BLOCKADE OF THE TRPV1 RECEPTOR AND OF THE FATTY ACID AMIDE HYDROLASE ENZYME IN A MOUSE MODEL OF NEUROPATHIC PAIN PREVENTS PAIN-LIKE BEHAVIOUR AND CASPASES ACTIVATION

Giordano Catia, Siniscalco Dario, Migliozzi Annalucia, Rossi Francesco, Di Marzo Vincenzo°, Maione Sabatino

°Istituto di Chimica Biomolecolare, CNR, Pozzuoli (NA), Italy
Department of Experimental Medicine, section of Pharmacology, Second University of Naples
Via S. Maria di Costantinopoli 16 – 80138 Naples, Italy - catiagiordano@hotmail.it

Aim of this research was to study the potential involvement of vanilloid and endocannabinoid systems in alleviating neuropathic pain in mice.
A mouse model of neuropathic pain consisting of spared nerve injury (SNI) of the sciatic nerve was used to examine the anti-allodynic and anti-hyperalgesic effect of a chronic treatment with N-arachidonoyl-serotonin (AA5HT), an inhibitor of the fatty acid amide hydrolase, and a TRPV1 receptor blocker.
Thermal withdrawal latency and mechanical withdrawal threshold were monitored to evaluate the AA5HT effect on thermal hyperalgesia and mechanical allodynia.
After behavioural analysis, the cortex was removed, minced and the proteins were extracted.
The protein levels were measured by western blot analysis.
Neuropathic mice treated chronically with vehicle developed thermal hyperalgesia and mechanical allodynia at 3, 7, 14, and 21 days post-surgery.
Western blot analysis showed increased Caspase-3 protein levels in the cortex at 3, 7, 14, and 21 days post-surgery.
The chronic treatment with AA5HT (5 mg/kg, i.p. once daily) was able to prevent the development of thermal hyperalgesia and mechanical allodynia at 7, 14, and 21 days post-surgery, and reduced Caspase-3 protein levels.
Our findings provide first evidence for an activation of Caspase-3 in the cortex of mice with neuropathic pain induced by spared nerve injury. Activation of Caspase-3 may be a marker of neuropathic pain. Caspase-3 inhibition may represent a target in neuropathic pain controlling.
The dual activity of AA5HT, on endocannabinoid metabolism and TRPV1 receptors, could be a novel strategy for newer pain-relievers.