Different effects of nitric oxide synthase inhibitors on convulsions induced by nicotine in mice

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Abstract:
Acute intraperitoneal (ip) administration of N⁵-nitro-L-arginine (NNA, 10, 20 and 40 mg/kg), a non-selective nitric oxide synthase (NOS) inhibitor, significantly and dose-dependently decreased the incidence of convulsions induced by ip nicotine (NIC) in mice, whereas 7-nitroindazole (7NI, 50 and 100 mg/kg ip), a selective neuronal NOS inhibitor, had a proconvulsant effect. Aminoguanidine (100 mg/kg ip), a specific inducible NOS inhibitor, remained without an effect on convulsive behavior. L-arginine, a nitric oxide (NO) precursor, which independently has no effect on convulsions, markedly reversed the anticonvulsant effect of NNA; yet only partially reversed the proconvulsant effect of 7NI when injected at 500 mg/kg ip. Convulsions evoked by intracerebroventricular injection of NIC were significantly suppressed by ip NNA (40 mg/kg ip) and enhanced by ip 7NI (100 mg/kg ip); however, these effects of NNA and 7NI were less potent than those seen when NIC was administered ip.

The present study revealed essential differences in the action of NOS inhibitors in NIC-induced convulsions. It appears that only NO produced by constitutive NOS is involved in the mechanism of NIC-induced convulsions. The proconvulsant effect of 7NI may result from the mechanisms unrelated to NOS inhibition.

Key words:
nicotine, nitric oxide, seizures, N⁵-nitro-L-arginine, 7-nitroindazole, aminoguanidine