Presynaptic and astrocytic role of Amyloid precursor protein signaling in the hippocampus

https://neurodegenerationresearch.eu/survey/presynaptic-and-astrocytic-role-of-amyloid-precursor-protein-signaling-in-the-hippocampus/

Name of Fellow
Institution
Funder

European Commission FP7-Seventh Framework Programme

Contact information of fellow
Country

EC

Title of project/programme

Presynaptic and astrocytic role of Amyloid precursor protein signaling in the hippocampus

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 50,000

Start date of award

01/02/14

Total duration of award in years

2.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Molecular and cellular neuroscience | amyloid beta | synaptic vesicle release | astrocyte | single synapse | fluorescence lifetime imaging | electrophysiology

Research Abstract
Amyloid beta peptide (Abeta) is a normal product of the amyloid precursor protein (APP)

proteolysis in the brain. While Abeta synaptotoxicity has been extensively studied as central to Alzheimer’s disease (AD) pathogenesis, the mechanisms by which physiological Abeta regulates synapse function remain unknown. Utilizing two-photon excitation laser scanning microscopy combined with fluorescence lifetime imaging, FM-based imaging of synaptic vesicle recycling at the single-synapse level and electrophysiology, I aim to explore the molecular mechanisms modulating synaptic and astrocytic properties by physiological Abeta signaling and its effects on neuronal integration in acute hippocampus slice preparations.
I will investigate the potentiation of presynaptic strength by Abeta and the transducing mechanism by answering the following questions: In the hippocampus, is the Abeta-dependent potentiation of neurotransmission synapse-specific? Can APP molecules form homodimers at presynaptic and astrocytic plasma membranes? Do local changes in the conformation of APP complexes convey intracellularly the Abeta signal? I will also investigate which effectors downstream to presynaptic APP dimers are modulated to induce Abeta-dependent potentiation of neurotransmission. I will measure the distance range at which axon-released Abeta regulates presynaptic functions during neuronal activity. With electrophysiological techniques, I will characterize the effects of Abeta on the functional input-output relationship in the hippocampal network. I will finally ask whether APP molecules also exist as dimers in astrocytes and whether APP conformation is dependent on Abeta levels and on membrane specialization in the vicinity of synaptic contacts.
At the end of the project, the training in neuroimaging will offer me a great opportunity to investigate structure-functions relationship in native single synapse using cutting-edge technologies with an important impact in the field of AD.

Types:
Fellowships

Member States:
N/A

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A