

Mice lacking M1 and M3 muscarinic acetylcholine receptors have impaired odor discrimination and learning

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The cholinergic system has extensive projections to the olfactory bulb (OB) where it produces a state-dependent regulation of sensory gating. Previous work has shown a prominent role of muscarinic acetylcholine (ACh) receptors (mAChRs) in regulating the excitability of OB neurons, in particular the M1 receptor. Here, we examined the contribution of M1 and M3 mAChR subtypes to olfactory processing using mice with a genetic deletion of these receptors, the M1^{-/-} and the M1/M3^{-/-} knockout (KO) mice. Genetic ablation of the M1 and M3 mAChRs resulted in a significant deficit in odor discrimination of closely related molecules, including stereoisomers. However, the discrimination of dissimilar molecules, social odors (e.g., urine) and novel object recognition was not affected. In addition the KO mice showed impaired learning in an associative odor-learning task, learning to discriminate odors at a slower rate, indicating that both short and long-term memory is disrupted by mAChR dysfunction. Interestingly, the KO mice exhibited decreased olfactory neurogenesis at younger ages, a deficit that was not maintained in older animals. In older animals, the olfactory deficit could be restored by increasing the number of new born neurons integrated into the OB after exposing them to an olfactory enriched environment, suggesting that muscarinic modulation and adult neurogenesis could be two different mechanism used by the olfactory system to improve olfactory processing. © 2017 Chan, Singh, Keshav, Dewan, Eberly, Maurer, Nunez-Parra

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Adult neurogenesis

Granule cell

Inhibition

Olfactory

Olfactory discrimination

muscarinic M1 receptor

muscarinic M3 receptor

age

animal cell

animal experiment

animal tissue

Article

associative learning test

controlled study

discrimination learning

female

gene deletion

habituation

knockout mouse

long term memory

male

mouse

nerve cell differentiation

nonhuman

novel object recognition test

olfactory bulb

olfactory discrimination

short term memory

stimulus response

visual discrimination

wild type