

# EFFECT OF COCARBOXYLASE ON TONE OF THE INTRACRANIAL AND EXTRACRANIAL VESSELS AND ON THE SYSTEMIC ARTERIAL PRESSURE

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When injected intravenously and intra-arterially, cocarboxylase lowers the tone of the intracranial and extracranial vessels.

The beneficial effect of cocarboxylase in diseases of the cardiovascular system has been demonstrated by several workers [1, 5, 7, 8]. However, no information on the effect of this compound on the cerebral hemodynamics could be found in the accessible literature.

This paper describes the results of an experimental study of the effect of cocarboxylase on tone of the intracranial and extracranial vessels, and on the venous, intracranial, and systemic arterial pressure.

## EXPERIMENTAL METHOD

Acute experiments were carried out on 23 cats weighing 2-3.5 kg under chloralose-urethane (0.04 and 0.6 g/kg, respectively) anesthesia. A preliminary intraperitoneal injection of hexobarbital (0.1 g/kg) was given. The tone of the intracranial and extracranial vessels was recorded by an autoperfusion method [6] using a two-channel resistograph, connected by cannulas to the carotid arteries. The corresponding cranial vessels were ligated.\*

The systemic arterial pressure was recorded in the common carotid artery by a mercury manometer. The venous pressure was measured by a water manometer in the external jugular vein, after appropriate

\*The method of ligation of the vessels is described in detail in the paper "Effect of pipolphen on tone of the intracranial and extracranial vessels" [Byull. Éksperim. Biol. i Med., No. 6, 54 (1970)].

TABLE 1. Effect of Cocarboxylase on Tone of Intracranial and Extracranial Vessels and on Systemic Arterial Pressure (in percent of initial level)

Dose of co-carboxylase, (mg/kg)	No. of expts.	Change in resistance of vessels		Change in arterial pressure
		intracranial	extracranial	
Intravenous injection of cocarboxylase				
3—5	6	$-14 \pm 6.9$ $P = 0,07$	$-14 \pm 2,5$ $P < 0,001$	$-18 \pm 4$ $P = 0,001$
10	6	$-17 \pm 4$ $P = 0,002$	$-21 \pm 3,4$ $P < 0,001$	$-19 \pm 3,7$ $P = 0,001$
Intracarotid injection of cocarboxylase				
0,3—1	4	$-12 \pm 1,6$ $P < 0,001$	$-23 \pm 3$ $P < 0,001$	No significant changes

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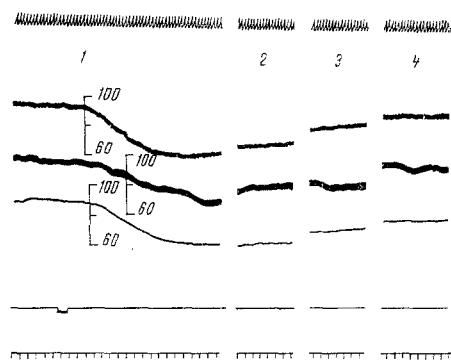


Fig. 1

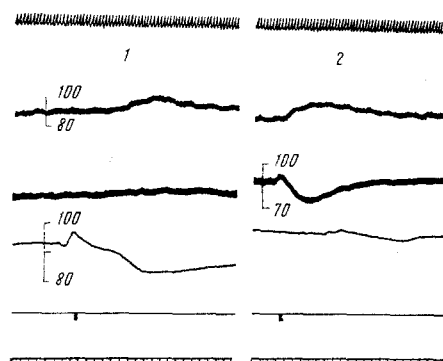


Fig. 2

Fig. 1. Changes in tone of cranial vessels following intravenous injection of cocarboxylase. From top to bottom: respiration (controlled); systemic arterial pressure; resistogram of intracranial vessels; resistogram of extracranial vessels; marker of injection of compound (10 mg/kg); time marker 5 sec. 1) Before and after injection of cocarboxylase; 2, 3, 4) 5, 10, and 30 min, respectively, after injection of cocarboxylase.

Fig. 2. Changes in tone of cranial vessels following intra-arterial injection of cocarboxylase. 1) Compound (1 mg/kg) injected into system of extracranial vessels; 2) compound (in same dose) injected into system of intracranial vessels. From top to bottom: legend as in Fig. 1.

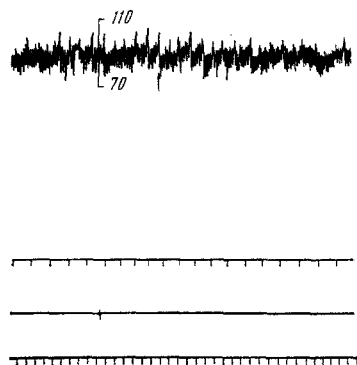


Fig. 3. Changes in volume velocity of blood in vertebro-basilar system following injection of cocarboxylase into lumen of vertebral artery in dogs. From top to bottom: systemic arterial pressure; blood flow (distance between strokes 3 mm); marker of injection of compound; time marker 5 sec.

In one experiment the tone of the vessels was increased by 6%. In all experiments the tone of the extracranial vessels was reduced on the average by  $14 \pm 2.5\%$  for between 10 and 30 min. Under the influence of these doses of cocarboxylase, the systemic arterial pressure was reduced on the average by  $18 \pm 4\%$  for between 10 and 20 min.

Following intravenous injection of cocarboxylase in a dose of 10 mg/kg, the tone of the intracranial vessels was reduced by  $17 \pm 4\%$ , that of the extracranial vessels was reduced by  $21 \pm 3.4\%$ , and the systemic arterial pressure was lowered by  $19 \pm 3.7\%$  (Fig. 1). The action of cocarboxylase began immediately after its injection, reached a maximum after 3-4 min, and after 20-30 min the initial values of the tone of the

ligation of its branches. The jugular vein was tied in the region of the neck, and a catheter introduced into its lumen in the cranial direction. In some experiments the catheter was introduced into the venous sinus through a burr-hole in the skull.

To measure the intracranial pressure, a hole was drilled in the parietal bone and a cannula connected to a water mercury fitted securely into it. The venous and intracranial pressures were determined visually from the readings of the manometers. Clotting of the blood was prevented by intravenous injection of heparin. All the experiments were carried out under controlled respiration using a suitable apparatus [3].

Cocarboxylase was injected intravenously (1-2.5% solution) in doses of 3-10 mg/kg and intra-arterially in doses of 0.3-1 mg/kg. Working solutions of cocarboxylase were prepared before the experiment from the official ampule-sealed preparation (in powder form), manufactured in Poland.

## EXPERIMENTAL RESULTS

Intravenous injection of cocarboxylase in doses of 3-5 mg/kg in 5 of the 6 experiments reduced the tone of the intracranial vessels by 6-50% for periods of between 3 and 20 min.

cerebral vessels and systemic arterial pressure were usually restored. In some experiments the tone of the extracranial vessels remained below its initial level for 1 h.

The reaction of the vessels to cocarboxylase was evidently due to the direct effect of the compound on neuromuscular elements in the vessel walls. This is confirmed to some extent by the experiments in which cocarboxylase was injected into the carotid arteries in doses of 0.3-1 mg/kg. Injection of cocarboxylase into the system of intracranial vessels lowered their tone by  $12 \pm 1.6\%$ , while injection of the same doses of the compound into the system of extracranial vessels of the head lowered their tone by  $28 \pm 3\%$ . The reaction affected only those vessels into which the compound was directly injected (Fig. 2). This reaction to cocarboxylase persisted after denervation of the carotid sinuses. The combined results of the experiments are given in Table 1.

The effect of cocarboxylase on the venous and intracranial pressure was investigated in a separate series of experiments. The results of these experiments showed that intravenous injection of cocarboxylase in a dose of 10 mg/kg lowered the pressure in the venous system of the brain by  $15 \pm 5.4\%$  ( $P=0.016$ ). In most experiments this effect continued for 10-20 min, and it exceeded 60 min only in a few cases. The intracranial pressure in three of seven experiments was lowered by 5-17%, and in the rest there were no significant changes.

Besides the experiments on cats, other experiments were carried out on dogs in which the blood flow was recorded in the vertebral arteries [4] by means of a flowmeter [2]. Intra-arterial injection (into the lumen of the vertebral artery) of cocarboxylase caused a definite increase in the volume velocity of the blood flow (Fig. 3). Since the systemic arterial pressure was unchanged, this also gives evidence that the reduction in vascular tone was evidently local.

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