THE MECHANISM OF THE ACTION OF PARA-AMINOBENZOIC ACID ON THE ORGANISM

REPORT 1. THE EFFECT OF ADMINISTRATION OF PARA-AMINOBENZOIC ACID ON THE GAS EXCHANGE AND TEMPERATURE OF THE BODY

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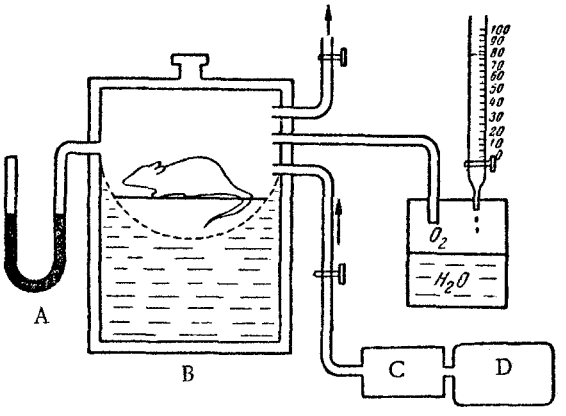
Previous reports [3, 4]have shown that novocaine and para-aminobenzoic acid possess similar actions on the organism, by increasing the chances of survival of albino rats subjected to anoxia. The mechanism of this phenomenon has not been clearly elucidated, although it is evident that it is based mainly on the general action of novocaine and para-aminobenzoic acid (PABA) on the body.

Reports in the literature of the effect of novocaine on metabolism are numerous [5-12], and most workers note a lowering of the body temperature of experimental animals and of their oxygen demand. It is possible that PABA has a similar general action. Its action on certain respiratory enzymes [1] confirms this suggestion.

The study of the effect of PABA on the body temperature and gas exchange is of considerable interest to the elucidation of the action of novocaine and PABA, especially in anoxia.

EXPERIMENTAL METHOD

The rats used in the experiment consumed oxygen in a specially constructed chamber (see figure). The animals were kept in an exsiccator with a capacity of 3 liters, two-fifths of which was filled with soda lime to absorb the expired carbon dioxide, while the remaining volume was left free. The oxygen consumed by the animals led to a decrease in the pressure inside the chamber, which was recorded by a water manometer. Under the control of the manometer, the oxygen consumed by the animals was replaced by pure oxygen added in measured amounts from a reservoir. In constant temperature conditions, the volume of oxygen utilized in equalizing the pressure inside the chamber corresponded to the oxygen absorbed. The absorption of carbon dioxide in the chamber was checked by means of a Haldene's apparatus and its concentration did not exceed 0.1%. In our experimental conditions the chamber was ventilated with a gas mixture containing 5% oxygen or air.



Scheme of the experiment to determine the oxygen absorbed by the animals. A) Water manometer; B) soda lime; C) pressure reducer; D) mixture poor in oxygen.

The body temperature was measured in the rectum. The oxygen consumption was measured in animals receiving for 24 h a diet containing 200 mg PABA/100 g [4].

The action of PABA was also studied in eight healthy human subjects aged from 21 to 40 yr. The Douglas–Haldene method was used to determine the basal metabolism and the resting metabolism, the former during admission to hospital, the latter in the laboratory. For control purposes the gas exchange was also determined at rest during the same time period. Altogether 70 observations were made in different conditions. The PABA used in these investigations was prepared at the Kalinin vitamin factory.

EXPERIMENTAL RESULTS

It is clear from Table 1 that the administration of PABA led to a decrease in the oxygen consumption of the animals, and that this effect was more marked in conditions of oxygen deficiency. The lowering of the oxygen consumption during respiration in a gas mixture poor in oxygen was also observed in the controls, but to a much lesser degree than after administration of PABA. It is evident that the increased resistance of the animals to anoxia after taking PABA was the result of the lowered oxygen demand.

TABLE 1. Effect of PABA on the Oxygen Consumption of Albino Rats with Differences in the Composition of the Inspired Air

Experimental conditions		No. of animals		Mean O_2 consumption by rats (in ml/h)
		used in expt.	survived	
Breathing atmospheric air	with administration of PABA	20	20	415 ± 2.3
	control	20	20	498 1 6.0
Breathing a gas mixture containing 5% O_2	with administration of PABA	20	17	387 ± 5.2*
	control	20	13	237 ± 5.0*

*Oxygen consumption only in the surviving rats.

TABLE 2. Effect of PABA on the Body Temperature of Rats

Expt. No.	Dose of PABA	Body temperature		Temperature difference	
		before administration	after administration		
	Parenteral injection				
1	20 mg per rat		Rat died		
2	15 " " "	36.8°	33.5°	−3.3°	Mean −1.2°
3	10 " " "	35.5°	35.2°	−0.3°	
4	10 " " "	36.8°	36.2°	−0.6°	
5	10 " " "	36.3°	36°	−0.3°	
6	10 " " "	35.9°	34.4°	−1.5°	
7	10 " " "	35.7°	35.1°	−0.6°	
8	10 " " "	35.2°	34.4°	−0.8°	
9	10 " " "	34.9°	34°	−0.9°	
10	10 " " "	36.8°	36.6°	−0.2°	
11	10 " " "	36 8°	32.4°	−4.3°	
	Given with the food				
12	200 mg/100 g food	35.4°	35.2°	−0.2°	Mean −0.8°
13	The same	36.8°	35.4°	−1.4°	
14	" "	36.2°	35.6°	−0.6°	
15	" "	38.5°	37.5°	−1°	
16	" "	35.3°	34.9°	−0.4°	
17	" "	36.2°	34.8°	−1.4°	

We also observed an effect of PABA on the body temperature, which was measured 1 h after the parenteral administration of the preparation and 24 h after its ingestion with the diet (Table 2).

Hence, the administration of PABA led to a decrease of the gas exchange and the body temperature. Reports in the literature [2, 5-9] suggest that this action of PABA might be due to its effect on the thyroid, causing a decrease

in hormone production [2]. To test this hypothesis we gave one group of animals PABA together with thyroidin in their food. The dose of thyroidin was 1 g/100 g of food, the iodine content of the preparation being 1.7-2.3 mg.

After the combined administration of PABA and thyroidin (Table 3), in only two cases was the body temperature lowered, and in the rest it was either unchanged or raised. This suggests that the thyroid gland is concerned in the mechanism of the effect of PABA on the organism. We were also interested to discover whether PABA had the same action on the basal metabolism in man (Table 4).

TABLE 3. Effect of Simultaneous Administration of PABA and Thyroidin on the Body Temperature of Albino Rats.

Expt. No.	Body temperature		Temperature difference	
	before taking preparations	24 h after taking PABA + thyroidin		
1	36°	34.9°	−1.1°	Mean −+0.6°
2	35.1°	35.6°	+0.5°	
3	35.2°	38°	+2.8°	
4	35.9°	36°	+0.1°	
5	35.2°	35.2°	−	
6	36.3°	37.2°	+0.9°	
7	34.9°	36.1°	+1.2°	
8	37.4°	38.7°	+1.3°	
9	36.9°	36.6°	−0.3°	
10	35.9°	36.1°	+0.2°	

TABLE 4. Effect of PABA on Basal Metabolism in Man

Subject's surname	Dose and mode of administration of PABA	Period of administration of preparation (in days)	Gas exchange	
			before taking PABA (Cal/h)	after taking PABA (Cal/h)
G-v	3 times a day, 200 mg	1	51.2	50.5
P-v	The same	3	51.2	41.5
K-v	" "	3	66.3	52.9
	" "	3	44.8	42
E-a	200 mg daily	10	87.5	56.4
	The same	20	87.5	61.8
	" "	30	87.5	60

TABLE 5. Effect of PABA on the Gas Exchange in Man at Rest, 4 h after Taking the Preparation

Subject's surname	Dose of preparation taken (in g)	Gas exchange	
		before taking preparation (in Cal/h)	after taking preparation (in Cal/h)
Sh-v	0.5	78.8	63.6
U-v	0.5	75.6	73.4
U-v	0.5	67.2	58.2
U-v	0.5	67.8	50.4
Sh-v	1	65.4	51.6
E-a	1	81	57.6
E-a	1	80.4	69.6
V-g	1	90.2	81.8

Administration of PABA in doses from 200 to 600 mg led to a decrease in the basal metabolism, which was clearly apparent on the 3rd-10th day of its administration. This effect was weak during the first 2 days. For this reason, when we studied the effect of PABA on gas exchange at rest, we increased the dose (Table 5).

It may be seen from Table 5 that administration of PABA led to a marked decrease in the gas exchange of the human subjects. It should be noted that in the control experiments the gas exchange either remained unchanged or was increased at this period, probably on account of a diurnal rhythm in the gas exchange, for the first determination was made at 10-11 A. M. and the second at 2-3 P. M.

The mechanism of this effect of PABA on the gas exchange has not been made sufficiently clear. We may postulate that this action is effected through the thyroid, although a direct action of PABA on tissue metabolism is perfectly feasible [1].

SUMMARY

A study was made of the effect exerted by para-aminobenzoic acid on gaseous exchange and body temperature of albino rats. As demonstrated, its administration decreases oxygen uptake; this phenomenon is especially pronounced in animals to which an oxygen-deficient gaseous mixture is given for respiration. Para-aminobenzoic acid administration also leads to a rise in the body temperature. The body temperature is not reduced in combined administration of para-aminobenzoic acid and thyroidin. Para-aminobenzoic acid given in doses of from 0.2 to 1.0 g reducted the BMR and metabolism at rest in healthy persons investigated. The mechanism of this phenomenon requires a further study.

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