S(-)-Nornicotine Increases Dopamine Release in a Calcium-Dependent Manner from Superfused Rat Striatal Slices

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Abstract: The present study demonstrates that \(S\)(-)nornicotine evoked a concentration-dependent increase in dopamine (DA) release from superfused rat striatal slices. The increase in DA release was indicated by an \(S\)(-)nornicotine-induced overflow of endogenous 3,4-dihydroxyphenyl-acetic acid (DOPAC) in the striatal superfusate and by an \(S\)(-)nornicotine-induced increase in tritium overflow from striatal slices preloaded with \(^{3}H\)DA. Low concentrations (0.01–1.0 \(\mu M\)) of \(S\)(-)nornicotine, which did not evoke endogenous DOPAC overflow, also were unable to modulate electrically evoked DOPAC overflow. The increase in DOPAC overflow induced by \(S\)(-)nornicotine was compared with that produced by \(S\)(-)nicotine. Comparing equimolar concentrations (0.1-100 \(\mu M\)) of \(S\)(-)nornicotine and \(S\)(-)nicotine, superfusion with \(S\)(-)nornicotine resulted in a significantly greater DOPAC overflow. In contrast to the effect of \(S\)(-)nicotine, \(S\)(-)nornicotine evoked a sustained increase in DOPAC overflow for the entire period of \(S\)(-)nornicotine exposure. Furthermore, DOPAC overflow evoked by \(S\)(-)nornicotine in control Krebs buffer was inhibited by superfusion with a low-calcium buffer. Moreover, in the low-calcium buffer, DOPAC overflow induced by 30 and 100 \(\mu M\) \(S\)(-)nornicotine was not different from that with no \(S\)(-)nornicotine. The results indicate that \(S\)(-)nornicotine, a constituent of tobacco products and a known metabolite of \(S\)(-)nicotine, increases DA release in a calcium-dependent manner in superfused rat striatal slices. It is interesting that unlike \(S\)(-)nicotine, there does not appear to be desensitization to this effect of \(S\)(-)nornicotine.