

Muscarinic Receptors and Memory Retrieval: Same Players, Different Grounds

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ABSTRACT

Hippocampus is the primary brain region responsible for formation and storage of episodic memories. Muscarinic cholinergic receptors are the key players of learning and memory processes. Blockade of these receptors leads to impaired episodic memory formation, however not much is known about the role these receptors play in memory retrieval. This study was aimed to identify the role of hippocampal muscarinic receptors in episodic memory retrieval. Moreover, we also dissected how different environmental, pathological and biochemical circumstances modulate muscarinic cholinergic receptor role in memory retrieval. Following memory formation for hippocampus dependent spatial memory and hippocampus-amygdala dependent fear memory, the mice were subjected to acute muscarinic antagonism, muscarinic receptor activation under physiological conditions, sub-chronic receptor modulation, chronic stress and dopamine antagonism prior to memory retrieval. We found significant involvement of hippocampus and medial entorhinal cortex muscarinic receptors in spatial and fear memory retrieval. The muscarinic cholinergic receptor activity was crucial for successful retrieval of hippocampus dependent spatial memories in male mice but not in female mice under all retrieval conditions. On the other hand, despite the involvement of muscarinic receptors in retrieving fear memories under physiological conditions our results showed an interplay between muscarinic activity, different retrieval circumstances and gender in fear memory retrieval. These findings suggest that role of muscarinic receptor activity in retrieving different types of memories depends on gender of subjects and the conditions during which memories are retrieved.
