structures (probably, shape changes), since it proceeds against the background of suppressed regeneratory-plastic processes and myocardial atrophy. It should be mentioned that exposure of an animal to a single total hyperthermia during a critical time period after which the animal can die induces such far-reaching disturbances in the intracellular regeneration in the cardiomyocytes that the consequences of these disturbances - changes in the cell architectonics - are permanent and become more pronounced by the 7th day of the experiment.

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The Effect of Morphine on RNA Synthesis in Some Brain Structures of Rats with Various Narcological Resistance

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Different incorporation of ^{3}H-uridine in RNA and increased RNA synthesis after the addition of morphine are demonstrated in all brain structures of resistant rats, as well as in the cortex, nucleus accumbens, griseum centrale, and nucleus ventriculus hypothalami of prone rats.

Key Words: *morphine; narcological resistance; transcription activity of nerve cells*

The predominant involvement of certain brain structures of the central nervous system (CNS), namely the sensorimotor cortex (SmC), cerebellar cortex (CbC), CA3 zone of the hippocampus (CH), amygdala (A), nucleus raphe magnus (NRM) griseum centrale (GC), nucleus ventromediali hypothalami (NVmH), and nucleus accumbens (NA) has been demonstrated in the development of drug and alcohol addiction [3,4]. With the exception of CbC, these structures have high contents of endogenous opioids and opiate receptors and play a

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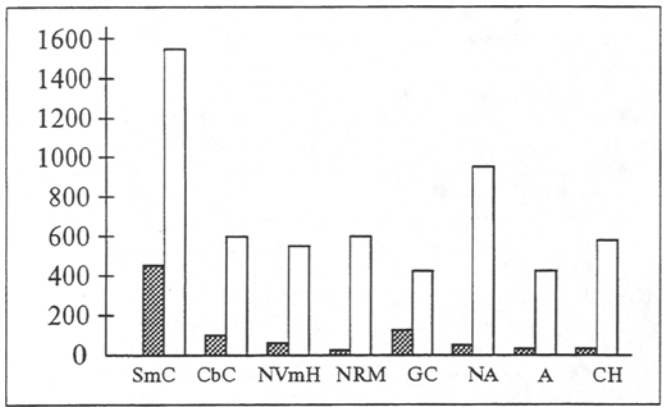

Fig. 1. ^{3}H–uridine incorporation in total RNA from nerve cells of different CNS structures of resistant rats. Here and in Fig. 2 ordinate: radioactivity (cpm/min × section weight). White bars: experiment; black bars: control.

role in the manifestation of emotional and analgetic effects of morphine. There is evidence that morphine affects the genetic apparatus of the cell, specifically RNA synthesis, and modulates the activity of some transcription enzymes [1,6-9].

The objective of the present study was to compare the response of chromatin in the nerve cells of the above-mentioned structures to morphine in animals prone and resistant to the development of morphine addiction. The propensity for drug use and the development of drug addiction may be related to individual genetic characteristics, which determine the drug pharmacology in each individual case [5].

MATERIALS AND METHODS

Individual sensitivity to the development of drug addiction was estimated as described elsewhere [5]. Fifty male Wistar rats were used in the study. The animals were decapitated, the cerebral structures were dissected, cut into 1×0.5×0.5 mm pieces, and incubated as described [2]. The preincubation time was 30 min. Some of the sections were further incubated with morphine (the final concentration in the incubation medium was 8 mM). ^{3}H-uridine (0.8 MBq/ml incubation medium, specific activity 350 GBq/liter) was added 60 min later and incubation was continued at 36°C for 30 min. Sections incubated in morphine-free medium served as the control. The results were expressed in specific radioactivity (counts per minute×mg wet weight). Evaluation of the absolute and relative incorporation of the label in RNA was described in [2]. The significance of differences was calculated using Student's *t* test.

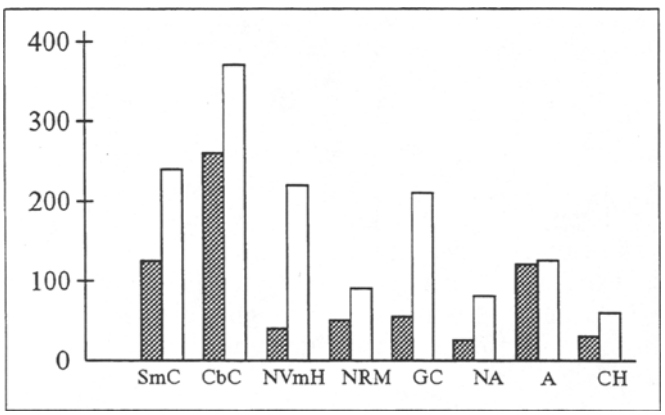

Fig. 2. ^{3}H–uridine incorporation in total RNA from nerve cells of different CNS structures of prone rats.

RESULTS

The results obtained attest to a variable transcription activity in the nerve cells of different CNS structures (Table 1). High control values were recorded for SmC of both groups, for CbC, and A of prone rats and for NA of resistant rats. The label incorporation in the SmC, CbC, NA, GC, and A was different in the control and experimental groups. This may confirm the genetic heterogeneity of the studied rats. Our results also corroborate the different sensitivity of these animals to morphine. The preparation induced an increase in both the absolute and the relative incorporation of ^{3}H-uridine in total RNA, the increment being much greater in resistant rats. In these animals a potentiating effect of morphine was elicited in all structures, the maximum label incorporation being recorded for NRM and GC, structures belonging to the endogenous nociceptive system (33- and 17-fold, respectively), and for A and CH, structures inolved in the manifestation of emotional reactions to pain (Fig. 1).

The mechanism of the effect of morphine on transcription activity is obscure [1]. The morphine receptors of the plasma membrane may be involved in signal transduction into the cell; however, the possibility that receptors also exist in the chromatin cannot be excluded [1,9]. The potentiating effect of morphine on the CbC, a structure which is practically devoid of opiate receptors, supports the latter hypothesis. If one assumes that morphine alters the transcription activity of the morphine-sensitive DNA sites [1], the effect observed in resistant animals may be indicative of activation of these sites. In nonresistant rats statistically significant changes were observed in the structures conveying pain signals - SmC, NA, GC, and NVmH (Fig. 2). Presum-

TABLE 1. Relative Incorporation of ^3H-Uridine in Total RNA from Nerve Cells of Different CNS structures of Rats Prone and Resistant to the Development of Drug and Alcohol Addiction ($M \pm m$)

Group	CNS structure							
	SmC	CbC	NVmH	NRM	NA	DG	A	SH
				Resistant				
Control	471±229.1	80±15.8	57±9.4	18±3.2	105±12.3	54±5.9	36±8.5	36±5.1
Exper.	1525±164.9*	603±73.5*	539±116.5*	591±112.3*	452±43.5*	942±201.2*	421±39.9*	579±60.8*
				Prone				
Control	121±25.2	256±45.1	37±9.1	45±12.4	48±6.8	27±9.1	121±46.8	34±12.9
Exper.	239±13.6*	371±35.3	217±52.1*	94±17.2	212±29.8*	86±6.5*	128±58.9	61±9.0

Note. Asterisk indicates values statistically significant at $p<0.05$. The data are presented in cmp/min×mg wet weight.

ably, the brain structures of nonresistant rats which did not respond to morphine have small numbers of morphine-sensitive sites or no such sites at all (NRM, GC, and the limbic system structures).

The morphine-induced changes in transcription activity are of a compensatory-adaptive nature. For example, the formation of specific types of RNA capable of binding morphine is quite possible; these RNA may prevent the development of cytophysiological effects of the preparation [7,8]. The rate of development of tolerance for and dependence on morphine should be much lower in animals in which the response of the transcription apparatus is accomplished in the above manner.

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