine how this affects synaptic transmission and plasticity within multiple amygdala nuclei (e.g. basolateral), and whether changes are related to NMDA receptor-dependent excitotoxicity. I will use DT-MRI to derive tracts in knock-in mice emanating within and between the amygdala to see how A? disrupts connectivity. Finally, I will explore amygdala-related behaviours to see whether these change in an age-dependent manner in the knock-in mice. This project will deliver a detailed investigation of how A? accumulation alters amygdala function. Understanding the neural circuity involved with AD in better mouse models will lead to the chance to treat social and anxietal deficits in AD.

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