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SHATI/NAT8L REGULATES DOPAMINE RELEASE-INDUCED BY NICOTINE IN NUCLEUS ACCUMBENS
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Many psychiatric disorders are caused by the abnormalities of the dopaminergic neuronal system. A novel N-acetyltransferase, Shati/Nat8l, was identified in the nucleus accumbens (NAc) of mice with methamphetamine (METH) treatment. Previously, we reported that suppression of Shati/Nat8l in the NAc enhanced METH-induced behavioral impairment via dopaminergic neuronal regulation by activation of group II mGluRs. In this study, we investigated the effects of Shati/Nat8l on the action of nicotine.

AAV vector containing the entire cDNA sequence of Shati/Nat8l (AAV-Shati/Nat8l vector) or AAV-Mock vector were injected in the NAc. Dopamine release were measured by in vivo microdialysis. The expression of nAChR mRNA were determined by RT-PCR. Shati/Nat8l mRNA in 6 times in AAV Shati/Nat8l-injected site. Overexpression of Shati/Nat8l in the NAc inhibited NIC-induced increasing of dopamine release. The effect of Shati/Nat8l was partially rescued by LY341495, the antagonist of mGluR2/3. Furthermore, Shati/Nat8l overexpressed mice, the expression of alpha7 nAChR mRNA was upregulated in the NAc compared with Mock mice. On the other hands, alpha4 nAChR mRNA in the ventral tegmental area was downregulated compared with Mock mice. These results indicate that Shati/Nat8l in the NAc, plays an important role of the mediation by nicotine of the extracellular dopamine level.