Entorhinal-hippocampal circuit dysfunction in AD mice

https://www.neurodegenerationresearch.eu/survey/entorhinal-hippocampal-circuit-dysfunction-in-ad-mice/

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Country

USA

Title of project or programme

Entorhinal-hippocampal circuit dysfunction in AD mice

Source of funding information

NIH (NIA)

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01/08/2015

Total duration of award in years

2

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): Spatial memory impairment and disorientation are a

common problem associated with aging and they are often one of the first symptoms of mild cognitive impairment and Alzheimer’s disease (AD). Understanding the properties of cells involved in the formation of spatial memory in a mouse model with early AD pathology will enhance our understanding of the earliest forms of cognitive decline in AD. The cells known to be important in spatial memory are place cells of the hippocampus (HPC) and grid and head direction cells of the entorhinal cortex (EC). We will use a novel approach to simultaneously record the electrophysiological properties of grid and place cells using 128-channel electrode recordings from 3 regions of the entorhinal cortex-hippocampal (EC-HPC) circuit in AD mice. We will then analyze the large-scale electrophysiological data and measure synaptic plasticity using a spike-timing dependent plasticity (STDP) model. Predictions from this model will be used as a guide to adjust spike timing in neurons, either enhancing or suppressing the synaptic strength of cell populations in affected regions of the EC-HPC, using optogenetic modulation. We anticipate that this will allow us to correct the spatial impairment deficits. To recapitulate te spatial orientation impairments seen in early-stage AD patients, behaviorally equivalent tasks in mice such as morphing open fields, spatial novel object recognition task and T-maze alternation tasks will be applied. These tasks have been chosen specifically to study the functioning of EC-HPC circuit neurons (CA1, CA3, dentate gyrus, lateral and medial entorhinal cortex) that get activated in relevant behavioral modes. The proposal brings together diverse fields (electrophysiology, molecular neuroscience and computational neuroscience) applying large-scale recording techniques simultaneously across multiple brain regions to develop analytical and predictive computational tests to interrogate and restore function in an important circuit that is dysfunctional in Alzheimer’s disease.

Lay Summary
PUBLIC HEALTH RELEVANCE: Early stage Alzheimer’s disease related cognitive impairment is thought to result from dysfunction in a circuit known as the entorhinal-cortex hippocampal circuit. To better understand the properties of cells in this circuit in an AD mouse model we will examine the firing properties of neurons, and then use a computational model to predict how to restore function. We will then test the model by using optogenetics to stimulate neurons accordingly.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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