on the terminal screen and led out to the printer. The mean values and standard deviations of spike activity are next calculated. Parameters of the systemic hemodynamics are entered from the digital volt meters and devices for measuring intersystolic intervals and are processed when the basic program is interrupted. Analysis of sympathetic bioelectrical activity is thus synchronized in time with evaluation of the parameters of the systemic hemodynamics. After values of the systolic and diastolic BP and the intersystolic intervals have been entered and processed, maximal and minimal values of each parameter for the time of the experiment are calculated and a final record of them is printed. An example of the record of an experiment and of documentation of the data after computer analysis is given in Fig. 3.

The CS is based on USSR-made instruments in large scale production. The design of the SADC is such that spike trains of varied origin can be transformed for entry into the computer whatever their amplitude and frequency characteristics. The pressure transducer can also be used to analyze parameters of venous pressure and volume velocity of the blood flow. Both the hardware and software of the CS are thus suitable for use in the optimization of experiments in many different fields of biology and medicine.

## LITERATURE CITED

1. V. N. Khayutin, R. S. Somina, and E. V. Lukoshkova, Central Organization of Vasomotor Control [in Russian], Moscow (1977).

# POSSIBLE ROLE OF POSITIVE REWARD ZONES IN PAIN REGULATION MECHANISMS AND THEIR CONNECTION WITH THE ENDOGENOUS OPIATE SYSTEM

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KEY WORDS: self-stimulation reaction; analgesia; naloxone

Morphine is a classical narcotic analgesic, whose spectrum of pharmocological activity also includes euphoric properties. The question accordingly arises whether this combination of pharmacological properties is essential for manifestation of the analgesic effect. Drugs with a euphoria-inducing action in experiments on animals have a facilitatory effect on the self-stimulation reaction (SSR) if the electrodes are located in the lateral hypothalamus (LH) and septum, i.e., in positive reward structures [1]. In turn, electrical stimulation of positive reward structures may lead to the devlopment of analgesia [3, 11].

In view of these considerations, and also data showing that the regions mentioned above contain large quantities of endogenous opioid peptides [5, 9, 10, 13], which can modulate both SSR and nociceptive sensitivity [3], it was decided to compare the character of involvement of opioidergic processes in SSR from the dorsal nucleus raphe (DNR) and LH, and the changes in nociceptive sensitivity arising under these conditions, with the aid of naloxone, a selective opioid antogonist.

## EXPERIMENTAL METHOD

Experiments were carried out on 36 noninbred male rats weighing 180-250 g, into which chronic unipolar electrodes were introduced under pentobarbital anesthesia (40 mg/kg, intraperitoneally) into LH (AP 1.5, L 1.5, H 8.5) and DNR (AP 7.0, L 0, H 7.0) in accordance with stereotaxic coordinates [8]. One week after the operation the animals were trained in SSR from LH (nine animals) and DNA (nine animals) respectively, until stable parameters of self-stimulation had been established by the method described above [1]. Next, in the experiments of series I, during a 10-min session, levels of the threshold of SSR and the number of

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TABLE 1. Effect of SSR and Naloxone on Thresholds of Pain Sensitivity (M ± m; n = 9)

| Brain structure from which self-stimulation (SS) was elicited | LP of tail withdrawal, sec | | | | |
|---|---|---|---|---|---|
| | background | immediately after session of SS | 30 min after session of SS | naloxone (2mg/kg) + session of SS 15 min later | 30 min after injection of naloxone (2 mg/kg) + session of SS |
| DNR | 1,80±0,28 | 4,22±0,18* | 1,72±0,18 | 4,82±0,40* | 1,90±0,20 |
| LH | 1,98±0,30 | 3,64±0,40* | 2,34±0,20 | 3,88±0,57* | 2,32±0,42 |

Legend. Here and in Table 2, *p < 0.05.

TABLE 2. Effect of Naloxone on Parameters of SSR (n = 9)

| Brain structure from which SS was elicited | Threshold of SSR, μA | | Frequency of SS per minute (number of self stimulations) for optimal current strength | |
|---|---|---|---|---|
| | background | Naloxone (2 mg/kg) | background | Naloxone (2 mg/kg) |
| DNR | 127 | 132 | 79 | 72 |
| LH | 72 | 128* | 104 | 71* |

self-stimulations per minute at threshold, optimal, and above-optimal current strengths were determined. Monophasic square pulses with a period of 6 msec, a duration of 3 msec, and with 20 pulses in a burst with an amplitude of 50-300 μA, from an ÉS-50-1 electrical stimulator, were used for SSR. The latent periods (LP) of withdrawal of the tail, immersed by three-quarters of its length in a jar of water at 55°C [7], were determined 15 min before the session of SSR, immediately after its end, and 30 min later.

In the experiments of series II the effect of naloxone (2 mg/kg, intraperiotoneally), injected 15 min before the beginning of SSR, induced from LH or from DNR, on the parameters of SSR ahd LP of tail withdrawal, measured at the same time intervals as in the experiments of series I, was studied.

In series III, to monitor the character of the effect of naloxone on opioidergic processes in the course of experiment, the effect of the drug in the above-mentioned dose was studied on LP of tail withdrawal in animals not subjected to the self-stimulation procedure, on which algesimetric testing was carried out at the same time intervals as in the experiments with SSR.

The results were subjected to statistical analysis by Student's test [4] and by the nonparametric differences method [12].

## EXPERIMENTAL RESULTS

As a result of SSR from both LH and NDR, a statistically significant increase of 2-2.5 times was found in LP of the tail withdrawal reflex, evidence of the development for analgesia under the influence of SSR. This effect was of short duration, for values of the above LP returned to their background level 30 min after the end of SSR. The specific opiate antagonist naloxone (2 mg/kg) did not abolish SSR-induced analgesia (Table 1).

The control experiments showed that at times other than during SSR naloxone, in the dose studied, if injected 30 min before testing the level of nociceptive sensitivity (i.e., to correspond to the time of ending of SSR), completely abolished analgesia caused by morphine (6 mg/kg, intreperitoneally, 15 min before testing), according to the tail withdrawal test. These facts suggest that the analgesia arising in response to SSR from both brain zones studied is nonopioidergic in nature. At the same time, it was shown that naloxone inhibits SSR from LH — its threshold increased by 1.8 times ($p < 0.01$) whereas the frequency of self-stimulation was reduced by 1.5 times ($p < 0.01$), but it had no effect on the parameters of SSR from DNR (Table 2). These facts demonstrate, on the one hand, involvement of opioidergic mechanisms in SSR from LH, and that the opioidergic system does not transmit SSR from DNR, on the other hand. Considering the fact that regions LH [9] and DNR [5, 9, 10, 13] contain large quantities of enkephalins and many opioid receptors, and that nalxone does not reverse analgesia induced by SSR from both zones, it can be tentatively suggested that the opioidergic systems of the regions under examination are not involved in the mechanism of analgesia produced by electrical stimulation of positive reward zones in the process of SSR.

These results to some extent contradict those of other investigations [3], which show that naloxone can abolish analgesia induced by SSR. This difference may perhaps be explained by the different neurochemical mechanisms forming the nociceptive response to stimuli of different modalities [6].

According to Borisenko [2], morphine has a facilitory action on SSR in rats only in a dose corresponding to $ED_{50}$ of the analgesic effect (3 mg/kg). Trimeperidine (4.5 mg/kg) did not affect it, fentanyl (40 mg/kg) reduced the intensity of self-stimulation, whereas pentazocine (20 mg/kg) completely suppressed it.

It can thus be concluded that the euphoria-inducing component is not essential for manifestation of the analgesic effect of narcotic analgesics.

## LITERATURE CITED


1. Yu. V. Borov and S. A. Borisenko, Byull. Éksp. Biol. Med., No. 6, 698 (1980).
2. S. A. Borisenko, Byull. Éksp. Biol. Med., No. 4, 432 (1976).
3. É. É. Zvartau, Byull. Éksp. Biol. Med., No. 11, 569 (1979).
4. N. A. Plokhinskii, Biometrics [in Russian], Moscow (1970).
5. J. D. Belluzzi, Nature, 266, 556 (1977).
6. O.-G. Berge, K. Hole, and S.-O. Ogren, Brain Res., 271, 51 (1983).
7. E. Fifková and J. Marsála, in: Electrophysiological Methods in Biological Research, J. Bures, M. Petran, and J. Zachar (eds.), Prague (1960), pp. 426-467.
8. K. B. J. Franklin and A. Robertson, Pharmacol. Biochem. Behav., 16, 433 (1982).
9. E. J. Glazer, H. Steinbusch. A. Verhofstad, and A. I. Basbaum, J. Physiol. (London), 77, 241 (1981).
10. D. J. Mayr, T. L. Wolfle, H. Akil, et al., Science, 174, 1351 (1971).
11. R. Meddis, Br. J. Psychol., 66, 225 (1975).
12. M. S. Moss, J. E. Glazer, and A. I. Basbaum, Adv. Pain Res. Ther., 5, 256 (1983).


# CORRELATION BETWEEN THE RATE OF ETHANOL ELIMINATION AND PSYCHOPHYSIOLOGICAL DIFFERENCES IN RATS


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The development of alcoholism as a multifactorial disease can be attributed to a number of environmental and genetically determined features [5, 13]. In particular, one feature of the genetic predisposition to alcohol addiction from the beginning is the high rate of its elimination [4]. It has also been shown that primary predisposition to alcohol consumption may be due to individual differences in higher nervous activity in a population of laboratory albino rats.

For the above reasons it was decided to study the rate of ethanol elimination (an indirect parameter of activity of ethanol-oxidizing enzyme systems) from the blood of rats distinguished *ab initio* with respect to their psychophysiological features, in order to discover if the general principles mentioned above can be identified in the complex system of predisposition to alcohol consumption in a model of experimental alcoholism.

## EXPERIMENTAL METHOD

Experiments were carried out on 12 laboratory male albino rats weighing 180-200 g, divided beforehand into two groups, by a method based on differences in behavioral activity


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