Summary

Tissue injury leads to increased sensitivity to noxious and innocuous stimuli due to mechanisms of peripheral sensitisation of primary nociceptors and central sensitization of neurons in the spinal dorsal horns. The subpopulation of capsaicin – sensitive sensory neurons plays an important role in this process. The capsaicin – sensitive neurons express capsaicin TRPV1 receptors (transient receptor potential 1) on their peripheral and central terminals, local high concentration capsaicin treatment can induce regional destruction of these endings. It is well estabilished that TRPV1 receptors play the key role in neural transmission of nociceptive information and its modulation. The aims of this study were to investigate the role of capsaicin – sensitive primary afferent fibers and the involvement of peripheral and central TRPV1 receptors in the development of hypersensitivity after surgical tissue trauma, to test the effect of high concentration capsaicin and the specific TRPV1 antagonist treatment on postoperative pain and to enlighten the function of central TRPV1 receptors in the neural mechanisms of nociception.

Using behavioral testing methods, the responses to mechanical (Von Frey filaments) and thermal stimuli (radiant heat source) were tested on the rat plantar incision model of surgical pain before and several times after the surgical procedure. In the first series of experiments the animals were treated intradermally with high concentration capsaicin 24 hrs before, 6 days before or 2 hrs after the plantar incision was made. Another group of experimental animals was treated with TRPV1 antagonist (SB 366791), either intrathecally or intradermally applied before the surgery. The magnitude of central sensitization of neurons in the spinal dorsal horns due to the plantar incision was also judged by the number of spinothalamic (STT) and postsynaptic dorsal column (PSDC) neurons expressing c – Fos in L3 – L5 segments of the lumbar spinal cord using immunohistochemical staining. In the last part of this study the changes of responsiveness to mechanical and thermal stimulation after intrathecal application of TRPV1 agonist (OLDA, N – oleoyldopamine), bradykinin and both compounds together were investigated using the same behavioral methods as described above.

The plantar incision caused rapid increase of responsiveness to mechanical and thermal stimuli in the control group of animals treated with vehicle. However, high dose of capsaicin applied intardermally before or after the surgical procedure significantly reduced the postoperative thermal and mechanical hyperalgesia, the numer of STT and PSDC neurons expressing c – Fos in the spinal dorsal horns was also greatly reduced in animals pretreated with capsaicin 24 hrs before the plantar incision was made in comparison to controls. Intradermal TRPV1 antagonist treatment had only moderate analgesic effect on postoperative thermal hyperalgesia and mechanical allodynia. In sharp contrast, the effet of TRPV1 antagonist was much more pronounced after intrathecal application, thermal hyperalgesia was blocked completely and mechanical allodynia was reduced remarkably in this group of animals. Even though intrathecal treatment with OLDA did not affect the responsiveness of animals to mechanical or thermal stimuli, it potentiated the sensitizing effect of intrathecally applied bradykinin significantly.

Local high concentration capsaicin treatment showed great analgesic effect on postoperative thermal and mechanical hyperalgesia. Also, intrathecal application of TRPV1 antagonist appeared to be very effective in the treatment of postoperative thermal hyperalgesia and mechanical allodynia. Acording to our results, not only peripheral, but also central TRPV1 receptors play an important role in the neural transmission of nociceptive information and its modulation and they seem to be essential for the developement of postoperative pain states.