ROLE OF PERIPHERAL CHEMOCEPTORS IN RESPONSES OF RATS TO BRIEF AND PROLONGED HYPOXIA

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The role of the carotid sinus chemoceptors in the responses of certain physiological systems of rats, especially the respiratory system, to hypoxic hypoxia was demonstrated experimentally. Deafferentation of the carotid sinus reflexogenic zones and of the portal zones in rats did not abolish but only reduced the degree of the compensatory responses. The oxygen lack in the muscle tissue was greater in the denervated than in the intact animals.

It is generally accepted that arterial chemoceptors are the only source of stimulation of respiration in hypoxemia [1, 2, 11, 12]. A leading role is ascribed to the carotid sinus reflexogenic zones [1]. In most investigations, for instance, the blocking of these zones led to total loss of the ventilatory response of the experimental animals to inhalation of a mixture deficient in oxygen [10]. Admittedly, in some species of animals it was also necessary to block the aortic reflexogenic zone in order to obtain this effect [2].

The role of the peripheral chemoceptors in the regulation of respiration has been studied almost entirely in animals such as dogs, cats, rabbits, and sheep. In rats, however, which are widely used in experiments with changes in the gas composition of the atmosphere, these reflexogenic zones have only rarely been studied [9]. The role of arterial chemoceptors in adaptation to prolonged hypoxia has also been inadequately studied [1, 5].

The method of denervation of the carotid sinus reflexogenic zones was used to investigate their role in responses of the respiratory, cardiovascular, and thermoregulatory systems of rats to acute hypoxia, and also in ensuring an adequate supply of oxygen to the body tissues under these conditions. In addition, some rats were subjected to deafferentation of the aortic reflexogenic zone.

To assess the importance of these chemoceptors in adaptation of the animal to prolonged hypoxia, denervated animals were exposed for 1 month to an atmosphere deficient in oxygen. The role of the arterial chemoceptors in adaptation to oxygen deficiency was judged from the ventilatory responses of the experimental animals to acute hypoxia during inhalation of air.

EXPERIMENTAL METHOD

Male albino rats weighing 200-300 g were used. Bilateral surgical denervation of the carotid sinus chemoceptors was carried out on some of the animals. The operation was performed under an operating microscope (magnification 10-20 times), and all nerve fibers leaving the region of bifurcation of the common carotid artery were removed, after which 10% phenol solution was applied to that region. The operative technique has been described earlier [6]. Deafferentation of the aortic zone was carried out by division of the corresponding nerve fibers [13]. Similar operations, but without division of the nerves or treatment of the arterial walls, was carried out on the rats of the control group. The response of the respiration of the

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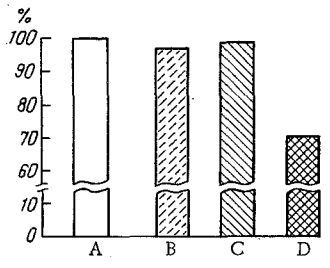

Fig. 1

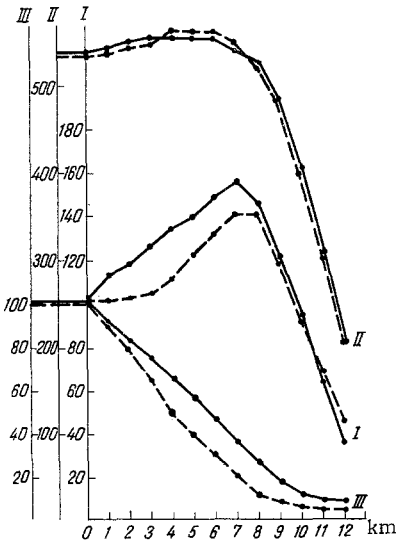

Fig. 2

Fig. 1. Ventilatory responses to inhalation of mixtures with 11% oxygen in intact rats (A) and in rats with blocked reflexogenic zones: carotid sinus (B), aortic (C), and carotid sinus and aortic combined (D), in percent of increase in ventilation of intact rats during inhalation of the same mixture.

Fig. 2. Dynamics of some indices in intact (continuous line) and denervated (broken line) rats during "elevation" to an altitude of 12,000 m: I) respiration rate (per minute); II) heart rate (per minute); III) pO_2 in thigh muscle (in percent of initial level).

experimental animals to hypoxia was studied by means of an apparatus of the authors' own design [7]. The volume of the pulmonary ventilation was measured during inhalation of the hypoxic mixture for 1 min and compared with that measured during inhalation of air.

In other cases hypoxia was induced by "elevating" the animals in a pressure chamber, while recording simultaneously their respiration rate by means of a carbon pick-up, the heart rate by an electrocardiographic method, the rectal temperature by means of an electrothermometer (Sanei), and the oxygen tension in the thigh muscle by a polarographic method [8]. Altogether 5 series of experiments were carried out on 72 intact and 45 denervated rats.

EXPERIMENTAL RESULTS

The results showed that in intact animals breathing a hypoxic mixture (11% O_2, pO_2 83.6 mm Hg) the ventilation increased significantly by 20.3% compared with its level while breathing air.

In animals after bilateral carotid sinus denervation the response to the hypoxic mixture showed no significant quantitative change. The same effect was found with rats after deafferentation of the aortic zone. However, if both these chemoceptor zones were blocked simultaneously, there was some decrease in the ventilatory response to acute hypoxia (Fig. 1).

Increasing hypoxia was induced by "elevating" the animals in a pressure chamber to an altitude of 12,000 m (pO_2 =30 mm Hg) at the rate of 25 m/sec, which was followed by a rapid "descent."

In the intact animals, the "elevation" was accompanied by a marked increase in respiration rate at an altitude of 1,000-7,000 m (Fig. 2). The respiration rate in the denervated rats began to rise later and was 15-25% lower than in the intact animals. Moderate hypoxia also induced an increase in the heart rate. No significant differences were found between the heart rates of the intact and denervated rats. Extreme degrees of hypoxia (over 7,000 m) led to sharp inhibition of respiration and of cardiac activity in both the intact and the denervated animals.

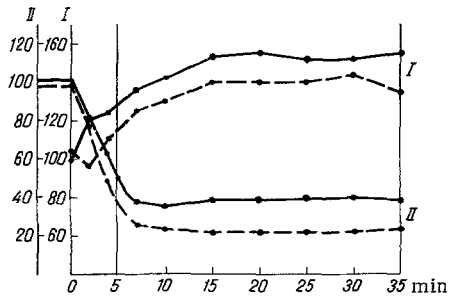

Fig. 3. Dynamics of some indices in intact (continuous line) and denervated (broken line) rats during "elevation" and during a stay of 30 min at an altitude of 5,000 m: 1) respiration rate (per minute); 2) pO_2 in thigh muscle.

During increasing hypoxia the decrease in pO_2 in the thigh muscle was more marked in the animals with blocked carotid sinus chemoceptors than in the intact rats. The difference was statistically significant at altitudes of 4,000-8,000 m, while at higher altitudes it tended to disappear. The decrease in rectal temperature was small and was the same in all animals (by 0.52°C on the average). To study responses of the rats to moderate hypoxia, they were "elevated" at the same rate to an altitude of 5,000 m (pO_2 85 mm Hg), at which they remained for 30 min.

During the period of "elevation" and during the first 10 min of their stay at the fixed "altitude" the intact animals showed a gradual increase in respiration rate (Fig. 3) which continued until the end of exposure.

Blocking the carotid sinuses did not completely abolish the response of the respiratory system to hypoxia. The respiration rate of rats with denervated carotid sinus chemoceptors was lower throughout the experiment than that of the intact rats.

In this series of experiments there was likewise no difference between the responses of the cardiovascular and thermoregulatory systems of the intact and denervated rats to hypoxia. After an initial increase there was a slight decrease in the heart rate, by 5% at the end of the experiment. The rectal temperature of the rats fell by 1.6°C (from 38.2 to 36.8°C) during the experiment.

As the air pressure fell in the pressure chamber the oxygen tension in the thigh muscle fell rapidly in all the animals and reached a steady level 1-3 min after elevation to an altitude of 5,000 m, remaining at approximately the same level until the end of the experiment. In the intact animals it was 50-60% below its initial level. In the rats with blocked carotid sinus chemoceptors the decrease in pO_2 in the thigh muscle was greater than in the intact animals.

These results show that blocking the carotid sinus chemoceptors in rats altered the intensity of the animal's respiratory responses to hypoxia but did not abolish them. Meanwhile, oxygen lack in the muscle tissue developed more rapidly in the denervated animals than in the intact during exposure to hypoxia, suggesting less efficient compensation of the hypoxic changes.

So far as regulation of the circulation in hypoxemia is concerned, it is nowadays generally accepted that the response of the cardiovascular system to hypoxia takes place not only through arterial chemoceptors, but also through the direct action of oxygen lack on the centers of innervation of the heart [3]. The results of the present experiments confirmed this hypothesis. From this point of view it was interesting to assess the altitude resistance of intact rats and of rats with blocked carotid sinus reflexogenic zones.

The altitude ceiling and the duration of survival at an altitude of 12,000 m, with a rate of elevation of 25 m/sec, was determined. In the second case the animals were fixed to a special bench. "Descent" took place after apnea lasting more than 15 sec. The altitude ceiling of the intact rats was 12,640 ± 252 m and of the denervated rats 12,280 ± 340 m; the survival times were 86 ± 16 and 68 ± 13 sec respectively. No hypoxic convulsions occurred in the denervated rats during exposure to acute hypoxia.

There was thus a tendency for the altitude resistance to be reduced somewhat in the denervated rats, although the difference between the animals of the two groups was not statistically significant. During exposure to extremely severe hypoxia, absence of the carotid sinus chemoceptors is evidently not of decisive importance. This is confirmed by the equality between pO_2 in the muscles of both groups of rats on reaching high "altitudes" (Fig. 2).

To investigate the role of the arterial chemoceptors in adaptation to hypoxia, intact and denervated rats were exposed for 1 month in a chamber containing 10-11% oxygen. In parallel tests, rats of another group were kept in a chamber filled with air. All the other parameters of the environment were identical in both chambers.

Neither in the intact rats nor in the rats with blocked carotid sinus chemoceptors were significant changes found in the ventilatory responses to inhalation of a mixture containing 11% oxygen during an exposure of 30 days.

These experimental results show that the peripheral chemoceptors play a definite role in the general adaptation of the animal to oxygen deficiency. At the same time, there is reason to suppose that the carotid sinus chemoceptors do not play a significant role in the responses of the cardiovascular and thermoregulatory systems to hypoxia. Their removal likewise has little effect on the resistance of rats to extreme degrees of rarefaction of the atmosphere.

A special word must be said about the respiratory responses. Since denervation of the carotid sinus zone did not lead to disappearance of the adequate ventilatory response to hypoxia, presumably this function in rats is also shared by other chemosensitive structures. These could be, in particular, the chemoceptors of the aortic zone. However, surgical division of the possible afferent chemoreceptor pathways arising from the region of the aortic arch in rats, which was performed on some animals, did not cause complete disappearance of the ventilatory responses to hypoxia.

It can thus only be assumed that chemosensitive information concerning hypoxia in rats arises not only from the well-known reflexogenic zones, but also from others which have not yet been investigated.

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