M1 muscarine receptors inhibit GABA release from striatal medium spiny neurons onto cholinergic interneurons.

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Whole-cell patch-clamp recordings were made from striatal cholinergic interneurons (ChINs) in P10-17 mice brain slices with restricted expression of channelrhodopsin-2 (ChR2) in the striatal medium spiny neurons (MSNs). Neurons were voltage clamped at -60 mV. Light stimulation evoked postsynaptic currents in the presence of glutamate and glycine receptor antagonists. These postsynaptic currents were blocked by $GABA_A$ receptor antagonist, bicuculline, suggesting they were $GABA_A$ receptor-mediated inhibitory postsynaptic currents (IPSCs). A muscarine receptor agonist, carbachol (1 μM), suppressed IPSCs by 49.5 $\pm$ 7.8% (n = 5). To examine the changes in GABA release probability, we calculated coefficient of variation (CV). The CV was not increased after application of bicuculline, suggesting the action site of bicuculline was postsynaptic $GABA_A$ receptors. On the other hand, CV after application of carbachol was significantly increased ($p = 0.004$). In addition, carbachol (10 μM) did not affect inward currents evoked by puff-applied GABA (100 μM). These results suggest that activation of M1 muscarine receptors presynaptically inhibits GABA release from MSNs onto ChINs.