STUDIES ON THE DIFFERENCE IN THE BIOLOGICAL ACTIVITIES INDUCED BY PYROGEN IN RABBITS RESTRAINED BY TWO DIFFERENT METHODS

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Accepted April 9, 1980

During the study of fever-reactions induced by pyrogen in rabbits we observed changes in the activities which depended on the positions of restraint. Pyrogen is related to various biological activities, including fever and increased heart rate (1, 2).

We investigated the relations between the fever and the increasing heart rate using two methods of restraint; supine-restraint (S-R) and prone-restraint (P-R).

Adult male Japanese albino rabbits, weighing 2.0 to 2.7 kg, were used. Experiments were performed in an air-conditioned room maintained at 22–24°C with a 40–60 % humidity. Pyrogen was obtained from the dried cells of E. coli UKT-b, by the phenol-water method (3). Rectal temperatures were measured as described previously (4). Heart rate was measured, in the second lead, by electrocardiogram (Nihon Koden, RBL-42). Urethane (1 g/kg) was administered s.c. 3 hours before the administration of pyrogen to establish the baseline rectal temperature and heart rate. All glassware and needles used were sterilized by dry-heat at 250°C for 2 hours to inactivate any contaminating pyrogen.

The conscious rabbits were restrained in the P-R and S-R positions, and the rectal temperatures fell gradually from 38.55±0.35°C to 37.55±0.40°C in P-R rabbits and to 36.95±0.30°C in S-R rabbits within 90 min, the same level being maintained during the entire experiment. As shown in Fig. 1, the rectal temperature of P-R rabbits increased with administration of pyrogen at a dose of 10 μg/kg, i.v., while that of the S-R rabbits remained

Fig. 1. Effect of pyrogen on rectal temperature in unanesthetized, restrained rabbits. Arrows denote the administration of pyrogen (10 μg/kg, i.v.). Each point represents the mean of five to ten rabbits. Vertical bars represent the standard-deviations.
Fig. 2. Effect of pyrogen on the heart rate in unanesthetized, restrained rabbits. Arrows denote the administration of pyrogen (10 μg/kg, i.v.). Each point represents the mean of five to ten rabbits. Vertical bars represent the standard-deviations.

unchanged.

On the other hand, as shown in Fig. 2, the heart rates of both the P-R and S-R rabbits showed no difference between them, and remained at the same level, for several hours. With the administration of pyrogen, the heart rate of P-R rabbits increased progressively from 240±10 beats/min to 270±11 beats/min within 30 min, the maximum level being about 290 beats/min. In the S-R rabbits also, the heart rate increased progressively from 248±9 beats/min to 280±7 beats/min within 30 min, reaching the maximum level of about 285 beats/min. Thus, there was no significant difference in the degree of tachycardia induced by pyrogen, in accordance with the positions of restraint.

In urethane anesthetized rabbits, the rectal temperature stabilized within 3 hr after the administration of the compound, and fell to 36.5±0.5°C in the P-R rabbits, and to 35.4±0.3°C in the S-R rabbits, the same level being maintained at the end of 3 hour experiments. The administration of pyrogen had no influence on the rectal temperature in either group of rabbits. In the case of the P-R rabbits anesthetized with urethane, the heart rate increased (270±10 beats/min), but such was not the case in the S-R rabbits (246±8 beats/min). In both groups anesthetized with urethane, the heart rate was neither increased nor decreased with the administration of pyrogen.

It was thus ascertained that the pyrogenic response and heart rate are markedly influenced by two different forms of restraint. The lower rectal temperature was seen in the S-R rabbits and in the urethane anesthetized rabbits, while an increase in rectal temperature with pyrogen administration was seen only in the P-R rabbits. In the S-R rabbits, the administration of pyrogen had no influence on the rectal temperature, and such was also the case in shorn rabbits (5). These data suggest that in the S-R rabbits, the caloric losses are greater than in the P-R rabbits, and the mechanisms of heat conservation are maximally operative prior to the administration of pyrogen and there is no increase in rectal temperature. However, increasing in the heart rate was observed in both groups treated with the pyrogen. Some effects of pyrogen are mediated by the release of catecholamines (6), therefore the tachycardia may be related to these amines. It has been demonstrated that urethane de-
creases the thermal sensitivity of the temperature sensitive neurons in the hypothalamus (7) as influenced by pyrogen (8, 9) and also that urethane has an antipyretic effect on the pyrogen-induced fever (10). Therefore, the urethane anesthetized rabbits may not show an increase in rectal temperature with pyrogen administration.

Positions of restraint may therefore affect the biological activities of pyrogen.

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CHANGES IN α-ADRENERGIC RECEPTORS IN RAT BRAIN IN VITRO BY PREINCUBATION WITH α-ADRENERGIC LIGANDS

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Accepted April 11, 1980

Interesting findings on α-adrenergic receptors in brain (1-4) and many peripheral organs (5-9) have been obtained using radiolabeled specific ligands with high specific activity for these receptors. It has been reported that (*H)WB4101, (*H)2-(2',6'-dimethoxy)phenoxo-