Role of intracellular calcium in acute thermal pain perception.

Galeotti N, Bartolini A, Ghelardini C.

Department of Preclinical and Clinical Pharmacology, University of Florence, Viale G. Pieraccini 6, 50139 Florence, Italy.

OBJECTIVE: The role of intracellular calcium in acute thermal nociception was investigated in the mouse hot-plate test.

RESULTS: Intracerebroventricular (i.c.v.) administration of TMB-8, a blocker of Ca++ release from intracellular stores, produced hypernociception. By contrast, i.c.v. pretreatment with thapsigargin, a depletor of Ca++ intracellular stores, produced an increase of the mouse pain threshold. Furthermore, non-analgesic doses of thapsigargin prevented the hypernociception produced by TMB-8. In mice undergoing treatment with heparin, an InsP3-receptor antagonist, or ryanodine, a ryanodine receptor (RyR) antagonist, a dose-dependent reduction of the pain threshold was observed. Pretreatment with D-myo inositol, compound which produces InsP3, and 4-chloro-m-cresol, a RyR agonist, induced an antinociceptive effect. The heparin hypernociception was prevented by D-myo inositol, but not by L-myo inositol, used as negative control. In the same experimental conditions, the antinociception induced by D-myo inositol was prevented by a non-hyperalgesic dose of heparin. Similarly, the reduction of pain threshold produced by ryanodine was reversed by non-analgesic doses of 4-chloro-m-cresol, whereas the antinociception induced by 4-chloro-m-cresol was prevented by non-hyperalgesic doses of ryanodine. The pharmacological treatments employed did not produce any behavioral impairment of mice as revealed by the rota-rod and hole-board tests.

CONCLUSION: These results indicate that a variation of intracellular calcium contents at a supraspinal level is involved in the modulation of acute thermal nociception. In particular, the stimulation of both InsP3- and Ry-receptors appears to play an important role in the induction of antinoiception in mice, whereas a blockade of these receptors is involved in an hypernociceptive response to acute thermal pain.

PMID: 15527827