SHORT COMMUNICATION

INHIBITORY EFFECT OF SOME NEUROACTIVE STEROIDS ON COCAINE-INDUCED KINDLING IN MICE

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Some neuroactive steroids which positively modulate GABA_A receptor activity suppress cocaine-induced kindling but a possible involvement of other neurochemical mechanism in their antiepileptogenic effect remains to be elucidated. To this end, in the present study, we evaluated effects of allo-pregnanolone, a positive modulator of the GABA_A receptor; its isomer without GABAergic activity – isopregnanolone and a negative-modulator of GABAergic transmission – dehydroepiandrosterone sulfate on cocaine-induced kindling in mice. Animals were pretreated daily with either vehicle or neuroactive steroid and then given cocaine (45 mg/kg) for 12 days. After a 14-day washout period in which drugs were not administered, the mice were challenged with the same 45 mg/kg dose of cocaine. Isopregnanolone (5 mg/kg) and dehydroepiandrosterone sulfate (20 mg/kg) administered daily with cocaine decreased number of mice exhibiting seizures. Allopregnanolone (5 mg/kg) also showed strong tendency to suppress cocaine kindling, however, its effect did not reach statistical significance. None of the neuroactive steroids had effect on acute cocaine (75 mg/kg ip)-induced clonic seizures. Further biochemical study showed that the veratridine- but not K+-stimulated release of D-[3H]-aspartate in hippocampal slices was higher in cocaine-kindled mice than in the control group. Isopregnanolone (100 μM) significantly attenuated the veratridine-induced D-[3H]-aspartate release in hippocampi of cocaine-kindled group. These data indicate that positive modulation of the GABA_A receptors is not a critical feature of neuroactive steroids that would determine their ability to prevent the cocaine-induced kindling.

Key words: neuroactive steroids, cocaine kindling, D-[3H]-aspartate release, seizures

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