

## SYNTHETIC AMYLOID- $\beta$ OLIGOMERS IMPAIR LONG-TERM MEMORY INDEPENDENTLY OF CELLULAR PRION PROTEIN

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by deposition of extracellular  $\beta$ -amyloid (A $\beta$ ) plaques and intracellular neurofibrillary tangles. The inability to form new memories is an early clinical sign of AD and evidence suggests that the A $\beta$  peptide plays a key role in this pathogenetic process. Specifically, soluble, bio-derived oligomers of A $\beta$  are proposed as key mediators of synaptic and cognitive dysfunction possibly through an interaction with the prion protein (PrP<sup>C</sup>). In the present study we investigated the effect of intracerebroventricular injections of synthetic A $\beta$ <sub>1-42</sub> oligomers in mice tested in the object recognition task, and the involvement of PrPC. Following intracerebroventricle injection of either A $\beta$ <sub>1-42</sub> monomer, oligomers or fibrils (1.0  $\mu$ M), mice underwent the familiarization phase on day 1 and the memory test phase on day 2. Memory abilities were determined calculating the discrimination index on both *PrP*<sup>+/+</sup> and *Prnp*<sup>-/-</sup> mice. In addition we verified the interaction between A $\beta$  oligomers and PrP<sup>C</sup> using the surface plasmon resonance technique. Our findings show that A $\beta$  oligomers impair consolidation of the long-term recognition memory, whereas mature A $\beta$ <sub>1-42</sub> fibrils and freshly dissolved peptide did not. Retrieval of stored memories was not affected. The deficit induced by oligomers was reversible and prevented by an anti-A $\beta$  antibody. Although we confirmed that A $\beta$ <sub>1-42</sub> oligomers interact with PrP<sup>C</sup>, with nanomolar affinity, PrP-expressing and PrP knock-out mice were equally susceptible to this impairment. These data suggest that A $\beta$ <sub>1-42</sub> oligomers are responsible for cognitive impairment in AD, and that PrPC is not required.