APOPTOTIC GENE EXPRESSION IN A MOUSE MODEL OF NEUROPATHIC PAIN: ROLE OF THE ENDOCANNABINOID SYSTEM

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We studied the involvement of the endocannabinoid system in the cortex neural apoptosis in mice with spared nerve injury (SNI) for 3, 7, 14, and 21 days.
Behavioural testing was performed to verify thermal hyperalgesia and mechanical allodynia.
The mRNA levels of the genes under analysis were measured by RT-PCR amplification.
Thermal hyperalgesia and mechanical allodynia became apparent after nerve injury.
RT-PCR analysis showed increased expression of the bax/bcl-2 ratio (40±2%), bid (16±2%), caspase-1 (84±3%), caspase-8 (53±6%), caspase-9 (25±6%), caspase-12 (58±2%), TNF (32±2%) genes in the cortex by 7 days post-injury.
SNI induced increased expression of the bax/bcl-2 ratio (30±2%), bid (38±3%), caspase-12 (75±2%), TNF (39±2%) genes in the cortex also by 14 days post-injury, without affecting the mRNA levels of the regulative caspases, such as caspase-1, caspase-8, and caspase-9.
The fatty acid amide hydrolase inhibitor, and a TRPV1 antagonist N-arachidonoyl-serotonin (AA5HT, 5 mg/kg, i.p. once daily) prevented the development of thermal hyperalgesia and mechanical allodynia at 7 and 14 days.
AA5HT treatment reduced the mRNA levels of the bax/bcl-2 ratio, bid, caspase-1, caspase-8, caspase-9, and caspase-12.
This study provides first evidence for apoptosis induction in the cortex in mice with neuropathic pain by spared nerve injury.
The inhibitors of endocannabinoid metabolism could be a novel strategy for their use as next-generation of drugs for neuropathic pain management.