Muscarinic modulation of basolateral amygdala

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The basolateral amygdala (BL) receives a dense cholinergic innervation from the basal forebrain. Despite the importance of muscarinic acetylcholine receptors (mACHRs) in fear learning, consolidation, and extinction, there have been no studies that have systematically investigated the functional role of mACHRs in regulating emotional processing in the BL. To address this critical knowledge gap we combined brain slice whole-cell recording, optogenetics, and immunohistochemistry to determine how muscarine, acting on mACHRs, to regulate neuronal oscillations, synaptic transmission and plasticity in the BL.

Neurons in the BL oscillate rhythmically during emotional processing, which are thought to be important to integrate sensory inputs, allow binding of information from different brain areas and facilitate synaptic plasticity in target downstream structures. We found that muscarine induced theta frequency rhythmic IPSPs in BL pyramidal neuron (PN). These IPSPs synchronized PN firing at theta frequencies. Recordings from neurochemically-identified interneurons revealed that muscarine selectively depolarized parvalbumin (PV)-containing, fast firing, but not PV, regular firing or somatostatin (SOM)-containing interneurons. This depolarization was mediated by M3 mACHRs. Dual cell recordings from connected interneuron-PN pairs indicated that action potentials in fast firing, but not regular firing interneurons were strongly correlated with large IPSCs in BLa PNs. Furthermore, selective blockade of M3, but not M1 mACHRs suppressed the rhythmic IPSCs in BLa PNs. These findings suggest that muscarine induces rhythmic IPSCs in PNs by selectively depolarizing PV, fast firing interneurons through M3 mACHRs. Furthermore, we found that rhythmic IPSCs were highly synchronized between PNs throughout the BLa.

The BL receives extensive glutamatergic inputs from multiple brain regions and recurrent collaterals as well. They are important for fear learning and extinction, which are tightly regulated by local GABAergic inhibition. We found that mACHRs activation suppressed external glutamatergic inputs in a frequency dependent and pathway specific manner but kept recurrent glutamatergic transmission intact. In addition, muscarine disinhibited BL PNs by attenuating feedforward and GABAergic inhibition. In agreement with these observations, long term potentiation (LTP) induction was facilitated in the BL by mACHRs activation.

Taken together, we provided mechanisms for cholinergic induction of theta oscillations and facilitation of LTP in the BL.