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Insulin-like growth factor II reverses memory and synaptic impairments in APP transgenic mice

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Insulin-like growth factor II (IGF2) is a circulating hormone, which together with insulin and insulin-like growth factor I (IGF1), belongs to the IGF/IGFBP (IGF/IGF binding protein) system. Insulin and IGF1, more than IGF2, have been related to the pathogenesis of Alzheimer's disease (AD). Nevertheless, a recent study showed that administering IGF2 in the hippocampus of rats significantly enhances memory retention and prevents forgetting, suggesting that IGF2 is critically involved in memory consolidation. Other studies showed that systemic administration of IGF1 reduced amyloid load without affecting memory function. Altogether, these findings point out that administering IGF2 in the hippocampus could be a promising alternative to the treatment of Alzheimer's disease (AD). In this study we used recombinant adeno-associated viral (rAAV) vectors to provide IGF2 and IGF1 specifically into the hippocampus of an APP mouse model. We found that IGF2 expression decreases in the hippocampus of AD patients, leading us to hypothesize that the administration of IGF2 could ameliorate AD symptoms. We report that increasing hippocampal levels of IGF2 and IGF1 via AAV-mediated expression rescue behavioural deficits, promote dendritic spine formation and restores normal hippocampal excitatory synaptic transmission in Tg2576 mice. Finally, AAV-IGF2-expressing mice have significantly less amyloid levels than AAV-IGF1-expressing or sham Tg2576 mice. Notably, the regulation of amyloid levels in neuronal population may occur through an interaction with the IGF2R. Hence, IGF2 may represent novel therapeutic targets for the treatment of AD.

Biography

Ana Gracia Osta received her Bachelor Degree and her PhD in Pharmacy from the University of Navarra, Spain. Her postdoctoral training was obtained in the Alberini's laboratory, in the Neuroscience Department at the Mount Sinai School of Medicine in New York. She joined the Neuroscience Department of CIMA in 2007. She is an Investigator in the laboratory of Neurobiology of Alzheimer's disease and she is interested in the investigation of molecular basis of dementia in Alzheimer Disease. As an independent group, she leads several projects related to the search for new therapeutic targets to reverse the dementia associated with the pathology of Alzheimer's disease.

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