**Oral Section**

**Hormetic effect of amyloid-beta peptide in hippocampal synaptic plasticity and memory**

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**ABSTRACT**

**Background:** The term hormesis refers to a biphasic dose-response phenomenon characterized by low-dose stimulation and high-dose inhibition represented by a J-shaped or U-shaped curve, depending on the parameter measured (Calabrese and Baldwin, Hum Exp Toxicol, 2002). Indeed, several, if not all, physiological molecules (i.e. glutamate, glucocorticoids, nitric oxide) are likely to present a hormetic effect, exhibiting opposite effects at high or low concentrations. In the last few years, we have focused on amyloid-beta (Aβ), a peptide widely known because it is produced in high amounts during Alzheimer’s disease (AD). Aβ is considered a toxic fragment causing synaptic dysfunction and memory impairment (Selkoe, Science, 2002). However, the peptide is normally produced in the healthy brain and growing evidences indicate that it might have a physiologic function. **Aim:** Based on previous results showing that picomolar concentrations of Aβ42 enhance synaptic plasticity and memory (Puzzo et al, J Neurosci, 2008) and that endogenous Aβ is necessary for synaptic plasticity and memory (Puzzo et al, Ann Neurol, 2011), the aim of our study was to demonstrate the hormetic role of Aβ in synaptic plasticity and memory. **Methods:** We used 3-month old wild type mice to analyze how synaptic plasticity, measured on hippocampal slices in vitro, and spatial reference memory were modified by treatment with different doses of Aβ (from 2 pM to 20 μM). **Results:** We demonstrated that Aβ has a hormetic effect (Puzzo et al, Neurobiol Aging, 2012) with low-doses (200 pM) stimulating synaptic plasticity and memory and high-doses (≥ 200 nM) inhibiting these processes. **Conclusions:** Our results suggest that, paradoxically, very low doses of Aβ might serve to enhance memory at appropriate concentrations and conditions. These findings raise several issues when designing effective and safe approaches to AD therapy.

**Keywords:** hormesis, peptide, hippocampus.

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