

Rat model of pathological pain in the central nervous system

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Aim

Neuronal events leading to development of long-term potentiation (LTP) in the nociceptive pathways may be a cellular mechanism underlying central hyperalgesia. The objective was to investigate the supraspinal network involved in a model of spinal LTP after noxious stimuli.

Methods and results

Female Sprague–Dawley rats weighing 250–350 g, adapted for minimum 10 days to environment and given food and water ad librum, were for the following experiments anesthetized with isoflurane gas. The left sciatic nerve was given a noxious high-frequency conditioning stimulation (HFS) to induce LTP (5 trains/1 s, 100 Hz, 1 ms pulses, 10 s intervals).

1) Field potentials was recorded from wide dynamic range neurons in the dorsal horn of the spinal cord (n=6). A clear LTP of the nociceptive transmission following sciatic nerve HFS was observed for over 3 hours.

2) FDG PET studies (Focus 120, Siemens) were performed at 2 consecutive days with dynamic scan over 60 min with measured attenuation correction prior to FDG injections. A normal blood glucose level was confirmed in rats prior to FDG injection. All rats underwent first day a rest study without any intervention. At second day FDG was injected either immediately (acute group, n=4) or 2,5 hours (late group, n=10) after HFS. Respective sham groups were acquired. Data were MAP reconstructed and summed between 30-60 minutes. Statistical group comparisons between rest and stimulation condition was performed with SPM

(<http://www.fil.ion.ucl.ac.uk/spm/>) after anatomic standardization to a MRI template fitted to the Paxinos and Watson atlas (5th edition, 2006) with normalization to the global mean value of the brain. Level of significance for was set at $p < 0.05$. Increased activity in the somatosensory cortex was observed in the acute, but not the late group. In contrast, the late group exhibited an increase bilateral amygdala (contra-> ipsilateral) and in midline periaqueductal grey (PAG). Decreased activity was in the acute group limited to the midline and ipsilateral dorsolateral pontine tegmentum (DLPT), and in the late group the extended bilaterally in DLPT in addition to a change in the rostroventral medulla (RVM). Further a relative increased activity was seen in cerebellum in the late group.

Conclusion

At supraspinal level the HFS led in the acute group to an activation in the somatosensory as response to the sensory stimulation HFS. The brain regions involved in the late group (amygdala, PAG, DLPT and RVM) constitutes a network of descending stress-induced analgesia, which apparently does not effectively inhibit the pathological activity in ascending spinal neurons. The results gives us insight into possible mechanism of hyperalgesia.