Novel roles by glutamatergic receptors in the synaptic effects of beta amyloid

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Principal Investigators

MALINOW, ROBERTO

Institution

UNIVERSITY OF CALIFORNIA SAN DIEGO

Contact information of lead PI
Country

USA

Title of project or programme

Novel roles by glutamatergic receptors in the synaptic effects of beta amyloid

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,724,431.19

Start date of award

01/04/1995

Total duration of award in years

22

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): Novel roles by glutamatergic receptors in the synaptic effects of beta amyloid Long-term potentiation and depression (LTP and LTD) are promising and widely studied examples of vertebrate synaptic plasticity in which there is a persistent synaptic enhancement or decrement, respectively, seen following brief conditioning periods of synaptic activity. In both these forms of plasticity, which are leading models of memory, NMDA receptors (-Rs) and AMPA receptors (-Rs) at synapses play key and distinct roles. The general aim of this grant has been to examine the subcellular signaling controlling LTP and LTD. Recently, we have found that beta amyloid (A?), a peptide strongly implicated as a causative agent in Alzheimer's disease, has pronounced effects on AMPA-R trafficking requiring a novel form of NMDA-R signaling. In this grant period, we will examine the different roles played by NMDA-Rs and AMPA-Rs and their associated proteins in the effects of A? on synapses. Our preliminary studies show that a non-ionic form of NMDA-R signaling as well as a specific subunit of AMPA-Rs are required for A? to modify excitatory synapses. Here we will examine these findings using several complementing methodologies including molecular biology, electrophysiology, and two-photon laser scanning microscopy. These studies will use heterologous cell lines, organotypic rat hippocampal slices and genetically modified mice. The results of these studies will elucidate the mechanisms underlying Alzheimer's disease as well as provide potentially efficacious treatment strategies. The specific aims are to determine: Specific Aim 1: The role played by NMDA-Rs and associated molecules in A?-induced synaptic depression Specific Aim 2: The role played by AMPA-Rs and associated molecules in A?-induced synaptic depression

Lay Summary

PUBLIC HEALTH RELEVANCE: Synapses, the sites of communication between nerve cells, are thought to be early targets of damage in Alzheimer's disease. Abnormally high levels of the peptide A? is thought to be causative in the disease. Understanding such a process may provide insight into treatment of Alzheimer's disease.

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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