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Effect of intermittent chronic exposure to hypoxia on feeding behaviour of rats

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Abstract. Healthy albino male rats were exposed to a simulated high altitude (HA) equivalent to 25000 ft (7620 m) for 6 h daily, continuously for 21 days to study the feeding behaviour. The 24-h food and water intake and body weight once in 3 days were recorded. Blood samples were drawn once a week from the retro-orbital venous plexus for blood sugar analysis. All the parameters were recorded before, during and after exposure to simulated HA. The results show a decrease in 24-h food and water intake and decreased gain in body weight during hypoxic exposure, which showed a tendency to come back to control during the post-exposure period. The blood sugar reflected a state of mild hyperglycaemia during exposure to HA.

Key words: Hypoxia – High altitude – Feeding behaviour – Hypophagia

Introduction

Man in his multifarious activities encounters varied ambient conditions and one such condition is to stay in the rarefied atmosphere at high altitude (HA) resulting in hypoxia. Most of the undesirable effects of HA are due to hypoxia. A considerable amount of research has investigated the problems arising due to HA exposure, such as acute mountain sickness (Heath and Williams 1989), pulmonary oedema (Menon 1984), frostbite (Mathew 1984) and sleep disturbances (Selvamurthy 1984; Selvamurthy et al. 1986). Hypophagia is another common complaint among those sojourning at HA; however, the problem of hypophagia has drawn very little attention from environmental physiologists.

Anand (1968) suggested that alterations in energy balance and food intake occurred at HA. Earlier investigations had suggested a decrease in food and water intake, and body weight on short-term exposure to hypoxic mixtures of air (Koob and Annau 1974). Gloster et al. (1974) subjected six young male guinea-pigs to a simulated altitude of 5000 m for 14 days and compared their intake with that of six controls of comparable body weight. The total weight of food consumed by the test animals was only 63% of that eaten by the controls. There have also been reports suggesting the protective influence of carbohydrate intake and deleterious effects of a high fat and protein diet in tolerating severe hypoxia (Purshottam et al. 1978). Thus investigations carried out so far have shown the occurrence of anorexia and hypophagia on exposure to hypoxic gas mixtures or a HA environment. However these studies do not provide any information about the feeding responses of the animals exposed to hypoxia for a longer duration in controlled conditions.

The controlled studies have been done for a maximum period of 24 h where known mixtures of oxygen were administered; the remaining investigations have only been under the conditions of HA without taking into consideration the simultaneous effect of temperature, which would be an additional stress at HA. Since hypoxia produces alterations in body temperature, which in turn influences the amount of food consumed, the effect of hypoxia on food intake needs to be studied while keeping the ambient temperature constant near the thermoneutral level and noting the changes in body temperature. It is also not clear how recovery from the effects of hypoxia would ensue upon termination of hypoxic exposure. Therefore the present study attempted to investigate the effect of chronic intermittent exposure to hypoxia on feeding behaviour and to explore the possible underlying mechanisms.

Materials and methods

Male albino Sprague-Dawley rats of body weight 150–200 g and bred and reared in the animal house of the Defence Institute of Physiology and Allied Sciences were used. The rats were handled in accordance with the recommendations of the ethical committee

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of the Institute. All the rats were housed in separate cages at a temperature of 27±2° C. The lighting conditions in the room were maintained at a regime of 12:12 h light/darkness. The powdered synthetic diet (Gold Mohur Laboratory Animal Feed, Lipton India Ltd.) was given in spill-proof containers holding a maximum of 120 g. The diet contained the following components by weight: crude protein 21%, ether extract 5%, crude fibre 4%, ash 8%, calcium 1.0%, phosphorus 0.6%, nitrogen-free extract 53%, and a complete vitamin supplement. Tap water was provided for drinking in a calibrated dispenser. The food and water intake was recorded daily in the morning at 0930 hours for 7 days to select normophagic, normodipsic and normoglycaemic rats. Those animals showing fluctuations in these parameters at the end of this time were discarded. The following parameters were determined subsequently: food and water intake, once a day; body weight, every third day; blood sugar and blood insulin, once a week. Rats were divided into experimental and control groups. The animals in the experimental group were exposed to simulated conditions of HA equivalent to 25 000 ft (7620 m) by placing them in a decompression chamber with a capacity of 0.5 m^3.

The temperature in the chamber was maintained at 27±1° C based on information provided by Folk (1969) that the lowest temperature at which the rat can maintain its body temperature at basal metabolic rate is 25° C. The report of Bhatia et al. (1969) of a neutral temperature (dry bulb temperature) of 33° C for maintaining the set point in rat was also taken into consideration. The relative humidity within the chamber was about 50% and fresh air was allowed to flow into the chamber at the rate of 5.5 l/min. The rats were exposed for 6 h daily from 1000 h to 1600 hours, continuously for 21 days. The control rats were kept under the same environmental conditions but without the hypoxic exposure. Both control and experimental rats were deprived of food and water between the exposure times. The parameters mentioned above were recorded in both the experimental and control groups before, during and after the termination of exposure to hypoxia.

Blood was withdrawn from the retro-orbital venous plexus under ether anaesthesia for blood sugar estimation between 0900 and 0930 hours. Blood glucose estimation was done by the enzymatic colorimetric method. The blood glucose kit was obtained from Boehringer, Mannheim, GmbH Diagnostica. Statistical analysis of the data was done by two-way analysis of variance using the criteria of Newman Keuls multiple range test. Comparisons were made between the pre-exposure values of food intake, water intake, body weight and blood sugar with the corresponding exposure and post-exposure values.

Results

The 24-h food and water intake showed a decrease during exposure to simulated HA conditions equivalent to 25000 ft (7620 m). A gradual decrease was seen within the first 2 weeks of exposure to HA, which was maintained in the last phase of exposure to HA (Fig. 1). During post-exposure the 24-h food intake recorded an increase and showed a tendency to return to near control levels.

The blood sugar level showed a state of mild hyperglycaemia. On exposure to hypoxia, the blood sugar level showed an increase on the 7th day to 68.2±8.8 mg/dl from the control value of 59.9±6.8 gm/dl. This increase continued even on the 15th and 21st days of exposure (Fig. 1). The post-hypoxic effect on blood sugar showed a reversal of this pattern towards pre-exposure level. Twenty-four hour water intake also followed the same pattern. The 24-h water intake registered a decrease from 33.3±0.8 to 20.6±0.5 ml ($P<0.001$) during the period of exposure to HA (Fig. 2). The post-exposure level of water intake showed a tendency to come back to near control levels. Body weight gain was lower ($P<0.001$) during exposure to HA (Fig. 3).

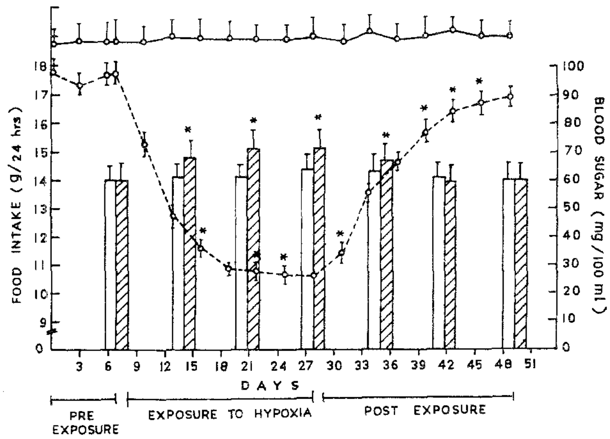

Fig. 1. Mean±SD 24-h food intake in g for control and experimental adult male rats during and after exposure to simulated high altitude (HA). The *columns* represent percentage change in the blood sugar level in experimental and control rats. Food intake: o——o control; o---o experimental. Blood sugar: □ control; ▨ experimental, *$P<0.001$

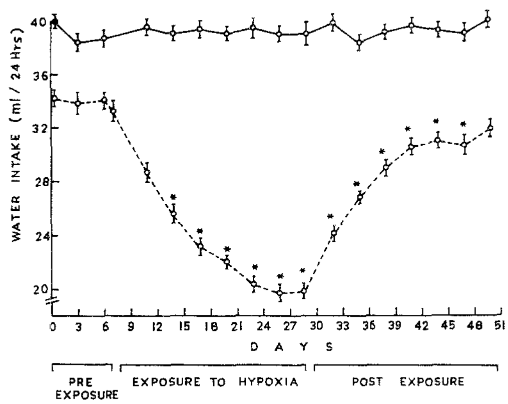

Fig. 2. Mean±SD 24-h water intake in ml for control and experimental rats during and after exposure to simulated HA. o——o Control; o---o experimental, *$P<0.001$

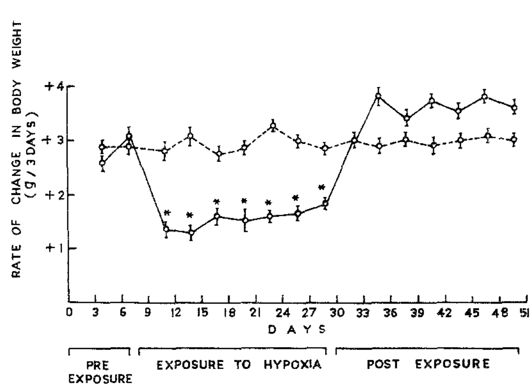

Fig. 3. Mean±SD body weight in g per 3 days for control and experimental rats during and after exposure to simulated HA. o——o Control; o---o experimental, *$P<0.001$

Discussion

Hypoxia resulting from an exposure to simulated altitude of 25000 ft (7620 m) produced a decrease in the total quantity of food consumed by the adult rats and this decrease occurred gradually. The changes in the mean pooled value of adult rats then stayed at a steady level with minor fluctuations. Thus the animals tended to maintain this new level of intake depending upon age and also the availability of different components of the food material. Koob and Annau (1974) had demonstrated a decrease in food intake on exposure to hypoxia for 24 h; the impression obtained from their observations was only a partial effect of hypoxia. Hypoxia in the adult rats not only leads to a reduced food requirement but also to a new base line in the homeostatic needs of the animals with the onset of reduced aerobic metabolic activity. It appears that the homeostatic mechanisms are diverted more to maintain the minimal level of metabolic activity that is just sufficient to sustain the vital functions of the organisms.

The rate of gain in body weight shows a considerable decrease during the phase of steep change in the level of food consumption. This observation of the present study confirms the results of Hunter and Clegg (1973) regarding the decrease in the rate of gain in body weight during hypoxia. Studies conducted by Ross et al. (1988) suggested that hypoxia can be a sufficient cause for the weight loss and decreased food consumption reported by mountain expeditions at HA. Boyer and Blume (1984) and Guilland and Klepping (1985) have observed negative nitrogen balance at extreme HA.

In addition to anorexia, increased basal metabolic rate and energy expenditure during conditions of moderate excercise can contribute to body weight loss at extreme altitude (Sridharan and Rai 1984; Butterfield et al. 1992). The measurements of the blood sugar level indicate that the animals continued to have relatively mild hyperglycaemia during exposure and also after the termination of hypoxia. The former finding is supported by reports of Morgan et al. (1959, 1961), showing an increase in hexokinase activity and its phosphorylation during hypoxic conditions; this indicates increased glucose mobilization and utilization. However Caldiron and Llerena (1965) have shown a low level of blood glucose in men living at HA. The difference in the level of blood sugar reported by Caldiron and Llerena (1965) and the results of the present study may be due to differences in the time of exposure to the environmental stress. Further studies are required of the effects of long-term continuous exposure to a simulated HA on feeding behaviour. The possible mechanisms underlying the pathophysiology of hypophagia at high altitude also need to be elucidated.

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