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Short communication

7-Nitroindazole, but not N^G-nitro-L-arginine, enhances the anticonvulsant activity of pregabalin in the mouse maximal electroshock-induced seizure model

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Abstract:
The objective of this study was to determine the effects of 7-nitroindazole (7NI – a preferential neuronal nitric oxide synthase (NOS) inhibitor) and N^G-nitro-L-arginine (NNA – a non-selective NOS inhibitor) on the anticonvulsant action of pregabalin (PGB – a third-generation antiepileptic drug) in the maximal electroshock (MES)-induced seizure model in mice.
Electroconvulsions were produced in mice by means of an alternating current (50 Hz, 500 V, 25 mA, ear-clip electrodes, 0.2 s stimulus duration, tonic hindlimb extension taken as the endpoint). The anticonvulsant action of PGB in the MES test was expressed as median effective doses (ED_{50} values) of the drug, protecting 50% of animals tested against MES-induced seizures. The acute adverse-effect potentials of PGB in combination with 7NI and NNA were evaluated in the chimney test (motor coordination), step-through passive avoidance task (long-term memory) and grip-strength test (skeletal muscular strength) in mice.
7NI (50 mg/kg, *ip*) significantly enhanced the anticonvulsant action of PGB by reducing the ED_{50} value of PGB from 145.0 mg/kg to 74.4 mg/kg ($p < 0.01$). Similarly, 7NI at the lower dose of 25 mg/kg also potentiated the anticonvulsant action of PGB by lowering the ED_{50} value of PGB from 145.0 mg/kg to 117.9 mg/kg, although the results did not attain statistical significance. In contrast, NNA (40 mg/kg, *ip*) had no impact on the anticonvulsant effects of PGB. Moreover, none of the examined combinations of PGB with 7NI and NNA affected motor coordination, long-term memory and skeletal muscular strength in mice.
Based on this preclinical study, one can conclude that 7NI significantly enhanced and NNA had no effect on the anticonvulsant activity of PGB against MES-induced seizures in mice.

Key words:
7-nitroindazole, N^G-nitro-L-arginine, nitric oxide, pregabalin, maximal electroshock seizure test