Effect of Partial Transection of Spinal Cord on Permeability of Cutaneous Vessels in Rats before and after Treatment with Neurotoxic Dose of Capsaicin

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Transection of the dorsal part of the spinal cord at the Th9 level disturbs permeability of blood vessels of thigh skin in rats. This effects is significantly inhibited by neurotoxic doses of capsaicin, which attests to the involvement of peptide-containing neurons. The data confirm the possibility of central modulation of the effector function of capsaicin-sensitive neurons.

Key Words: *spinal cord transection; vascular permeability; capsaicin; neuropeptides*

Recently considerable attention was focused on afferent-efferent function of subpopulation of capsaicin-sensitive neurons (CSN), which transmit impulses to higher centers during warm and noxious stimulation and control cutaneous blood flow and vascular permeability by releasing vasoactive neuropeptides: substance P and calcitonin gene-related peptide [4]. The somas of CSN are located in spinal ganglia, and transmission of the sensory signals is partially mediated by intercalated enkephalin-containing neurons in the dorsal horns of the spinal cord (SC). It was previously considered that the effector functions of sensory neurons are implemented via axon-reflexes, which cannot be modulated centrally. However, various clinical data attesting to participation of neuropeptides in the genesis of psychosomatic pathologies, as well as experimental evidence for the development of the neurodegenerative processes in peripheral tissues provoked by destruction of the dorsal cord structures containing central CSN projections [1,6] do not support this view.

In the present study we explored modulation of vascular permeability in rat thigh skin via CSN after transection of the dorsal SC at the Th9 level, which partially disrupts the connections of CSN with ventral cord without disturbing the integrity of sensory ganglia and central terminals of CSN. The involvement of CSN in this process was tested by applying capsaicin in high doses at terms corresponding to depletion of neuropeptide stores in peripheral sensory terminals [4].

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MATERIALS AND METHODS

The study was carried out on male Wistar rats (body weight 180-200 g). Partial transection of the dorsal SC was performed under nembutal anesthesia (40 mg/kg intraperitoneally) 2 h prior to sacrifice. Effectiveness of surgery was accessed by photographs of non-fixed SC microtome sections. Some rats were sham-operated, i.e. SC was opened at the Th9 level without destruction its structures.

Peripheral peptidergic terminals were blocked by daily subcutaneous injections of 1% capsaicin (Sigma) in a medium containing 10% ethyl alcohol, 10% Twin 80, and 80% isotonic NaCl performed under weak ether anesthesia for 3 days. Single doses were 25, 50, and 75 mg/kg, while the total dose was 150 mg/kg. After 2 weeks some rats were killed, and vascular permeability was assessed, while in others SC was transected at the Th9 level. The rats injected with vehicle alone and capsaicin-treated sham-operated rats served as the control.

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Permeability of skin vessels on the external side of the thigh was assessed by accumulation of Evans blue injected intravenously in a dose of 50 mg/kg 1 h before decapitation. The dye was extracted from skin specimens as described previously [7] with our modifications. Optical density of the extract was measured on an SF-46 spectrophotometer at 620 nm. The concentration of the dye was determined by calibration curves. The results were analyzed statistically using Student's *t* test.

RESULTS

In intact rats accumulation of the dye in the skin was minor (6.0±4.2 μg/mg tissue). After injection of the solvent, vascular permeability was 7.0±3.1 μg/mg.

Two weeks after injection of a neurotoxic dose of capsaicin, the body weight decreased by 22.6±0.58%. Ulcerated areas were in the interdigital space, snout, and ears. Ulceration of the skin was accompanied by increased dye accumulation (22.0±8.1 μg/mg tissue, $p<0.05$). This increase was probably caused by primary release of vasoactive neuropeptides from capsaicin-sensitive terminals followed by depletion of peptide stores in CNS, because the primary stages of neurogenic inflammation are characterized by enhanced release of tachykinins (substance P [3]), while weakening of the neural control results in deficiency of skin homeostasis and can provoke delayed hypersensitivity reaction [5].

Two hours after transection of the dorsal portion of SC in intact rats, vascular permeability significantly increased to 59.0±11.6 ng/mg ($p<0.05$); sham operation produced no significant changes in this parameter.

Transection of SC in rats treated with capsaicin 2 weeks before surgery produced less pronounced changes in vascular permeability. Two hours postoperation, dye concentration in the skin did not exceed 20.0±6.9 μg/mg tissue. Sham operation in capsaicin-treated rats insignificantly decreased this parameter to 17.0±6.2 μg/mg.

It should be noted that vascular permeability in peripheral tissues significantly changes after blockade of neural traffic from primary sensory neurons to structures of the ventral cord. This effect was markedly inhibited by preliminary depletion of neuropeptide stores in peripheral terminals, which attests to involvement of CSN in central modulation of peripheral vasodilation and the possibility of regulating this process via the first sensory relay stage in SC. Pharmacological blockade of enkephalin-containing intercalated neurons in SC that relay impulse traffic from sensory neurons to the ventral cord structures considerably decreases the release of substance P in response to irritating agents [2]. Thus, it can be concluded that the centrifugal influences of the central nervous system can be transmitted not only via the sympathetic, parasympathetic, or hormonal pathways. Anatomically, the interaction of the central nervous system with peripheral tissues may be realized via CNS subpopulation, which according to modern views performs a dual afferent-efferent function.

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