Role of the lateral habenula in nicotine addiction: interaction with the dopaminergic system

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Nicotine is the tobacco neuroactive compound mediating its rewarding/reinforcing properties by acting on the dopaminergic system. The lateral habenula (LHb) is a structure known to modulate the DA system activity both directly and indirectly, suggesting that it might represent a possible target for the action of nicotine in the CNS. We used an in vivo electrophysiological recording approach to investigate the nicotine-induced response of single LHb/DA neurons. Systemic administration of nicotine increased the LHb neuronal activity in vivo in rats. Following nicotine chronic treatment, this response was drastically decreased. To further elucidate the LHb role in central nicotine effects, we recorded the activity of VTA putative-DA neurons following LHb electrolytic lesion in both drug-naïve and nicotine chronically treated animals. Systemic administration of nicotine induced a significant increase in the neuronal activity of putative-DA neurons located in the paranigral nucleus (PN) of the VTA. This effect was completely abolished by LHb electrolytic lesion. Conversely, neurons located in the parabrachial pigmented nucleus (PBP) of the VTA responded significantly to nicotine administration only after LHb lesion. Following chronic nicotine treatment, putative-DA VTA neurons recorded from LHb sham-lesioned rats showed a nicotine-induced response pattern similar to LHb-lesioned drug-naive animals, while nicotine failed to increase the neuronal activity of both PN and PBP putative-DA neurons in LHb-lesioned rats. Our evidence strongly suggests that nicotine modulates LHb activity and plays an important role in mediating the effects of nicotine on the midbrain DA system thus participating in the mechanisms of addiction and aversion to this drug.

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