DOPA AND DOPAMINE LEVELS IN THE HYPOTHALAMUS AND BRAIN STEM OF RATS WITH EXPERIMENTAL GASTRIC ULCER TREATED BY ACUPUNCTURE

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Several studies of the neurochemical mechanisms of cortico-visceral disturbances have been undertaken [2, 4, 5]. We know that catecholaminergic systems of the brain play an essential role in acupuncture (AP) processes [1, 8, 9, 11]. Accordingly an attempt was made to study concentrations of certain catecholamines, namely dopa and dopamine (DA), in autonomic brain regions (hypothalamus and brain stem) of rats with experimental gastric ulcers, under treatment with a course of AP.

EXPERIMENTAL METHOD

Experiments were carried out on 90 male albino rats weighing 190-220 g. The animals as a whole were divided into five groups. Group 1 (control) consists of intact animals. In the rats of groups 2, 3, and 4 an experimental gastric ulcer (EGU) was induced by mechanical irritation of the pyloroduodenal region with Pean's forceps for 10 min [3]. Rats of group 5 underwent a mock operation. Animals of groups 3 and 4 started a course of AP, 24 h after the operation, by insertion of steel needles to a depth of 1-2 mm at symmetriical Ho-Ku points for 20 min [10]. AP was given once a day. The course consisted of 10 sessions. Mock AP was carried out on the rats of group 4, needles being inserted into skin zones of the lower third of the limbs where there are no AP points, for the same period of time.

Six animals from each experimental group were decapitated at the end of the 1st, 3rd, and 10th days of the experiments and the hypothalamus and brain stem was removed in the cold. Weighed samples were kept at −25°C for 2-3 days. Concentrations of dopa and DA were determined spectrofluorometrically [7]. Development of the pathological process on the gastric mucosa was monitored macro- and microscopically. The results were subjected to unifactorial dispersion analysis and the significance of differences between the control and experimental groups was assessed by the value of Dunnett's coefficient, whereas the significance of differences between parameters of the experimental groups was determined by Duncan's method [6].

EXPERIMENTAL RESULTS

Data on dopa and DA levels in the hypothalamus and brain stem in the control and experimental groups are given in Table 1.

The dopa level in animals with EGU 24 h after the operation and after one session of AP (group 3) showed an increase of 45% compared with the control, whereas in rats undergoing the mock operation the dopa level under the same conditions was reduced by 30%. This parameter did not change significantly in the other groups. However, dispersion analysis revealed no significant differences compared with the control ($F_{4,25} = 2.2$; $p > 0.05$), which can be regarded as the existence of a tendency for the parameter tested to change as a result of the experimental procedures. Meanwhile, on the basis of postdispersion analysis of the data on the dopa concentration in the experimental groups, significant differences were established between them ($F_{3,2} = 3.5$; $p < 0.05$). The dopa level in the hypothalamus of the rats of group 3 was about twice as high as in the rats of group 5 ($p_{3-5} < 0.01$).

The dopa concentration in the brain stem of rats with EGU after a single session of AP (group 3) showed an increase of 7.2 times ($p < 0.005$) compared with the control. In other

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TABLE 1. Effect of AP on Dopa and DA Levels in Hypothalamus and Brain Stem of Rats with EGU (in nmoles/g tissue)

Catecholamines	Time, days	Groups				
		1 (control)	2 (EGU)	3 (EGU + AP)	4 (EGU + mock AP)	5 (mock operation + AP)
Hypothalamus						
Dopa	1	0,20±0,05	0,23±0,02	0,29±0,05 $p_{3-5}<0,01$	0,23±0,01*	0,14±0,03
	3		0,15±0,02 $p_{2-3}<0,01$	0,33±0,04* $p_{3-4}<0,001$ $p_{3-5}<0,001$	0,13±0,01	0,11±0,01
	10		0,08±0,01*	0,08±0,02*	0,06±0,02*	0,07±0,01*
DA	1	0,71±0,20	1,86±0,44*	1,36±0,08	1,94±0,06*	1,58±0,15*
	3		0,79±0,18 $p_{2-3}<0,005$	1,70±0,26* $p_{3-4}<0,005$ $p_{3-5}<0,001$	0,72±0,05	0,61±0,04
	10		0,55±0,05 $p_{2-4}<0,05$	0,74±0,19 $p_{3-4}<0,005$	0,24±0,05* $p_{4-5}<0,005$	0,80±0,03
Brain stem						
Dopa	1	0,04±0,009	0,11±0,02 $p_{2-3}<0,005$	0,29±0,06* $p_{3-4}<0,005$ $p_{3-5}<0,001$	0,11±0,006	0,06±0,008
	3		0,07±0,02 $p_{2-3}<0,001$	0,23±0,02* $p_{3-4}<0,001$ $p_{3-5}<0,001$	0,09±0,02	0,04±0,004
	10		0,04±0,002 $p_{2-4}<0,05$	0,05±0,01 $p_{3-4}<0,05$	0,07±0,006* $p_{4-5}<0,005$	0,035±0,004
DA	1	0,70±0,04	1,0±0,16	1,15±0,24*	0,79±0,32	0,82±0,07
	3		0,49±0,10 $p_{2-3}<0,05$	1,13±0,28 $p_{3-4}<0,05$ $p_{3-5}<0,05$	0,58±0,03	0,60±0,05
	10		0,39±0,04	0,62±0,20 $p_{3-4}<0,01$	0,19±0,02* $p_{4-5}<0,01$	0,63±0,02

Legend. Asterisk indicates significant differences compared with control (Dunnett's test), p) the same, compared with corresponding columns (Duncan's test).

experimental groups, although changes were noted, they were not significant, but at the same time, they differed significantly from the value of this parameter in group 3.

At the end of the 1st day of the experiments the DA concentration in the hypothalamus of the animals of groups 2, 4, and 5 was significantly increased by 2-3 times ($p < 0.025$) compared with the control; in rats with EGU (group 2) and with EGU and undergoing mock AP (group 4), these changes were most significant and almost identical. Mock AP evidently does not cause a significant change in the DA level in rats with experimental gastric ulcer.

The DA level in the hypothalamus of animals undergoing true AP and EGU also was twice as high as in the control, but much lower than the corresponding parameters in the other groups. Dispersion and postdispersion analysis revealed no significant differences in this case.

The DA concentration in the brain stem of all experimental animals at the end of the first day of the experimetnal programs was higher than in the control but the increase in this parameter was significant only in the rats of group 3 (by 64% above the control, $p < 0.05$). Postdispersion analysis revealed no significant differences between the parameters at this stage of the experiments.

In the animals of groups 2, 3, and 4, 24 h after the beginning of the experiments, an abundant hemorrhagic effusion was found macroscopically in the lumen of the stomach, with thinning of its membranes, extensive hemorrhages and defects of the mucosa. The macroscopic picture at this time in all the above-mentioned animals likewise was identical and corresponded to an acute inflammatory process around the ulcer.

Toward the end of the 3rd day of the experiments, the dopa level in the hypothalamus of the animals of groups 2, 4, and 5 was lower than in the control, whereas in group 3 (EGU + AP) the dopa level in this brain structure remained significantly higher than in the control (by 68%, $p < 0.025$). Postdispersion analysis confirmed that this parameter was sig-

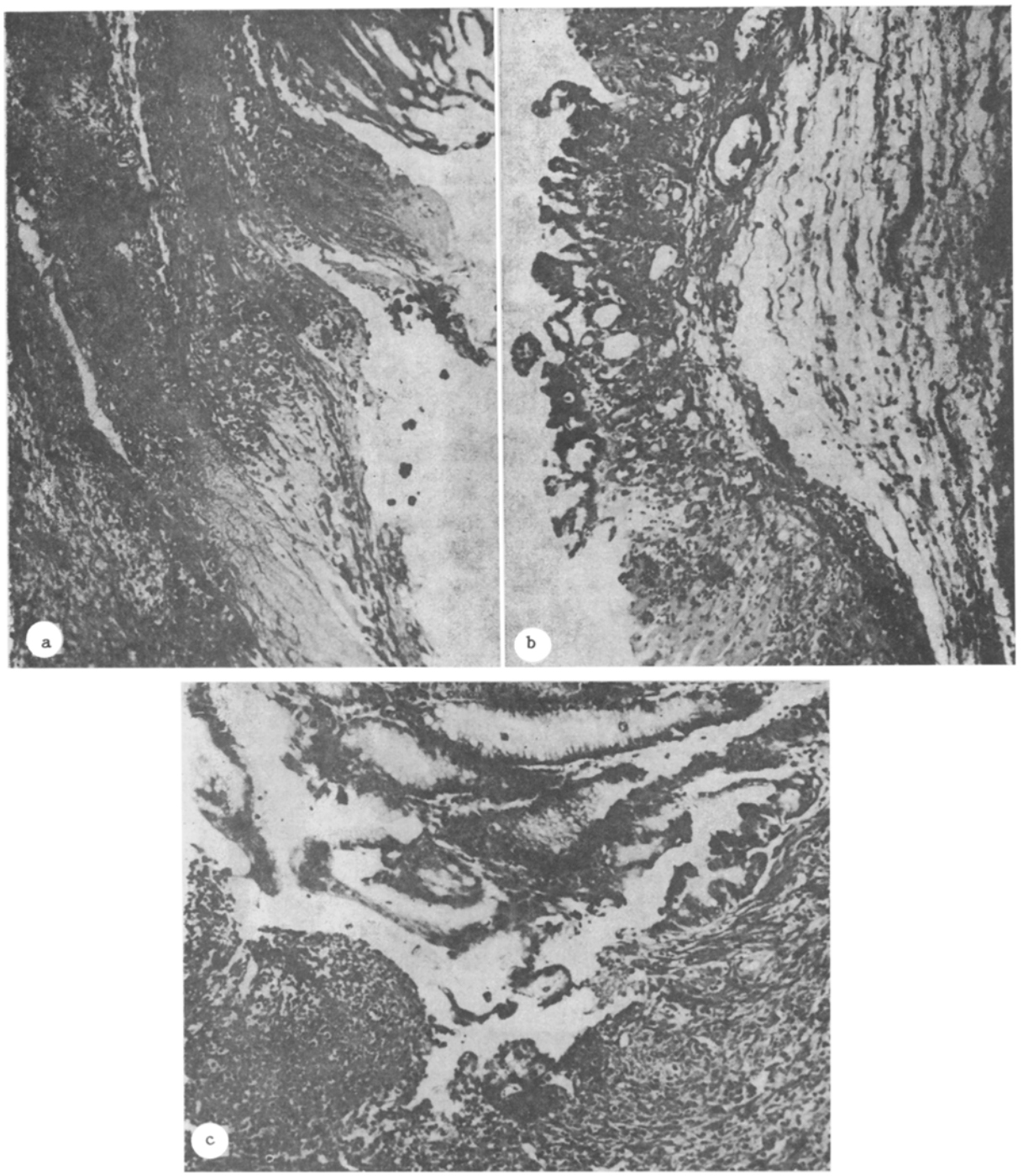

Fig. 1. State of gastric mucosa of rats on 3rd day of experiments. Hematoxylin and eosin. a) EGU (56×), b) EGU + AP (56×), c) EGU + mock AP (140×).

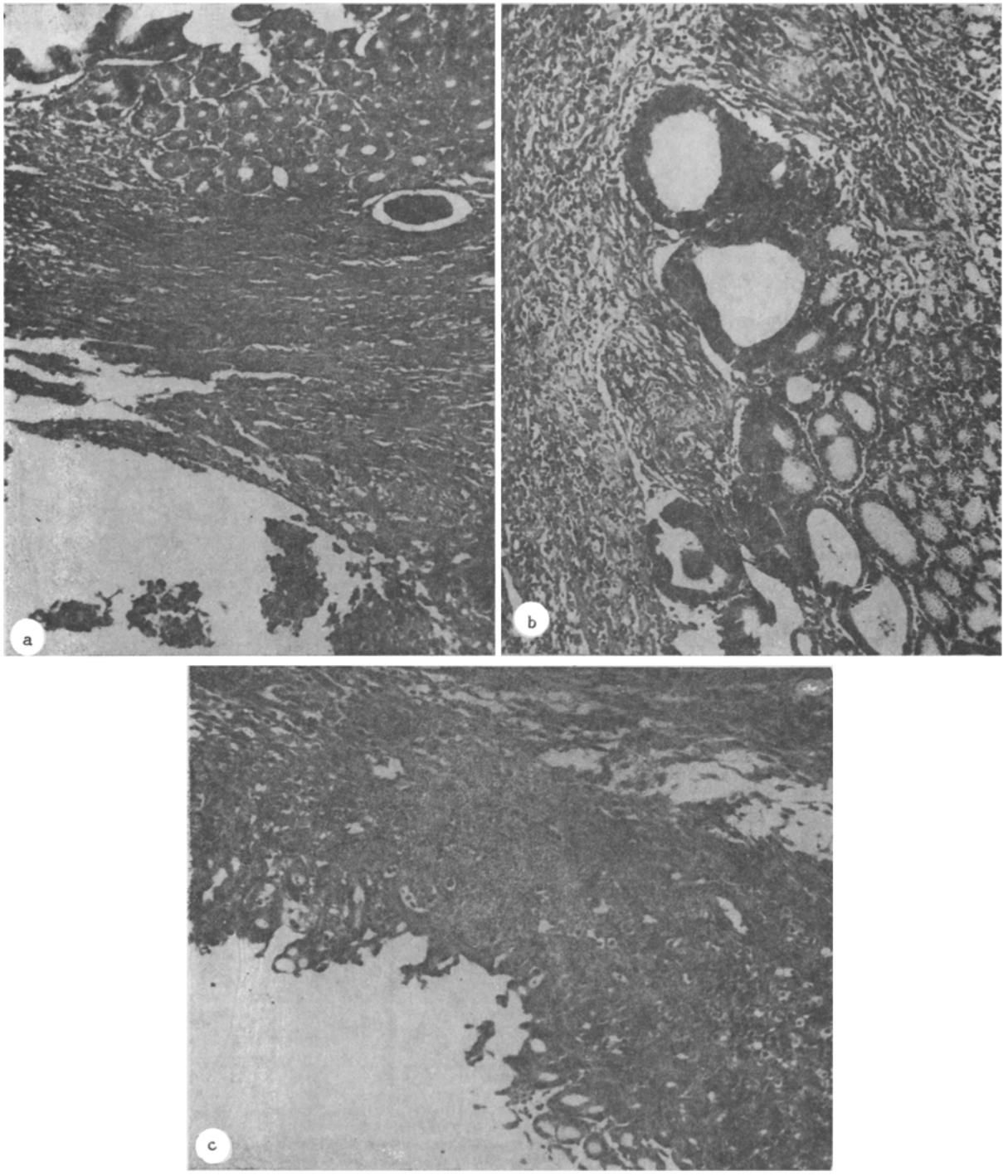

Fig. 2 State of gastric mucosa of rats on 10th day of experiments. Hematoxylin and eosin. a) EGU (56×), b) EGU + AP (140×), c) EGU + mock AP (56×).

nificantly higher in rats with EGU after three sessions of AP than in rats of the other experimental groups ($F_{3,2} = 17.95$, $p < 0.001$).

The dopa concentration in the brain stem of the animals of groups 2, 3, and 4 still remained higher than in the control at this period and in rats with EGU and treated by AP (group 3), moreover, this parameter reached its highest value (6 times higher than in the control, $p < 0.005$). Postdispersion analysis showed that the dopa level in the brain stem in the rats of group 3 was 2.5 times higher ($p < 0.001$) than in the rats of group 4, receiving mock AP, and 3.5 times higher ($p < 0.001$) than in rats with EGU (group 2). Consequently, AP at active points of the skin, in animals with experimental gastric ulcer, has the most significant influence on the dopa levels in the various brain formations.

The DA concentration in the hypothalamus of the rats of group 3 after 3 days of experiments was 2.5 times higher ($p < 0.05$) than in the control. In animals of the other groups this parameter reverted to the control level at this period, but as postdispersion analysis showed, these data differed from the value of the parameter in group 3 ($F_{3,2} = 8.77$, $p < 0.005$).

After 3 days the DA level in the brain stem was lower in the animals of groups 2-5 than in the control and than the initial data on the 1st day of the experiments. Although dispersion analysis did not give reliable results, postdispersion analysis showed that the DA concentration in the brain stem of rats with EGU after three sessions of AP was significantly (2-2.5 times) higher ($p < 0.05$) than the corresponding parameter in animals of the other groups.

Microscopic investigation of the gastric mucosa of the rats of group 2 toward the end of the 3rd day of the experiments revealed large areas of necrosis with inflammatory changes (Fig. 1a). After three sessions of AP, given to rats with EGU (group 3), islands of regeneration and partial proliferation appeared in the ulcer defect (Fig. 1b). Regeneration of the ulcer defect after mock AP (group 4) was weak (Fig. 1c).

Toward the end of the experimental programs (on the 10th day) the dopa level in the hypothalamus of the animals of groups 2-5 was approximately the same, and was 37-40% lower than in the control ($p < 0.01$); no purpose could therefore be served by postdispersion analysis.

The dopa level in the brain stem of animals of all groups was lower than this same parameter on the 1st and 3rd days, and was close to the control value. Only in rats of groups 3 and 4 was the dopa concentration in this part of the brain a little higher than in the control, and it differed significantly, according to the results of postdispersion analysis, from the parameters studied in animals of the other groups.

By the end of the experiments the DA concentration in the hypothalamus and brain stem of the rats of groups 2 and 4 had fallen below the control value. Ten sessions of AP in rats both with EGU and undergoing the mock operation led to normalization of the DA level in the structures tested, but dispersion analysis did not confirm the significance of the results ($F_{4,25} = 3.07$, $p > 0.05$).

Microscopic data on investigation of the gastric mucosa of rats on the 10th day of the experiments (10 days of EGU; group 2) revealed a large area of deep necrosis, surrounded by diffuse leukocytic infiltration (Fig. 2a); in the rats of group 3 the ulcer defect was almost completely covered with epithelium, and differentiation of glandular structures was observed (Fig. 2b); after mock AP (group 4) the defect in the mucosa was only partially covered by epithelium, and regeneration proceeded slowly.

Thus AP introduces significant corrections into the distribution of dopa and DA in the autonomic centers of the brain in animals with experimental gastric ulcer.

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GLUCONEOGENETIC EFFECT OF PROSTAGLANDIN $F_{2\alpha}$ UNDER NORMAL CONDITIONS AND IN MYOCARDIAL INFARCTION

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Biological and physiological aspects of the action of prostaglandins (PG) under normal and pathological conditions are widely familiar [1, 8]. Studies in the field of cardiology have been particularly numerous [2, 6, 9, 10]. It is not disputed that the differences in the action of PG of different classes may be ultimately due to changes in metabolism. However, the metabolic action of PG, especially at the whole body level, remains virtually unstudied.

The aim of this investigation was to study changes in gluconeogenesis in rats with myocardial infarction (MI) by comparison with normal rats. Gluconeogenesis is the resultant of major components of metabolism and it undergoes significant changes in MI [4].

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 232 g. The animals were divided into two groups. Animals of group 1 received no PG, those of group 2 received $PGF_{2\alpha}$. Both groups 1 and 2 included normal rats (control) and rats with MI (3rd, 10th, and 20th day after injection of $PGF_{2\alpha}$ and ligation of the coronary artery).

To discover the dose of PG, the preparation was injected into the caudal vein of rats in doses of 25, 50, or 100 μg/kg body weight. The glucose concentration was then determined in their peripheral blood after 30 sec, 1, 3, 5, 10, and 30 min, and 1, 2, 3, 4,5, and 24 h. The greatest rise of the rats' blood glucose level occurred 5 min after injection of $PGF_{2\alpha}$ in a dose of 50 μg/kg. This time and dose were working values and were used to study the metabolic action of PG. The rats were starved beforehand for 24 h. MI was induced by the method in [5], and its presence was monitored histologically and electrocardiographically.

Concentrations of glucose and lactate in the blood were determined by enzymic methods, pyruvate by a modified Umbreit's method, urea with the help of diacetylmonooxime, ammonia, and glutamine [7]. The glycogen concentration was determined in the liver and heart and skeletal muscles, and activity of the two key enzymes of gluconeogenesis, namely glucose-6-phosphatase (G6Pase) and fructose-1,6-diphosphatase (F-1,6-DPase) was determined in tissues of the liver and renal cortex by methdos in [11, 12]. Protein was determined by Lowry's method. The experimental results were subjected to statistical analysis by "Yamaha" computer.

EXPERIMENTAL RESULTS

After intravenous injection of $PGF_{2\alpha}$ the blood glucose level of the normal rats showed a statistically significant increase ($p < 0.02$) but the lactate and pyruvate levels rose by 25 and 18% respectively (Table 1). Meanwhile the blood urea of the rats rose by 2.44 times, and glutamine by 1.24 times, whereas the ammonia concentration showed a tendency to fall ($p > 0.05$). $PGF_{2\alpha}$ probably stimulates glucose synthesis in normal rats from noncarbohydrate, mainly

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