Cholinergic modulation of layer V interneurons in the mouse prefrontal cortex

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The prefrontal cortex (PFC) is a vital cortical area in the processes of attention and working memory, and it has been identified as a site for intracortical integration. It has been shown that nicotine increases attention skills in humans. Although cholinergic neurotransmission has been well-characterized at the neuromuscular junction and in other parts of the central nervous system, how acetylcholine modulates the PFC microcircuit is poorly understood. The current work addresses the effects of cholinergic transmission via nicotinic acetylcholine receptors (nAChRs) on the function of interneurons in the PFC microcircuit using both electrophysiology and single cell RT-PCR. Layer V interneurons were visually identified and classified by morphology and action potential profile. Spontaneous excitatory inputs (sEPSCs) to these cells were subsequently measured in voltage clamp. The frequency of sEPSCs to layer V fast-spiking (FS) interneurons of PFC slices was increased by bath application of nicotine, whereas sEPSCs to non-FS interneurons were unaffected. Furthermore, local application of nicotine showed that non-FS interneurons exhibit somatic nicotinic currents, indicating expression of somatic nAChRs, whereas FS interneurons did not respond to local nicotine application. Layer V pyramidal neurons also showed no somatic nicotine-induced current, but sEPSCs were increased. We are now using single cell RT-PCR on pyramidals and interneurons to complete interneuron classification and identify nAChR subunit expression by these neurons. We expect that in addition to expressing markers for GABA, these different interneuron subtypes will express different calcium binding proteins and a divergent nAChR subunit composition. The combination of our electrophysiological and molecular data will provide a first glimpse into the effects of cholinergic modulation of interneurons in the PFC.

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