Anti-convulsant effects of foot-shock stress in mice: Involvement of endogenous cannabinoids and opioids

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Abstract: Different types of acute stress such as swim stress and foot-shock stress exert anti-convulsant effects. The studies showed that endogenous opioids are released during acute stress. There is also some evidence for neuroprotective effects of endogenous opioids and cannabinoids in different seizure models. There are functional interactions between these two receptor systems in many pharmacological studies.

Purpose: In the present study we evaluated whether endogenous cannabinoids and opioids are involved in anti-convulsant effects of acute foot-shock stress. AM251, specific CB1 receptor antagonist and naltrexone, a non-specific opioid receptor antagonist were administered intraperitoneally. Clonic seizure threshold was determined by pentyleneetrazole (PTZ, 0.5%) infusion at a constant rate of 1 ml/min into the tail vein of male NMRI mice (23-29 g). Minimal dose of PTZ (mg/kg of mice weight) needed to induce clonic seizure was considered as an index of seizure threshold. Animals were exposed to prolonged and intermittent foot-shock stress for 30 min (5 pulses delivered each 30 s for 30 min ). Acute foot-shock stress significantly increased the seizure threshold. Pre-treatment with non-effective doses of AM251 (1 pg/kg, 1 ng/kg, 1, 10 and 100 µg/kg ) and non-effective doses of naltrexone (1 and 2 mg/kg ) prevented the stress-induced anticonvulsant effects. The low doses of naltrexone (0.3 mg/kg ) or ultra-low dose of AM251 (1 fg/kg ) that are sub effective doses prevented the stress induced anti-convulsant properties.

Conclusion: Acute foot-shock stress significantly increases the PTZ-induced clonic seizure threshold in mice. We demonstrated for the first time that endogenous cannabinoids and opioids are involved in the anti-convulsant effects of foot-shock stress.

Keyword: Foot-shock stress, Seizure, endogenous Opioids, endogenous Cannabinoids, Mice