Involvement of nitric oxide in the effect of caffeine on the pentylenetetrazole-induced seizure threshold in mice

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Abstract

Background: Effect of caffeine on seizure is controversial in animal models of epilepsy. Caffeine is non-selective antagonist of A₁ and A₂A adenosine receptors. Meanwhile, nitric oxide-soluble guanylate cyclase-cyclic guanosine monophosphate (NO-sGC-cGMP) pathway is partly involved in the central effects of caffeine.

Objective: The aim of this study was to investigate the effect of acute caffeine administration on seizure threshold and levels of nitric oxide metabolites in pentylenetetrazole (PTZ) model in mice.

Methods: In this study, 35 NMRI mice (25-30 g) were divided into 5 groups (7 animals in each group). Clonic seizure threshold induced by PTZ was assessed in intact control group or 30 min after acute intraperitoneal administration of caffeine (5, 100, and 150 mg/kg) or saline. Nitric oxide metabolites (NOx) were measured in the brain tissues of all groups at the end of experiments. Data were analyzed by ANOVA and followed Tukey test for multiple comparisons.

Findings: Acute administration of 5 mg/kg of caffeine significantly decreased seizure threshold compared to saline (P<0.01). While 100 and 150 mg/kg of caffeine did not change seizure threshold. NOx levels significantly decreased following acute administration of caffeine (100 and 150 mg/kg) compared to saline (P<0.05).

Conclusion: The results of study showed that different doses of caffeine had different effects. It seems that effect of higher doses of caffeine is partly mediated through modulation of nitric oxide pathway.

Keywords: Seizure, Caffeine, Nitric oxide, Pentylenetetrazole