In cats anesthetized with chloralose nociceptive heating of the skin of the foot to 44-60°C led to a two- to fourfold increase in amplitude of primary cortical responses to direct stimulation of neurons of the spinocervical tract receiving information from the heated area of skin, but did not affect primary responses evoked by stimulation of axons of these neurons in the dorsolateral funiculus, and actually inhibited the response to stimulation of the nerve innervating the heated area of skin. Inhibition was accompanied by depolarization of central terminal of low-threshold fibers of this nerve: During heating the amplitude of the antidromic discharges evoked in the nerve by stimulation of its presynaptic endings in the spinal cord was increased two- to threefold. After abolition of presynaptic depolarization with picrotoxin (0.2-0.7 mg/kg, intravenously) or as a result of asphyxiation, nociceptive heating acquired the ability to facilitate primary responses arising as a result of stimulation of the nerve also. The amplitude of the responses was increased under these circumstances by 3-20 times. It is concluded that acute nociceptive stimulation causes such powerful presynaptic inhibition of impulse transmission from low-threshold fibers of the cutaneous nerve that it virtually abolishes the facilitating effect of nociceptive impulses on sensory neurons of the spinal cord. It is suggested that it is this inhibitory mechanism which prevents the development of hyperalgesia during acute nociceptive stimulation.

INTRODUCTION

Chronic slowly increasing nociceptive stimulation, caused by inflammation developing in the skin, facilitates responses of the somatosensory system to testing stimulation of low-threshold nerve fibers which innervate the affected area of skin [1-3, 12, 25]. By contrast to this, acute nociceptive stimulation in the form of powerful tissue-damaging procedures or electrical stimulation of high-threshold fibers of cutaneous, muscular, or visceral nerves, not only do not facilitate, but may often actually inhibit the response of the somatosensory system to stimulation of low-threshold primary afferents [9, 10, 15, 17, 19, 22]. These data are matched by clinical and psychophysiological observations, according to which only chronic nociceptive stimulation, connected mainly with inflammatory processes in the peripheral tissue, is accompanied by the development of hyperalgesia — by lowering of the pain threshold of damaged and even of undamaged tissues, if the latter have afferent connections with those same sensory projection neurons of the spinal cord that receive excitatory influences from the pathological focus also [18]. Acute nociceptive stimulation, on the other hand, leads to a directly opposite phenomenon — raising of the pain threshold [6, 16, 21]. Why there should be this difference in responses of the somatosensory system to these two types of nociceptive stimulation (acute and chronic) is not known. The investigation described below was devoted to a study of this problem.

EXPERIMENTAL METHOD

Experiments were carried out on 27 cats anesthetized with α-chloralose (50-70 mg/kg, intraperitoneally) and immobilized with tubocurarine or diplacine, and artificially ventilated. Primary responses (PR) were derived by monopolar silver ball electrodes, which were lightly pressed by miniature springs against the surface of the posterior sigmoid gyrus in the representation of the hind or fore-limb. The reference electrode (a steel needle) was secured in the nasal bones. PR were evoked by stimulation of low-threshold fibers of cutaneous nerves (superficial peroneal and superficial radial) or by direct stimulation of lemniscal structures — the zone of neuron bodies of the spinocervical tract (SCT) at level L₈₋₉, SCT itself at level L₂₋₃ or the caudal part of C₅.
Fig. 1. Effect of nociceptive heating of skin of foot on transmission of signals along lemniscal system from low-threshold fibers of cutaneous nerve. 1) Primary responses (PR) of cortex of right hemisphere to threshold stimulation of neurons of spinocervical tract and 2) of superficial peroneal nerve on opposite side; 3) antidromal discharges in superficial peroneal nerve of left hind limb evoked by stimulation of central terminals of that nerve in posterior horn of spinal cord segment L7. PR and antidromic discharges evoked before (a) and 30-40 sec (b) and 3-4 min (c) after beginning of continuous nociceptive heating (up to 47°C) of dorsal surface of foot of left hind limb. Calibration: 30 (for 1, 2) and 300 (for 3) μV, 40 (for 1, 2) and 10 (for 3) msec.

Fig. 2. Effect of nociceptive heating of skin of foot on transmission of signals along lemniscal system from low-threshold primary afferents after blocking of presynaptic inhibition by asphyxia, a-f) Primary responses (PR) at lateral border of cruciform fissure of right hemisphere to threshold stimulation of superficial radial nerve and m-r) of fasciculus cuneatus on opposite side of body. g-i) PR at symmetrical point of cortex of left hemisphere to threshold stimulation of superficial radial nerve of right forelimb. Responses recorded before nociceptive stimulation (a, g, m) and 60-90 sec (b, h, n) and 3-4 min (c, l, o) after beginning of nociceptive stimulation of left forelimb, and also 60-70 sec (d, j, p), 6-7 min (e, k, q) and 9-10 min (f, l, r) after its end. Nociceptive stimulation produced by heating dorsal surface of foot of left forelimb to 53°C. Calibration: 300 μV, 15 msec.

and also the fasciculus cuneatus at level C2, C3. The methods of determining the optimal position of the microelectrode to stimulate neurons of SCT were described previously [4]. Excitability of central terminals of the superficial peroneal nerve in the posterior horn of the spinal cord was determined by Wall's method [26]. The nerves were stimulated by a bipolar technique through platinum wire electrodes with an interelectrode distance of 5 mm, the spinal cord by a monopolar method using steel needle electrodes with a tip 15-20 μ in diameter, insulated with Bakelite varnish or viniflex everywhere except at the tip. The reference electrode (anode of the stimulating current) was located in the muscles surrounding the operation wound. To prevent exposed regions of nerves, the spinal cord, and the cerebral cortex from drying, they were covered with warm mineral oil.

Presynaptic inhibition was blocked either by intravenous injection of picrotoxin (dose 0.2-0.7 mg/kg), or by acute asphyxia (a procedure which depresses first and foremost the activity of interneurons, including those participating in presynaptic inhibition) [8, 13, 14, 20, 23]. Acute asphyxia was induced by switching off the breathing apparatus for 3-5 min. This procedure was repeated several times with each animal.

Acute nociceptive stimulation was produced by heating the skin to 44-60°C by means of a contact thermode, covering the whole dorsal surface of the foot of the hind or fore-limb. The skin temperature beneath the thermode was monitored by a thermocouple. After switching on the thermode the temperature on the skin surface reached a maximum (44-60°C) in the course of 15-20 sec.