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2. Title

The Role of DOPAergic Neurotransmission in the Actions of Nicotine

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4. Summary

We proposed that L-DOPA, a precursor of dopamine, acts as a neurotransmitter by itself. Nicotine, an ingredient in tobacco products that can lead to addition, released L-DOPA as well as dopamine from the nucleus accumbens (NAc) and caudate putamen (CPu) of in vivo rats in a mecamylamine-sensitive manner. Coordinately, some of the acute action of nicotine was attenuated by L-DOPA cyclohexyl ester, a L-DOPA antagonist. In vivo microdialysis of the CPu, mecamylamine alone decreased the basal level of L-DOPA but not dopamine. Recently, GPR143/OA1 was identified as a receptor for L-DOPA. The GPR143 immunoreactivies or mRNA were expressed in the CPu, NAc, substantia nigra (SN) and ventral tegmental area (VTA). Nicotinic receptor subunits, α4 and α7 were co-expressed with GPR143 in some of the tyrosine hydroxylase (TH)-positive neurons in the SN and VTA. Importantly, both acute and chronic actions of nicotine were attenuated in Gpr143-gene deficient mice when compared to wild type mice. Furthermore, genetic association studies revealed that a single-nucleotide polymorphism in the Gpr143 gene was associated with traits of smoking behavior in Japanese male individuals. These findings suggest that GPR143, a L-DOPA receptor, is involved in acute and/or chronic actions of nicotine in men as well as rodent animals.