EFFECT OF PROCAINE ON CONTENT AND NUCLEOTIDE COMPOSITION OF RNA FROM THE LIVER AND CEREBRAL HEMISPHERES AND ON THE RATIO BETWEEN RIBOSOMAL AND TRANSFER RNA IN THE LIVER OF YOUNG RATS

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When injected subcutaneously in a dose of 10 mg/kg body weight, procaine caused an increase in the RNA content in the liver and cerebral hemispheres of young rats. The increase in RNA content was accompanied by changes in the nucleotide composition of the RNA, reflected in a decrease in the base ratio (G + C)/(A + U). Administration of procaine led to an increase mainly in the ribosomal RNA in the liver of young rats.

Histochemical investigations [1, 2] have shown that prolonged subcutaneous injection of small doses of procaine into rabbits leads to an increase in the RNA content in the liver. The writers' previous investigation [5] showed that a single subcutaneous injection of procaine into adult rats causes an increase in the RNA content in the cerebral hemisphere and liver of rats.

In young animals the intensity of nucleic acid synthesis is higher, and for this reason the study of the effect of procaine on the content, nucleotide composition, and relative proportions of the RNA fractions in young animals is particularly interesting. The investigation described below was carried out for this purpose.

EXPERIMENTAL

Young male Wistar albino rats weighing 120-150 g were used. Procaine was injected subcutaneously in a dose of 10 mg/kg body weight in 0.9% NaCl solution. Rats receiving injections of the same volume of 0.9% NaCl solution acted as the control. The animals were decapitated 30 min after the injection of procaine. RNA and DNA were separated and RNA determined quantitatively by the method of Schmidt and Thannhauser in Munro and Fleck's modification [9]. In the final stages the RNA content was determined by a modified Meibaum's method [3]. RNA was isolated for determination of the nucleotide composition by a modified Munro and Fleck's method [9], and after hydrolysis (in 0.3 N KOH at 37°C) for 18 h the nucleotides of the RNA were then separated by the method of Katz and Comb [8] on Dowex 50 × 4, 200-400 mesh, H^+ form.

Total RNA was isolated by Scherrer's method [12] from rat livers and fractionated on calcium phosphate gel [4]. The experimental results were subjected to statistical analysis.

TABLE 1. Effect of Procaine on RNA Content in Cerebral Hemispheres and Liver of Young Rats (in mg% of fresh weight)

Organ	No. of expts.	Control	Expt.	P
		$M \pm m$		
Liver ...	20	569,14±29,69	647,40±16,23	<0,05
Cerebral hemispheres	20	105,87±7,18	146,30±10,10	<0,01

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TABLE 2. Effect of Procaine on RNA Content in Cerebral Hemispheres and Liver of Young Rats (in mg% of fresh weight)

Organ	No. of expts.	UMP	GMP	AMP	CMP	$\frac{G+C}{A+U}$	Purines/ pyrimidines
		$M \pm m$					
Liver	20						
expt.		25,74±0,62	17,82±0,66	18,09±0,39	38,28±1,00	1,28±0,03	0,57±0,02
control		25,47±1,25	23,02±0,83	15,97±0,70	35,54±0,93	1,43±0,03	0,62±0,04
P		>0,5	<0,001	<0,02	<0,1	<0,01	>0,2
Cerebral hemispheres	20						
expt.		33,72±2,23	11,88±1,04	19,57±1,19	34,72±1,88	0,88±0,04	0,46±0,02
control		27,61±1,85	15,53±1,38	20,33±1,09	36,51±2,05	1,08±0,08	0,57±0,04
P		<0,05	<0,05	>0,5	>0,5	<0,05	<0,05

EXPERIMENTAL RESULTS AND DISCUSSION

The results (Table 1) show a statistically significant increase in the RNA content in the cerebral hemispheres and liver of the young rats after a single dose of procaine.

It will be clear that the young rats are far more sensitive to the action of procaine than adult rats [5].

Besides an increase in the RNA content, after administration of procaine qualitative changes were found in the RNA, with changes in the molar proportions of nucleotides and a decrease in the base ratio (G + C)/(A + U) (Table 2). The results obtained for the base ratio in the control rats were in agreement with those given in the literature [4, 6, 7, 10].

Subcutaneous injection of procaine caused a significant decrease in the molar percentage of GMP and an increase in that of AMP in the liver RNA, and these changes were accompanied by a significant decrease in the base ratio (G + C)/(A + U). The molar percentage of UMP was increased and that of GMP was reduced in the cerebral hemispheres, and this also led to a decrease in the base ratio.

In the modern view ribosomal RNA (rRNA) has a lower base ratio than transfer RNA (tRNA) [4, 11]. It can therefore be postulated that after the administration of procaine there is a preferential increase in the rRNA content in the brain and liver tissues of rats.

To test this hypothesis, fractions of liver rRNA and tRNA were fractionated on calcium phosphate gel and the relative contents of the fractions were determined under normal conditions and after administration of procaine. After fractionation in a phosphate buffer gradient (pH 6.8) two clearly defined heterogeneous peaks corresponding to RNA were obtained [4]. Whereas in the control the ratio of tRNA/rRNA was 1.22, after administration of procaine the ratio fell significantly ($P < 0.05$) to 0.98, indicating an increase in the fraction of rRNA and thereby confirming the hypothesis that the ribosomal fraction of RNA is predominantly increased after administration of procaine.

It is difficult at present to give an acceptable explanation of the observed increase in RNA biosynthesis under the influence of procaine. One probable explanation could be that p-aminobenzoic acid formed during the breakdown of procaine participates in nucleic acid biosynthesis. The qualitative change in the RNA composition is evidence in support of the influence of procaine on transcription.

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