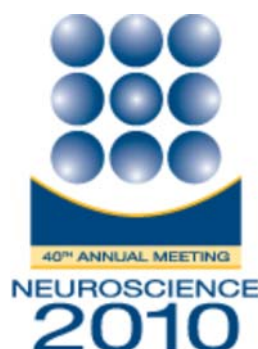


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Presentation Abstract

Program#/Poster#: 138.5/E37

Title: M1-like muscarinic acetylcholine receptors regulate fast-spiking interneuron excitability in rat dentate gyrus

Location: Halls B-H

Presentation Time: Sunday, Nov 14, 2010, 8:00 AM - 9:00 AM

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Abstract: Cholinergic transmission through muscarinic acetylcholine receptors (mAChRs) plays a key role in cortical oscillations. Although fast-spiking (FS), parvalbumin-expressing basket cells (BCs) are proposed to be the cellular substrates of gamma oscillations, previous studies reported that FS nonpyramidal cells in neocortical areas are unresponsive to cholinergic modulation. Dentate gyrus (DG) is an independent gamma oscillator in the hippocampal formation. However, in contrast to other cortical regions, the direct impact of mAChR activation on FS BC excitability in this area has not been investigated. Here, we show that bath-applied muscarine or carbachol, two mAChR agonists, depolarize DG BCs in the acute brain slices, leading to action potential firing in the theta-gamma bands in the presence of blockers of ionotropic glutamate and γ -aminobutyric acid type A receptors at physiological temperatures. The depolarizing action persists in the presence of tetrodotoxin, a voltage-gated Na⁺ channel blocker. In voltage-clamp recordings, muscarine markedly reduces background K⁺ currents. These effects are mimicked by oxotremorine methiodide, an mAChR-specific agonist, and largely reversed by atropine, a non-selective mAChR antagonist, or pirenzepine, an M1 receptor antagonist, but not by gallamine, an M2/4 receptor antagonist. Interestingly, in contrast to M1-receptor-mediated depolarization, M2 receptor activation by the

specific agonist arecaidine but-2-ynyl ester tosylate down-regulates GABA release at BC axons - the effect is occluded by gallamine, an M2 receptor antagonist. Overall, muscarinic activation results in a net increase in phasic inhibitory output to the target cells. Thus, cholinergic activation through M1-like receptor enhances BC activity and promotes the generation of nested theta and gamma rhythms, thereby enhancing hippocampal function and associated performance.

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Keyword(s): MUSCARINIC ACETYLCHOLINE RECEPTORS
DENTATE GYRUS
GABAERGIC INTERNEURON

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