

Evolution of Alzheimer's Disease: From dynamics of single synapses to memory loss

<https://neurodegenerationresearch.eu/survey/evolution-of-alzheimer%c2%92s-disease-from-dynamics-of-single-synapses-to-memory-loss/>

Principal Investigators

Institution

Contact information of lead PI

Country

European Commission

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Evolution of Alzheimer's Disease: From dynamics of single synapses to memory loss

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The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Research Abstract

A persistent challenge in unravelling mechanisms that regulate memory function is how to bridge the gap between inter-molecular dynamics of single proteins, activity of individual synapses and emerging properties of neuronal circuits. The prototype condition of disintegrating neuronal circuits is Alzheimer's Disease (AD). Since the early time of Alois Alzheimer at the turn of the 20th century, scientists have been searching for a molecular entity that is in the roots of the cognitive deficits. Although diverse lines of evidence suggest that the amyloid-beta peptide (Abeta) plays a central role in synaptic dysfunctions of AD, several key questions remain unresolved. First, endogenous Abeta peptides are secreted by neurons throughout life, but their physiological functions are largely unknown. Second, experience-dependent physiological mechanisms that initiate the changes in Abeta composition in sporadic, the most frequent form

of AD, are unidentified. And finally, molecular mechanisms that trigger Abeta-induced synaptic failure and memory decline remain elusive.

To target these questions, I propose to develop an integrative approach to correlate structure and function at the level of single synapses in hippocampal circuits. State-of-the-art techniques will enable the simultaneous real-time visualization of inter-molecular dynamics within signalling complexes and functional synaptic modifications. Utilizing FRET spectroscopy, high-resolution optical imaging, electrophysiology, molecular biology and biochemistry we will determine the casual relationship between ongoing neuronal activity, temporo-spatial dynamics and molecular composition of Abeta, structural rearrangements within the Abeta signalling complexes and plasticity of single synapses and whole networks. The proposed research will elucidate fundamental principles of neuronal circuits function and identify critical steps that initiate primary synaptic dysfunctions at the very early stages of sporadic AD.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

European Commission

Diseases:

Alzheimer's disease & other dementias

Years:

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Database Categories:

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