

Titolo del progetto

ROLE OF EXOCYTOTIC PRESYNAPTIC PROTEINS-INDUCED ALTERATIONS OF SYNAPTIC PLASTICITY IN AGING-ASSOCIATED COGNITIVE DECLINE

Abstract

A growing body of evidence suggests that cognitive decline associated to brain aging is determined by a reduction of synaptic plasticity (Burke & Barnes 2006). It is well known that synaptic plasticity is determined by changes at both pre- and post-synaptic levels (e.g., Kullmann & Lamsa 2007), and some evidence, although scanty, exists supporting a role for altered presynaptic expression in brain aging (Powell 2006; Corradi et al 2008). The hypothesis we intend to verify is that in cognitively impaired subjects (fish, rats and humans) expression of presynaptic proteins (PP) that contribute to neurotransmitter release is differentially regulated, thus altering synaptic plasticity and determining behavioral abnormalities. Finally, we also aim at developing a novel biomarker for cognitive decline by using human platelets.

AIMS:

Aim 1

- To demonstrate that, in aged animals (fish and rats), the expression of some PP in cognitively impaired (I) animals is different from that of not impaired (NI) ones;
- to correlate the time course of the expression of proteins exhibiting changes in I animals with cognitive performance;
- to characterize the neurotransmitter phenotype of axon terminals expressing these proteins;
- to demonstrate that these changes correlate with alterations of synaptic plasticity in telencephalon (hippocampus and neocortex for rats).

Aim 2:

- To show that the platelet level of PP identified in animal studies correlate with cognitive performance in healthy elderly subjects and in MCI subjects; and
- to identify novel biomarkers for the cognitive decline that characterize most aged brains.