Role of dopamine receptors in modulating nicotine-induced tremor in mice

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We previously demonstrated that nicotine elicited kinetic tremor by activating the inferior olive neurons via α 7 nACh receptors (*Behav. Brain Res.*, 314, 173-180, 2016). Since α 7 nACh receptors are known to enhance monoamine release, we here explored the role of dopamine receptors in modulating nicotine-induced tremor. Male ddY mice were treated with nicotine (1 mg/kg, i.p.) to induce tremor. Various dopamine agonists or antagonists were injected 15 min before the nicotine injection. Brain levels of dopamine and its metabolites, DOPAC and HVA, were analyzed in mice treated with nicotine (1 mg/kg) using HPLC. Treatment of mice with the D_1 receptor antagonist SCH-23390 significantly enhanced nicotine-induced tremor whereas the D_1 agonist SKF-38393 significantly suppressed the tremor induction. The nicotine-induced tremor was inhibited the D_3 receptor antagonist U-99194, but potentiated by the D_3 agonist PD-128,907. Neither the selective D_2 antagonist L-741,626 nor D_4 antagonist L-745,870 affected nicotine-induced tremor. In addition, nicotine elevated the levels of dopamine and DOPAC in the medulla oblongata containing the inferior olive. These results suggest that D_1 and D_3 receptors exert inhibitory and facilitatory influences on nicotine-induced tremor, respectively.