STRESS ANALGESIA IN EXPERIMENTAL BURN SHOCK

L. N. Sinitsyn and S. S. Gelashvili

UDC 617.001.17-001.36-092.9-07:616.8-009.614-02:616.831-008.939.43

KEY WORDS: burn shock; afferent systems; endogenous opiates; stress analgesia; naloxone.

Modern views on stress analgesia, that it is due to hyperproduction of endogenous opiates, are generally accepted [1, 5-8]. Burn shock is accompanied by severe disturbances of CNS activity [3], but these have not yet been adequately studied.

The aim of this investigation was to study the transmission of excitation in the afferent and efferent systems of the brain in experimental burn shock and to establish the possible mechanisms of their disturbances.

EXPERIMENTAL METHOD

Experiments were carried out on 30 adult cats immobilized with succinylcholine, anesthetized with chloralose (10 mg/kg), artificially ventilated, and with their body temperature maintained within normal limits. The effect of burn trauma was studied on evoked potentials (EP) in specific, association, and nonspecific structures of the cerebral cortex, diencephalon, and mesencephalon in response to somatic, acoustic, and photic stimulation. Burn shock was induced by infliction of a contact burn of the IIIB degree affecting 20-30% of the body surface by means of an electric heater with contact thermometer, maintaining the temperature of the buring surface at 100°C (exposure 30 sec).

EP were recorded by means of a 6-channel amplifier (Alvar, France) and cathode-ray oscilloscope with driven sweep, by the repeated superposition on photographic film method. For electrical stimulation of the sciatic nerve paired (interval 100 msec) or single square pulses were applied with a frequency of 1 Hz. Acoustic and visual stimulation was obtained by converting these pulses into acoustic and photic stimuli.

The effect of burn trauma on transmission of excitation in the efferent visceral systems was studied under similar conditions by a method of local electrical stimulation of structures of the cerebral cortex, diencephalon, and mesencephalon and recording of the neurogenic arrhythmias (NA), hypertensive responses (HR), and changes in the general arterial pressure level (BP) arising under these circumstances. The ECG was recorded in standard lead II and BP was recorded in the femoral artery by means of an electrocardiograph and electromanometer (Alvar, France). For electrical stimulation of the brain structures square pulses (5-10 V, 1 msec, 200 Hz) were applied with intervals of 5 min.

EXPERIMENTAL RESULTS

Starting with the 2nd hour after burn trauma, inhibition of EP mainly in the association and nonspecific cortical areas was observed in the afferent system; this inhibition gradually increased to reach a maximum by the end of the first day. This effect of inhibition was expressed as a decrease in amplitude and increase in duration and latent period of EP. Similar changes took place in association and nonspecific structures of the diencephalon and mesencephalon. Disturbances of tranmission of excitation in the specific afferent systems were much less marked (Fig. 1). Signs of inhibition in the somatic system were more marked than in the auditory and visual systems.

In efferent visceral systems burn shock caused pronounced facilitation of excitation transmission. HR to stimulation of the sensomotor cortex and nonspecific structures of the

Laboratory of Pathophysiology and Experimental Surgery, Research Institute of Traumatology and Orthopedics, Ministry of Health of the RSFSR, Gor'kii. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 95, No. 4, pp. 37-39, April, 1983. Original article submitted September 30, 1982.

0007-4888/83/9504-0447$07.50

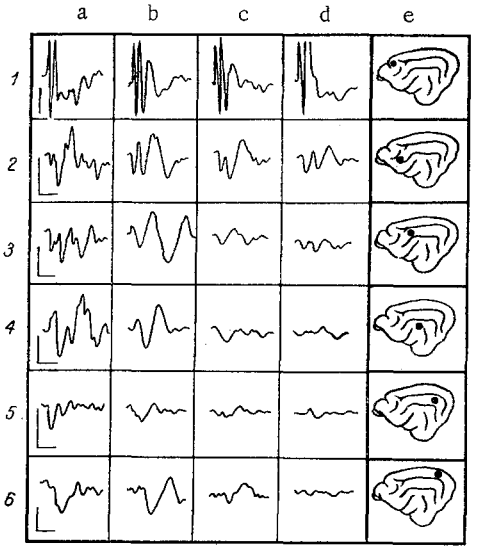

Fig. 1. Effect of burn shock on cortical EP in response to sciatic nerve stimulation. a) Initial background; b) 10 min, c) 8 h, d) 18 h after burning; e) location of recording electrodes. 1) Specific projection area; 2, 3, 5) association projection areas; 4, 6) nonspecific projection areas. Vertical lines, amplitude 100 μV; horizontal lines — time 100 msec.

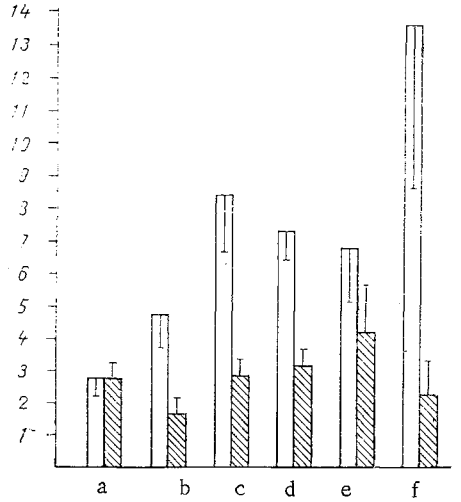

Fig. 2. Effect of naloxone on elevation of visceral pain threshold in albino rats with experimental burn shock. Ordinate, values of pain threshold (in relative units). Initial pain threshold, estimated from vocalization response after stimulus, taken as 1. a) 2 h after burning, b) 10 min, c) 30 min, d) 60 min, e) 2 h, f) 24 h after injection of naloxone, 5 mg/kg. Vertical lines indicate confidence limits. Unshaded columns — control animals receiving physiological saline, shaded columns — animals receiving naloxone (10 rats in each group).

diencephalon and mesencephalon increased on average by 81% after burn trauma and remained at this level for 24 h, after which their intensity gradually declined. The duration of NA increased on average by 3.7 times during the first 2 h of burn shock. This effect gradually diminished but was also observable for 24 h. The general BP level rose on average by 18% during the first hour after burning. This state of hypertension persisted in most experiments for 24 h. Later, however, the general BP level fell to or even below its initial values.

Analysis of the results showed that burn shock causes changes in excitation transmission in the afferent and efferent systems of the brain similar to those found after administration of narcotic analgesics of the morphine group [4]. It was accordingly decided to carry out the next series of experiments to study the effect of burn shock on somatic and visceral nociceptive sensation. Experiments were carried out on albino rats weighing 180-200 g. Burn shock was produced by the method described above. Nociceptive electrical stimulation was applied in the form of groups of square pulses (10 pulses, 1 msec in duration, per group) through bipolar needle electrodes in the upper third of the tail or in the peritoneal cavity. Pain thresholds were estimated from the appearance of a motor response and a vocalization response during and after stimulation. Threshold strengths of the stimulating current were determined for each response by means of a S1-19 cathode-ray oscilloscope by recording the voltage drop on a measuring resistance.

The results showed that burn shock induces elevation of the thresholds of somatic and visceral nociceptive sensation in albino rats, as shown by the vocalization response during and after stimulation, on average by 5-10 times. Elevation of the pain thresholds begins 1 h after trauma, reaches a maximum toward the end of the first day, and continues, steadily declining, for the next 5 days.

To analyze the possible mechanism of development of stress analgesia in experimental burn shock the effect of antagonists of narcotic analgesics and endogenous opiates on elevation of the pain threshold in burned animals was studied. The effect of rausedil, which reduces the catecholamine content in presynaptic endings of central neurons [2], and of naloxone was studied. These drugs were injected intravenously.

The experimental results showed that rausedil, in a dose of 20 μg/kg, delayed the rise of the pain threshold of somatic sensation compared with the control. Naloxone, under similar experimental conditions and in a dose of 5 mg/kg, delayed elevation of thresholds of somatic and visceral pain senstation caused by the burn in albino rats. The action of the drug reached a maximum 10 min after its injection. The fall in the pain threshold ceased to be significant after 1 h. However, on the 2nd day the pain threshold in animals treated with naloxone still remained significantly lower than in the control (Fig. 2). Lowering of the threshold of pain sensation on the 2nd day was also distinctly present in the experiments with rausedil.

These results suggested that stress analgesia in experimental burn shock is due to hyperproduction of endogenous opiates. To confirm this suggestion, the total opiate-like activity (β-endorphin, β-lipotropin) of extracts of the anterior brain regions of albino rats with burn trauma was determined and compared with its value in control animals. Radioimmunoassay was carried out with diagnostic kits from Immunonuclear Corporation (USA). Radioactivity was determined on an automatic Gamma-counter (LKB, Sweden).

The experiments showed that total opiate-like activity in rats of the control group was 121.64 ± 11.9 counts/mg, whereas in albino rats killed 2 h after thermal trauma the opiate-like activity increased to 193.12 ± 10.9 counts/mg, and in animals killed on the 2nd day after burning the total opiate-like activity was 199.15 ± 21.6 counts/mg. The results of these experiments confirm the fact that burn shock led to an increase in opiate-like activity compared with the control by 75.5 counts/mg 2 h, and 77.55 counts/mg 24 h after trauma ($P < 0.05$). The experimental results thus show that in burn shock stress analgesia is present and is evidently due to increased production of endogenous opiates.

LITERATURE CITED

1. E. V. Golovanov, S. B. Parin, and V. V. Yasnetsov, Byull. Éksp. Biol. Med., No. 6, 60 (1982).
2. V. V. Zakusov, Pharmacology of Central Synapses [in Russian], Moscow (1973), p. 116.
3. B. A. Saakov and É. A. Bardakhch'yan, Urgent Problems in the Pathogenesis of Burn Shock [in Russian], Moscow (1979).
4. L. N. Sinitsyn, "Effect of neurotropic drugs on afferent and efferent visceral systems," Author's Abstract of Doctoral Dissertation, Moscow (1974).
5. J. Faden and J. Holaday, J. Pharmacol. Exp. Ther., 212, 441 (1980).
6. W. K. K. Ho, H. K. Wang, and H. L. Wen, Neuropharmacology, 18, 865 (1979).
7. J. W. Holaday, G. L. Belenky, A. J. Faden, et al., in: Neuropsychopharmacology, Vienna (1978), p. 503.
8. D. D. Kelly and R. L. Bodnar, Acupunct. Elect.-Ther. Res., 4, 159 (1979).