# ROLE OF THE CENTRAL GRAY MATTER OF RATS IN REGULATION OF PAIN SENSITIVITY DURING AURICULAR ELECTRICAL STIMULATION

E. O. Bragin, G. F. Vasilenko, and R. A. Durinyan

UDC 612.884-06:612.825

KEY WORDS: auricular electrical stimulation; analgesia; central gray matter.

As a result of research into the central mechanisms of analgesia, an important role has been postulated for the central gray matter (CGM). Injection of microdoses of morphine or opiate peptides or electrical stimulation of CGM has been shown to reduce sensitivity to pain [2, 7, 10, 12]. The analgesic effect of these procedures is evidently linked with activation of the neurochemical systems of CGM in the brain, in which neurons of different chemical nature are found, such as opiate [5, 11] and monoamine [3]. The role of the CGM in the mechanisms of morphine analgesia is revealed by data showing that injury to CGM in rats causes marked depression of the analgesic effect of morphine [4].

Previous experiments yielded data indicating the role of CGM in mechanisms of depression of sensitivity to pain during auricular electrical stimulation. This is shown by the fact that analgesia as a result of stimulation of zones in the region of auricular acupuncture points is accompanied by changes in the level of opiate-like compounds [9] and of electrophysical neuronal activity in CGM [1].

In the investigation described below the influence of CGM on the sensitivity of rats to pain was studied during auricular electrical stimulation.

## EXPERIMENTAL METHODS

Experiments were carried out on male albino rats weighing 200-250 g, anesthetized with pentobarbital (40 mg/kg), into which electrodes were inserted stereotaxically into CGM, taking coordinates AP +0.6, L ± 0.5, VD +4.0 to +4.2 from the atlas [8], and CGM was destroyed electrolytically by a current of 1 mA applied for 25-30 sec. Rats of the control group underwent a mock operation: The electrode was inserted into brain tissue to a depth of 2.0-2.5 mm relative to the dura mater. The experiments began 2 weeks after the operation.

Auricular electrical stimulation was carried out by means of clip electrodes, fixed to the conchae auriculae in the region of projection of the "lung" points. Stimulation was applied with a current of 1 mA (frequency 4 Hz, pulse duration 0.4 msec) for 15 min.

Sensitivity to pain was assessed from the latent periods (LP) of responses to nociceptive stimulation. Two methods were used: the hot-plate method (HP) and the tail-flick method (TF). In the first case the rats were placed in a chamber the floor of which had a temperature of 55°C. The time from the moment of contact of the rats with the hot plate and the first time it licked its hind limbs was taken as LP. The mean value of LP was determined on the basis of two measurements made at an interval of 15 sec. In the second case the rats were placed in a constraining box, and the tail was subjected to temperature stimulation by means of the focused beam of light from a 150-W projection lamp. LP corresponded to the time from switching on the lamp to the first movement of the rat's tail. The mean value of LP was obtained from the results of 5-7 measurements at intervals of 7-10 sec.

The duration of the initial LP was determined 7-10 min before auricular electrical stimulation, and thereafter LP was determined at regular time intervals.

---

Laboratory of Neurochemistry and Histochemistry, Central Research Institute of Reflex Therapy, Moscow City Council Main Health Authority. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 7, pp. 11-13, July, 1982. Original article submitted December 25, 1981.

 0007-4888/82/9407-0860$07.50 

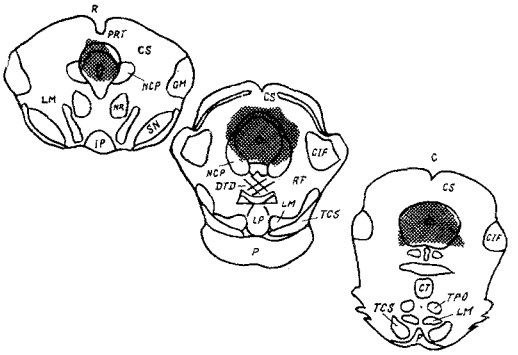


Fig. 1. Location of lesion of CGM (shaded) at different levels of rat midbrain (rostral AP +2.0, middle AP +1.0, caudal AP +0.4). C) caudalis, ClF) colliculus inferior. CS) colliculus superior, CT) nucl. centralis tegmenti, DTD) decussatio tegmenti dorsalis, GM) corpus geniculatum mediale, IP) nucl. interpreduncularis, LM) lemniscus medialis, NCP) nucl. proprius commissural posterior, NR) Nucl. ruber, P) pons, PRT) area praetectalis, RF)formatio reticularis, R) rostralis, SN) substantia nigra, TCS) tractus corticospinalis, TPO) nucl. tegmenti pontis.

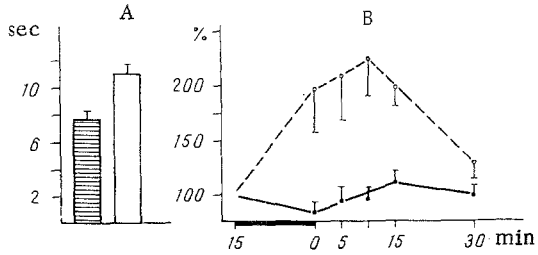


Fig. 2. Effect of destruction of CGM on duration of LP measured by hot-plate method before (A) and after (B) auricular electrical stimulation. Shaded column and broken line represents duration of LP in rats undergoing mock operations, unshaded column and continuous line represent LP in rats with destruction of CGM. Bold line on abscissa shows duration of stimulation (in min); ordinate: A) duration of LP (in sec), B) the same (in % of initial value).

At the end of the experiment the animals were decapitated, the brain was fixed in 10% neutral formalin solution, and after 3-4 days sections were cut to a thickness of 60 μ on a freezing microtome. The sections were fixed on slides and photographed.

## EXPERIMENTAL RESULTS

In animals operations to block CGM, on recovery from anesthesia changes were observed in their behavior, which was characterized by periodic paroxysms of intensive motor activity, arising in the absence of any visible external stimuli, or in response to them (light touch,

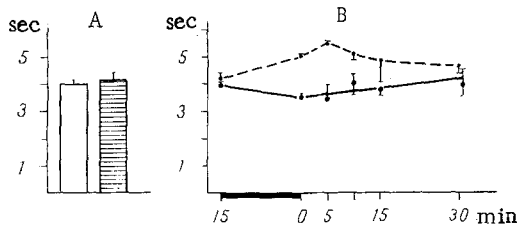


Fig. 3. Effect of destruction of CGM on duration of LP measured by tail-flick method. Ordinate, in b: duration of LP (in sec). Remainder of legend as in Fig. 2.

shaking of the cage in which the animals were kept, very weak but unexpected acoustic and photic stimuli). The motor hyperactivity was characterized by rapid turning around the longitudinal axis of the body and movements along the cage walls. Uncoordinated jumps were often observed. In the intervals between paroxysms the rats were quiet. At the end of 2-4 h their normal behavior was restored and it was indistinguishable from that of animals of the control group. Similar changes in behavioral responses after blocking of CGM were described in [4]. It can be tentatively suggested that these changes were connected with functional disturbances of brain structures responsible for regulation of movement coordination.

The results of the histological study of the location of the lesion in CGM, illustrated in Fig. 1, show that by the use of this method the greatest extent of the lesion produced in CGM in the rostro-caudal direction was 2.0-2.8 mm. In some cases the lesions were found to spread beyond the lateral boundaries of CGM (Fig. 1).

Determination of the values of LP showed that in rats with destruction of CGM the initial LP, measured by the HP method, was significantly longer ($P < 0.05$) than in the control: $11.0 \pm 0.3$ and $7.7 \pm 0.5$ sec, respectively (Fig. 2). A rather different result was obtained when LP was measured by the TF method: In rats with lesions of CGM LP differed only a little from its values in rats of the control group: $4.0 \pm 0.1$ and $4.2 \pm 0.2$ sec, respectively (Fig. 3).

The results of experiments to study the effect of CGM on LP of responses to pain after auricular electrical stimulation showed (Figs. 2 and 3) that values of LP measured by the HP method in rats with destruction of CGM after the end of stimulation were indistinguishable from the initial values for 30 min. In the control group, however, electrical stimulation led to an increase in LP up to 200% (compared with the initial level) immediately after the end of stimulation, with a peak of up to 230% ($P < 0.001$) by the 10th minute, and a gradual decline until the 30th minute. Statistical analysis showed that LP of responses to nocicpeptive stimulation were significantly lower at all times of the experiment after electrical stimulation in rats with destruction of CGM than in the control.

Measurement of sensitivity to pain by the TF method showed that in rats with destruction of CGM the duration of LP after auricular electrical stimulation was unchanged compared with the initial value for 30 min (Fig. 3). In the control group, this procedure led to a significant increase in LP immediately after the end of stimulation ($S = 6.76$; $P < 0.05$), and also 5 min ($P < 0.05$) and 10 min ($P < 0.01$) later. Comparison of the results for comparable groups of animals showed that LP in rats with destruction of CGM was significantly lower than in the controls until the 10th minute ($P < 0.05$).

It can thus be concluded from these results that CGM participates in mechanisms of regulation of sensitivity to pain during auricular electrical stimulation. The possibility likewise cannot be ruled out that the effect obtained in this investigation may also be due to injury to the posterior raphe nucleus, located in the ventral part of the caudal zone of CGM. However, analysis of the histological data showed that in most cases this region of the brain was only partly damaged or completely undamaged. In addition, the results of a study of morphine analgesia [6] show that the posterior raphe nucleus does not participate in this form of analgesia, and that a more important structure is the large raphe nucleus, which gives rise to descending serotoninergic pathways of the spinal cord.

## LITERATURE CITED


1. O. N. Moskovets, "Electrophysiological analysis of antinociceptive effects of electrical stimulation of the concha auriculae in cats," Author's Abstract of Candidate's Dissertation, Moscow (1981).
2. J. K. Chang, B. T. W. Fong, A. Pert, et al., Life Sci., 18, 1473 (1976).
3. A. Dahlstrom and K. Fuxe, Acta Physiol. Scand., 62, Suppl. No. 232, 1 (1965).
4. J. F. W. Deakin and J. O. Dostrovsky, Br. J. Pharmacol., 63, 159 (1978).
5. M. Kuhar, C. Pert, and S. Snyder, Nature, 245, 447 (1973).
6. S. A. Lorens and L. M. Yunger, Pharm. Biochem. Behav., 2, 215 (1974).
7. D. J. Mayer and D. D. Price, Pain, 2, 379 (1973).
8. L. J. Pellegrino, A. S. Pellegrino, and A. J. Cushman, A Stereotaxic Atlas of the Rat Brain, New York (1979).
9. A. Pert, R. Dionne, E. Bragin, et al., Abstracts Neurosci., 10, 50 (1980).
10. D. V. Reynolds, Science, 164, 444 (1969).
11. R. Simantov, M. Kuhar, G. Pasternak, et al., Brain Res., 106, 189 (1976).
12. R. L. Yaksh, J. C. Yeung, and T. A. Rudy, Brain Res., 114, 83 (1976).