FUNCTIONAL ACTIVATION OF Bv8 RECEPTORS (PKR1-2) IN RAT SENSITIVE NEURONS AND GLIAL CULTURES

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Bv8 is a small protein secreted from amphibian skin. It belongs to a novel family of highly conserved proteins from invertebrates to humans, and it is involved in the modulation of the pain threshold (here: Metere et al.).
Bv8 receptors have been cloned and their primary structures indicate that they belong to GPCR family; in agreement with the effects of Bv8 on nociception, apoptosis and angiogenesis, the activation of these receptors promotes, in different cellular models, intracellular calcium mobilization and p44/42 MAPK phosphorylation.
Some evidences suggest that p44/42 MAPK phosphorylation and glial stimulation are involved in maintenance of pain sensitization.
By RT-PCR, we showed the presence, in the rat CNS, of mRNA codifying for Bv8 analogs (mBv8) and Bv8 receptors. We therefore investigated the ability of Bv8 to activate p44/42 MAPK in purified cultures of astrocytes and microglia deriving from neonatal rat cerebral cortex.
The stimulation of astrocytes with 1 to 20 nM Bv8 increased p44/42 MAPK phosphorylation by about two fold. Conversely, the stimulation of microglia with 1 nM to 1 µM Bv8 had not effect.
Because we found that Bv8-receptor mRNA was present in dorsal root ganglia (DRGs) and that Bv8 induced long-lasting sensitization of cutaneous nociceptors, we investigated the ability of Bv8 to mobilize calcium in cultures of DRGs sensory neurons obtained from neonatal rats.
We showed that 0.5 to 2 nM Bv8 produced 3 to 5 fold increase in calcium release in small-diameter sensory neurons that probably express Bv8 receptors.