Involvement of the hippocampal CA3-kappa opioid system in episodic-like memory in mice

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The hippocampus plays a central role in various forms of learning and memory. Its specific architecture and the presence of an auto-associative network support the hypothesis of a major implication of the CA3 area in episodic memory (memory of personal events). The inputs arrive to the CA3 sub-region via two different pathways : a direct one, called the temporoammonic (TA) pathway from the entorhinal cortex, and an indirect one, the mossy fiber (MF) pathway from the dentate gyrus. Giant synapses of the MF contain a high density of opioid peptides, mainly dynorphins, which are localized together with glutamate and Zn++ in neurotransmitter vesicles. These peptides have been shown to modulate glutamate release and synaptic plasticity. Kappa opioid receptor activation can impair spatial learning in Morris water maze whereas kappa-opioid specific antagonists (nor-binaltorphamide, nor BNI) do not improve learning. Involvement of kappa opioid systems in episodic-like memory is unknown.

In this study, we investigated the role of the kappa opioid system in episodic-like memory in mice with two different paradigms: Contextual Fear Conditioning (CFC) and a Delayed Matching to Place (DMP) water-maze procedure. Mice were microinjected in the CA3 area. Injection of an agonist (U50488H) blocked contextual learning at a dose of 5 nmol but not at 2 nmol, whereas norBNI had no effect at any tested dose. This impairment of acquisition by U50488H depends on the stimulation of kappa opioid receptors, since it was fully reversed by norBNI. In the DMP test, drugs were injected before the beginning of the last task to run. The same results were obtained as in CFC, i. e. U50488H impaired the capacity of the mouse to improve its performance in acquiring the new location of the platform, whereas norBNI reversed this impairment.

This study points that the kappa opioid system might play a crucial role in the neuromodulation of the MF-CA3 plasticity involved in episodic-like memory in mice.

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