"Dr. Jekyll or Mr. Hyde? The strange case of amyloid-beta peptide from physiology to Alzheimer’s disease."

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Abstract

For several years Amyloid-beta peptide (Aβ) has been considered the main pathogenetic factor of Alzheimer’s disease (AD). According to the so called Amyloid Cascade Hypothesis the increase of Aβ triggers a series of events leading to synaptic dysfunction and memory loss as well as to the structural brain damage in the later stage of the disease. However, several evidences suggest that this hypothesis is not sufficient to explain AD pathogenesis, especially considering that most of the clinical trials aimed to decrease Aβ levels have been unsuccessful. Moreover, Aβ is normally produced in the brain, where it is regulated by synaptic activity, primarily through vesicle exocytosis. In the last 10 years, we have been investigating whether and how Aβ plays a physiological role in the healthy brain. We have demonstrated that concentrations of synthetic Aβ resembling the physiological content in the brain enhances synaptic plasticity and memory in mice, and that endogenous Aβ is needed for these processes. Interestingly, the effect of both exogenous and endogenous Aβ was mediated by modulation of neurotransmitter release and α7-nicotinic receptors (α7-nAchRs). Recently, we have deepened the mechanisms underlying the physiological role of Aβ by focusing on its crosstalk with cyclic nucleotides.

Based on these findings, we propose a new model interpreting AD pathogenesis as an alteration of the negative feedback loop between Aβ and its physiological receptors.

The lecture will take place at 14.30 – Aula E – Istituti biologici

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