Mapping AD Memory Failure: Molecules to Connectivity of Brain Network

https://neurodegenerationresearch.eu/survey/mapping-ad-memory-failure-molecules-to-connectivity-of-brain-network/

Principal Investigators

KACZOROWSKI, CATHERINE COOK

Institution

UNIVERSITY OF TENNESSEE HEALTH SCI CTR

Contact information of lead PI
Country

USA

Title of project or programme

Mapping AD Memory Failure: Molecules to Connectivity of Brain Network

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

383486.2385

Start date of award

15/08/2015

Total duration of award in years

2

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Basic Behavioral and Social Science... Behavioral and Social Science... Brain Disorders... Dementia... Mental Health... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s Disease (AD) dementia currently afflicts over 5 million people in the United States and is projected to rise to 11-16 million elderly by the year 2050. Recently my colleagues and I demonstrated that spatial memory deficits in mouse

models of aging and AD correspond to a decrease in excitability of neurons of the hippocampus. However, the molecular mediators of these intrinsic changes and the consequence of excitability changes at the individual neuron level once they are embedded into an active neural network remains unknown. The present proposal is based on our new preliminary data showing that memory deficits in an AD mouse model correspond to changes in the expression of a specific subset of excitatory and inhibitory receptors. These changes in expression are indicative of a shift in the balance of excitatory and inhibitory influences on hippocampal neural networks. An appropriate balance has been shown to be crucial for the generation normal gamma band oscillatory network activity and for the long range synchronization of beta and gamma oscillations. We have new electrophysiological pilot data, showing that spatial memory deficits in our AD mouse model is correlated with a significantly reduced coherence of hippocampus (Hip) and prefrontal cortical (PFC) oscillatory network activity in the beta and gamma frequency ranges. Additional preliminary data on receptor expression provide a probable mechanistic explanation for the observed reduction in Hip-PFC coherence. It is posited that either misregulation of plasma membrane proteins normally required for memory (via de novo synthesis) and plasticity, or the dysfunction of Hip-PFC network coherence, or both, underlie spatial memory deficits in AD that will be tested in ensuing aims. Outcomes of the proposed research have the potential to make a major impact on the identification of new treatments for AD-related memory disorders. Our molecular and network level analysis may also discover biomarkers that could be used to detect potential onset of Alzheimer’s disease well in advance, so that treatment could begin earlier with better success rates.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A