

## THE ROLE OF DOPAMINERGIC ACTIVITY ON RECOGNITION MEMORY: IMPLICATIONS FOR ALZHEIMER'S DISEASE.

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Recently, it has been shown that the deregulation of dopamine could be involved in Alzheimer's disease (AD) both in humans and in transgenic mice models. For some time, we have investigated the role of dopaminergic activity on recognition memory consolidation. Therefore, we have studied the relationship between dopamine activity and cognitive dysfunction in a model of transgenic mouse of AD, as well as by exogenous administration of  $\beta$  amyloid oligomers in wild-type mice. We found that the accumulation of beta-amyloid decreased dopamine levels and converted in vivo long-term potentiation (LTP) into long-term depression (LTD) after high-frequency stimulation, which led to a deterioration of recognition memory. Surprisingly, increases in cortical dopamine levels rescued LTP and recognition memory. Our results suggest that A $\beta$ -induced dopamine depletion is a central mechanism underlying early synaptopathy and the recognition memory alterations observed in AD.

- Cadena-del-Castillo C., Valdes-Quezada C. Carmona-Aldana A., Arias C., Bermúdez-Rattoni F., and Recillas-Targa F. Age dependent increment of hydroxymethylation in the brain cortex in the triple-transgenic mouse model of Alzheimer's disease. *Journal of Alzheimer's Disease*. 41: 1-9; 2014.
- Guzmán-Ramos K, Moreno-Castilla P, Castro-Cruz M, McGaugh JL, Martínez-Coria H, LaFerla FM, Bermúdez-Rattoni F. Restoration of dopamine release deficits during object recognition memory acquisition attenuates cognitive impairment in a triple transgenic mice model of Alzheimer's disease. *Learning & Memory*, 19(10): 453-60, 2012.
- Moreno-Castilla P, Rodríguez-Duran LF, Guzman-Ramos K, Barcenas-Femat A, Escobar ML, Bermudez-Rattoni F. Dopaminergic neurotransmission dysfunction induced by amyloid- $\beta$  transforms cortical long-term potentiation into long-term depression and produces memory impairment. *Neurobiology of Aging*, 41:187-99, 2016.
- Moreno-Castilla P, Pérez-Ortega R, Violante-Soria V, Balderas I, Bermúdez-Rattoni F. Hippocampal release of dopamine and norepinephrine encodes novel contextual information. *Hippocampus*. 27: 547-557, 2017.
- Morin JP, Cerón-Solano G, Velázquez-Campos G, Pacheco-López G, Bermúdez-Rattoni F, Díaz-Cintra S. Spatial memory impairment is associated with intraneural amyloid- $\beta$  immunoreactivity and dysfunctional arc expression in the hippocampal-ca3 region of a transgenic mouse model of Alzheimer's disease. *Journal of Alzheimer's Disease*. 51: 69-79, 2016.