Hippocampal Neurovascular Plasticity in CVN-AD Mouse: Fornix-Septal Stimulation

https://neurodegenerationresearch.eu/survey/hippocampal-neurovascular-plasticity-in-cvn-ad-mouse-fornix-septal-stimulation/

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Country

USA

Title of project or programme

Hippocampal Neurovascular Plasticity in CVN-AD Mouse: Fornix-Septal Stimulation

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

387614.6789

Start date of award

01/09/2016

Total duration of award in years

1

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Cerebrovascular... Dementia... Neurodegenerative... Neurosciences

Research Abstract
? DESCRIPTION (provided by applicant): Current understanding of Alzheimer’s disease focuses on accumulation of amyloid and tau proteins, enhanced disease progression with vascular factors (ie, APoE), a large reduction in metabolism and substrate/energy supply to the brain, significant changes in neurovascular coupling, neuronal damage leading to memory and

cognitive abnormalities, cholinergic cell loss, and diffuse brain atrophy. Though a large number of treatments are in trials, the underlying basis of Alzheimer's disease remains unclear. Thus, similar to dopamine replacement therapy for Parkinson's disease, the clinical focus for Alzheimer's disease has been to treat symptoms (ie, memory) rather than the underlying (unknown) cause. Thus, available human treatments focus on acetylcholinesterase inhibition to improve cholinergic function and memory. Other clinical approaches to enhance cholinergic cell function and memory loss in Alzheimer's patients have involved nerve growth factor [NGF] gene therapy into nucleus basalis Meynert and deep brain stimulation [DBS] applied to the fornix, both currently in trials. However, human fornix stimulation has also been noted to show widespread metabolic changes in the brain. Though the focus of this DBS approach has been on memory enhancement, fornix and septal stimulation also induces cholinergic stimulation, which can affect blood vessel reactivity and neurovascular coupling and improve metabolism throughout the brain. We hypothesize that fornix DBS stimulation is also causing secondary septal stimulation of cholinergic nuclei, affecting neurovascular coupling and blood flow, in addition to direct hippocampal physiological effects. Septal stimulation would lead to diffuse cholinergic enhancement of hippocampal function, causing changes in excitatory transmission, neurovascular coupling and enhanced substrate/metabolic supply to the brain, likely improving the widespread vascular changes noted in Alzheimer's disease. We propose to study both physiological and vascular effects of fornix/septal stimulation in a mouse model of Alzheimer's disease that shows a clear, progressive deterioration with representative histological changes (ie, plaques and tangles) over months [CVN-AD].

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