

ENDERPIN CONTENT IN THE MYOCARDIUM OF ANIMALS IN
ONTOGENY AND ALCOHOL INTOXICATION

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The writers showed previously [1-3] that endogenous alkaloid-like substances are present in animal tissues. It was subsequently demonstrated that the level of these enderpins (RPI, RP2, RP3) reflects stress states of the body as they affect organs and tissues such as the myocardium, hypothalamus, and adrenals.

In this investigation an attempt was made to explain the function of enderpins from these same standpoints by determining changes in their content in the myocardium of newborn rats (intact animals and rats born from animals which were "hereditary alcoholics") and also in adult rats (intact animals and "hereditary alcoholics").

EXPERIMENTAL METHOD

Experiments were carried out on 110 adult male Wistar rats and on 160 newborn rats of the same line aged 1 day. The hearts of 6-8 young rats from the same litter were pooled. Hearts of adult rats were investigated singly. Isolation and the first stages of purification of the enderpins were carried out in accordance with the method described previously [1]. The enderpin content was determined fluorometrically on a KM-3 chromatogram spectrophotometer (Opton) at an excitation wavelength of 270 nm. For this purpose, in the final stages of purification the enderpins were isolated by chromatography on "Silufol" disks (Cavalier) in the system acetone-carbon tetrachloride-iso-octane-light paraffin-n-propanol (25:25:25:25:50). Enderpins RPI, RP2, and RP3 with electrophoretic mobilities of 0.78, 0.49, and 0.1 respectively, were eluted with a mixture of chloroform and methanol (2:1) and applied as spots 5 mm in diameter on DC Alufolien Kieselgel 66/Kieselguhr F-254 disks (Merck) in the same way as enderpins of known concentration for calibration curves. The results were expressed in μg RPI, RP2, and RP3/g wet weight of tissue. Altogether 810 quantitative determinations of the enderpin content were undertaken.

In the experiment with acute alcohol intoxication, the adult rats were given 40% ethanol *per os* by means of a catheter in a dose of 2 ml/100 g body weight under light ether anesthesia. The animals were killed after 3 h. In the experiment with chronic alcohol poisoning, the rats were given 20% ethanol *ad lib*, instead of water daily for 4 months. To study the effect of alcohol on the enderpin content in the progeny, litters were taken from rats receiving alcohol in five generations. The progeny from intact rats served as the control. The animals were killed by a blow to the head.

EXPERIMENTAL RESULTS

Administration of alcohol to the animals led to an approximately twofold increase in the content of all three types of enderpins whether under chronic or acute experimental conditions (Table 1).

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TABLE 1. Effect of Acute Alcohol Intoxication of Rats on Enderpin Content (in $\mu\text{g/g}$ tissue) in Myocardium ($M \pm m$)

Experimental conditions	RP1		RP2		RP3	
	control	experiment	control	experiment	control	experiment
Acute experiment	29,23 \pm 3,46 (n=17)	60,80 \pm 6,21 (n=10)	11,83 \pm 0,81 (n=17)	20,35 \pm 2,05 (n=10)	23,53 \pm 1,28 (n=17)	36,40 \pm 2,35 (n=10)
Chronic experiment	32,19 \pm 1,46 (n=15)	55,26 \pm 3,81 (n=20)	7,46 \pm 0,32 (n=15)	18,65 \pm 1,26 (n=20)	18,31 \pm 0,92 (n=15)	29,05 \pm 1,87 (n=20)

Legend. Control — intact animals, experiment — animals receiving alcohol. Differences significant at $P < 0.01$. Here and in Tables 2 and 3, number of animals shown in parentheses.

TABLE 2. Effect of Chronic Alcohol Intoxication on Enderpin Level (in $\mu\text{g/g}$ tissue) in Myocardium of Progeny of Rats ($M \pm m$)

RP1		RP2		RP3	
control	experiment	control	experiment	control	experiment
53,95 \pm 5,55 (n=12)	129,88 \pm 15,01 (n=9)	33,44 \pm 3,65 (n=12)	35,42 \pm 3,94 (n=9)	53,95 \pm 5,72 (n=12)	73,32 \pm 15,64 (n=9)
$P < 0,01$		$P > 0,1$		$P > 0,1$	

Legend. Control — intact young rats, experiment — young rats from hereditary "alcoholics."

TABLE 3. Content of Enderpins (in $\mu\text{g/g}$ tissue) in Myocardium of Adult and Young Rats ($M \pm m$)

RP1		RP2		RP3	
control	experiment	control	experiment	control	experiment
32,96 \pm 1,54 (n=50)	53,95 \pm 5,55 (n=12)	9,32 \pm 0,43 (n=50)	33,44 \pm 3,65 (n=12)	20,05 \pm 0,91 (n=50)	53,95 \pm 5,72 (n=12)

Legend. Control — adult rats, experiment — young rats. Differences significant at $P < 0.01$ level.

In the progeny of rats receiving dilute ethanol instead of water for a long period of time this phenomenon also was reproduced. The level of all types of enderpins in the myocardium of these young rats also was raised, but the increase was significant only for RP1 (Table 2). Yet another characteristic fact was noted: The level of all three types of enderpins was higher in the myocardium of the newborn rats than in that of the adult animals. This difference was particularly marked for RP2, for which it was almost fourfold (Table 3).

The results with respect to alcohol intoxication can be explained on the grounds that elevation of the enderpin level in the myocardium under the experimental conditions described is probably an adaptogenic response to a stress factor (alcohol), and a reaction of the same type also was preserved in the progeny of the "rat-alcoholics."

The results of the other series of experiments to determine the enderpin level in the myocardium during ontogeny of the rats suggest that the sharply increased content of these substances in newborn rats is somehow linked with intensive processes of biosynthesis in the early stages of development of the animals. Consequently, the function of the alkaloid-like substances (enderpins) must be regarded not only as adaptogenic in stress situations, but also as responsible for certain biosynthetic processes. The possibility likewise cannot be ruled out that the adaptogenic functions of enderpins are realized by a mechanism of intensification of biosynthetic processes.

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