

## ORIGINAL ARTICLE

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## Effect of high altitude on sensitivity to the taste of phenylthiocarbamide

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**Abstract** Sensitivity to the taste of phenylthiocarbamide (PTC) was studied using the Harris-Kalmus method in healthy human volunteers at sea level and then subsequently at an altitude of 3500 m over a period of 3 weeks, after which they were brought back to sea level. Blood sugar, insulin and blood cortisol levels were estimated weekly. The results indicated that, out of 51 subjects studied, 26 (55%) were PTC tasters at sea level. Eight of those unable to taste PTC at sea level tested as tasters at high altitude, and 2 of them reverted to being non-tasters on return to sea level. In the blood, an increase in cortisol and blood insulin levels was seen without any significant change in sugar levels. All the changes recorded at high altitude tended to return to basal values after re-induction to sea level. The study suggests that high-altitude hypoxia in some way, possibly involving changes in hormonal profile among other factors, causes an alteration in sensitivity to the taste of PTC, resulting in some of the individuals shifting to lower PTC sensitivity.

**Key words** PTC taste sensitivity · Taster · Non-taster · High altitude

### Introduction

Sensitivity to the taste of phenylthiocarbamide (PTC) has triggered scientific interest because of the different frequencies of tasters and non-tasters in the human population (Facchini et al. 1990). Sensitivity to the taste of PTC is determined genetically, and shows a bimodal distribution that divides the population into tasters and non-tasters of these substances. An interesting study by Frank and Korchmar (1985) examined the differences in gustatory processing for tasters and non-tasters of PTC by as-

sessing the reaction times intensity for judging of taste in these two groups.

Several investigators have found that sensitivity to PTC-like compounds predicts sensitivity not only to substances that are chemically similar to PTC but also to sweet and bitter tastants that are chemically unrelated to PTC, like caffeine, urea, saccharine and sucrose (Bartoshuk 1979; Gent and Bartoshuk 1983; Hall et al. 1975). Even though sensitivity to PTC is genetically determined, it can be modulated by changes in internal milieu, as observed in hormonal imbalances (Rao and Sisodia 1970; Brand 1963).

Studies by Whissell-Buechy and Wills (1989) have shown that girls who could taste PTC reached maturity 3–8 months earlier than did non-tasters, suggesting that PTC polymorphism may involve the hypothalamic pituitary-gonadal axis and the sex hormone pathway. A recent study by Drewnowski and Rock (1995) suggests that the tasters and super-tasters of 6-n-propylthiouracil may also differ from non-tasters in their taste preferences and in their patterns of food rejection and food acceptance.

Altitudes above 3050 m have been shown to cause symptoms of acute mountain sickness. At high altitude (HA) there is almost always loss of appetite and a decreased tolerance for food. Exposure to HA hypoxia may result in changes in appetite and an increased desire for sweets (Drewnowski and Rock 1995; Klain and Hannon 1970; Singh et al. 1996, 1997a, b). Carbohydrate supplements are reported to have beneficial effects at HA and may lessen the symptoms and severity of acute mountain sickness (Consolazio et al. 1969; Hansen et al. 1972). Maga and Lorenz (1972) studied the responsiveness to different taste stimuli and determined the thresholds for six women tasting increasing concentrations of sucrose, sodium chloride, citric acid and caffeine at 1520 m, observing increased thresholds. Experiments from our laboratory using human volunteers have shown that there is an increase in the thresholds for glucose and sodium chloride and a decrease in thresholds for citric acid and quinine sulfate at 3500 m (Singh et al. 1997b).

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It is apparent that sensitivity to PTC is influenced by physiological and pathological conditions, and may also be affected by altitude. The present work was undertaken to study the effect of HA on sensitivity to the taste of PTC during 3 weeks of acclimatization at 3500 m.

## Materials and methods

The investigation was conducted on 51 healthy male volunteers, aged 21–32 years. The approval of the Ethical Committee of the Defence Institute of Physiology and Allied Sciences (DIPAS) was obtained. The procedure was explained in detail to the volunteers and their written consent was obtained.

The volunteers were selected on the basis of a clinical examination. A short history, including ethnic origin, alcohol consumption, food habits and the use of nicotine, was taken. Out of the 51 volunteers, 14 were smokers. Volunteers who had suffered from the common cold, cough, fever and stomach upsets in the recent past were excluded from the study.

Three observations each were recorded during the three phases, i.e. at sea level, (SL) (phase I), HA (phase II) at 3500 m in the Western Himalayas and on reinduction to SL (phase III). The temperature at HA ranged from  $4\pm 2^\circ\text{C}$  (minimum) to  $26\pm 2^\circ\text{C}$  (maximum) and the relative humidity was 50%. All the volunteers were air-lifted to the HA base camp where the studies were carried out and were flown back to SL for phase III of the study. Each phase lasted for 3 weeks. All the subjects received the same type of food throughout the duration of the study. It consisted of rice, wheat pancakes, legumes and lentil preparations, fresh vegetables (mainly potatoes, cabbage, cauliflower, carrots, peas etc.) and mutton and chicken preparations.

### Parameters recorded

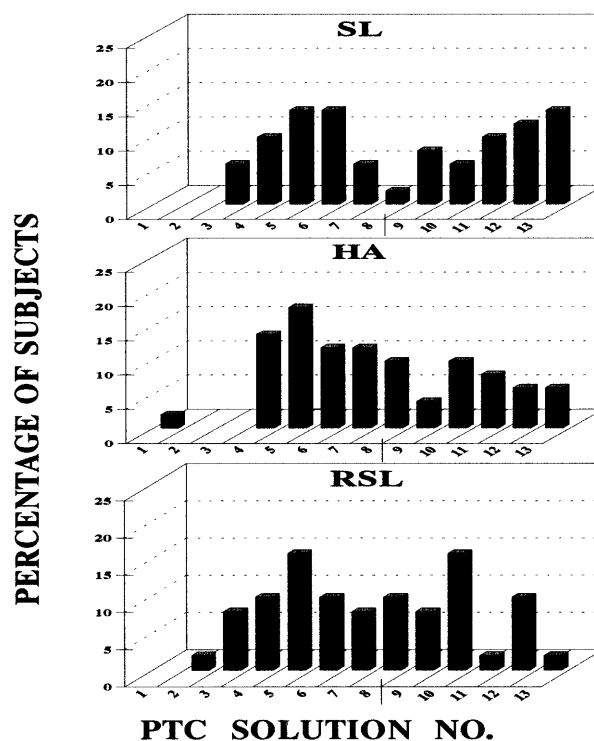
The test of sensitivity to the taste of PTC was administered according to the method of Harris and Kalmus (1949) in a laboratory maintained at  $25\pm 1^\circ\text{C}$ , 2 h after breakfast. A standard PTC solution was prepared containing 1.3 g PTC diluted in 1 l distilled water (solution 13). Twelve serial half-dilutions of this were made until solution 1 was obtained. These solutions were given to the volunteers, starting with solution 1 (concentration=0.00003% by weight) followed by the other solutions up to number 13 (0.13 g % by weight). Subjects thoroughly rinsed their mouths with tap water before each stimulus and between stimuli until no trace of the previous stimulus remained. The subjects were then instructed to taste the solutions by rolling them around on the tongue and palate before spitting them into a beaker. They were instructed to indicate the solutions in which they were able to detect a definite taste. The PTC concentration of the solution in which the volunteer was able to detect a bitter taste was noted. Volunteers who were able to detect PTC in solution 1–8 (concentrations 0.00003%–0.004%) were labelled as tasters and those who were unable to detect PTC in any of the solutions or were only able to detect PTC in the solutions 9–13 (concentrations 0.008%–0.13%) were labelled as non-tasters.

Blood was withdrawn from the antecubital vein under aseptic conditions. The blood sugar, insulin and cortisol levels were estimated once a week during each phase of the study.

The data were analysed statistically by the non-parametric Cochran *Q*-test. The blood glucose, insulin and cortisol values were analysed by Student's *t*-test.

## Results

The studies conducted in phase I established 26 of the 51 human volunteers to be tasters and 25 to be non-tasters. Those who were non-tasters mainly fell into classes



**Fig. 1** Frequency distribution (%) of subjects tasting phenylthiocarbamide (PTC) at exponentially increasing concentrations (solution 1=0.0003% by weight at sea level (SL), high altitude (HA) and on reinduction to sea level (RSL)

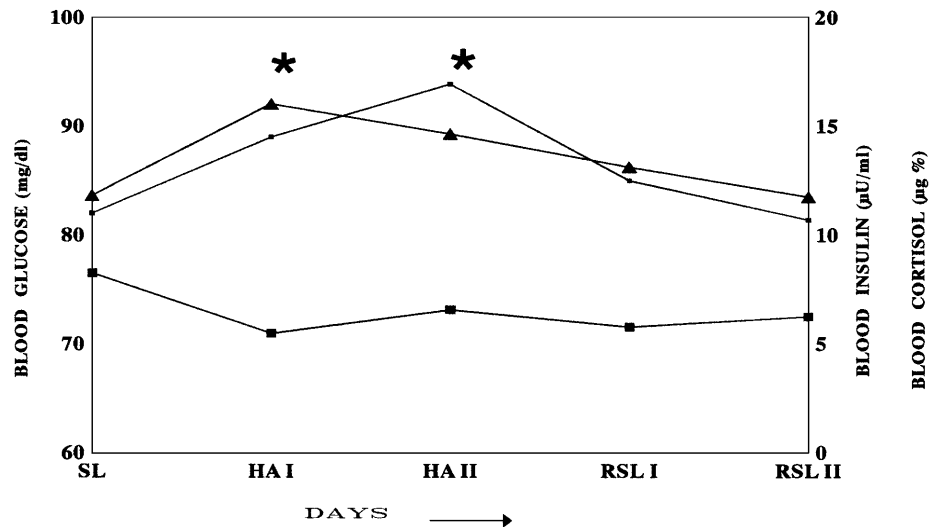
11–13; i.e. they could detect the bitter taste at PTC concentrations of 0.0032%–0.13% only. Out of the 25 non-tasters, 8 individuals tested as tasters at HA (phase II) and of these, 6 remained tasters even 3 weeks after their return to SL. The percentage distribution of the subjects into the different classes (solution numbers) during the different phases is given in Fig. 1.

Of the non-tasters who had been able to detect PTC in solutions 9 and 10, 6 now became able to perceive the taste of PTC in solutions 6, 7 and 8. They continued to perceive PTC at these lower concentrations until the third week of testing after the return to SL (phase III). Also, at phase II, 2 of the non-tasters hitherto falling into classes 10, 11 and 12 became able to perceive PTC in solutions 7 and 8. By the end of phase III, however, these subjects reverted to being able to taste PTC at higher concentration only.

The Cochran *Q*-test showed that the increase in the number of tasters at HA was statistically significant ( $P<0.005$ ) when compared to SL values. Similarly, comparison between the number of tasters at SL and the number who were tasters after returning to SL was found to be statistically significant ( $P<0.005$ ), because 6 of the non-tasters who had tested as tasters at HA continued to be tasters even three weeks after returning to sea level.

The blood sugar value at SL was 76.56 (SEM 8.53) mg dl<sup>-1</sup> and after a week at HA it was 70.96 (SEM 7.9) mg dl<sup>-1</sup>. The difference in values was not statistically significant (Fig. 2).

**Fig. 2** Graph showing mean  $\pm$  SEM values of blood glucose (■), insulin (■) and cortisol (▲) determined weekly during the three different phases of the study. \*  $P < 0.01$



The blood insulin levels showed a statistically significant increase at HA ( $P < 0.01$ ). The maximum level recorded after the second week at HA was 16.93 (SEM 7.96)  $\mu\text{U}$  (micro units)  $\text{ml}^{-1}$  as compared to the SL value of 11.04 (SEM 6.45)  $\mu\text{U}$   $\text{ml}^{-1}$  (Fig. 2)

The blood cortisol levels showed an increase after 1 week's stay at HA. The value increased to 16.03 (SEM 2.23)  $\mu\text{g}$   $\text{dl}^{-1}$  from the basal value at SL of 11.82 (SEM 2.45)  $\mu\text{g}$   $\text{dl}^{-1}$ , and this increase was statistically significant ( $P < 0.01$ ). After the first week of return, the blood cortisol levels recorded a slight decline and returned to near SL values by the second week of phase III (Fig. 2).

## Discussion

The results show changed sensitivity to the taste of PTC in 8 volunteers, who were non-tasters at sea level but became tasters at HA. Increases in the levels of blood cortisol and blood insulin were recorded during their stay at HA.

It is difficult to explain these changes in taste sensitivity to PTC at HA. We earlier reported changes in the taste thresholds and preferences for the four basic stimuli at HA (Singh et al. 1997b) and showed an increase in taste thresholds for glucose and sodium chloride and a decrease in the thresholds for citric acid and quinine sulfate solutions. Higher concentrations of glucose received higher pleasantness ratings at HA than at SL. Bhatia et al. (1990) have studied the gustatory differences in hypothyroid and hyperthyroid tasters and non-tasters and reported that decreased perceptions of sweet and bitter tastes were much more prominent in non-taster than in taster hypothyroid subjects. They also emphasized the role of elevated levels of vitamin A and reduced zinc levels in the serum. A greater hedonic value for salt was largely observed among hypothyroid tasters. It was further observed (Bhatia et al. 1990) that 60% of the hyperthyroid subjects and 40% of the hypothyroid subjects, were tasters implying that, in hyperthyroid subjects, the

percentage of those able to taste PTC is greater than in the hypothyroid subjects.

Bhatia et al. (1981) studied the responsiveness of subjects in certain physiological conditions e.g. during the menstrual cycle to PTC and glucose, and showed that these responses were dynamic and there was a tendency for non-tasters to become tasters during the ovulatory phase. PTC sensitivity also changes during pregnancy (Bhatia and Puri 1991).

Laroche and Johnson (1967) and Moncloa et al. (1966) have reported that humans transported from SL to an altitude of 3962–4267 m showed an increase in serum total and free thyroxine concentrations. An increase in thyroid function has been noted after acute exposure to HA; however, in rats, a decrease in thyroid function has been reported after chronic exposure. Field studies conducted by Rastogi et al. (1977) and Sawhney and Malhotra (1991) have shown higher levels of triiodothyronine and thyroxine at HA (3500 m) in both acclimatized lowlanders and HA natives than are found in SL residents. The acclimatized lowlanders, in spite of having increased levels of triiodothyronine and thyroxine, were clinically euthyroid.

There was an increase in the blood insulin level with a concomitant slight decrease in blood glucose during the time at HA in our study. An increase in insulin levels may cause glycogenesis and bring about a slight decrease in blood glucose level during the stay at HA, as observed in the present study. Studies from our laboratory, in rats, exposed to a simulated HA hypoxia of 7620 m for 21 h daily and continuously for 18 days, showed hypoglycaemia (Singh et al. 1997a). We have previously reported an increase in blood glucose level and blood insulin level in the rats exposed to simulated HA hypoxia of 7620 m for 6 h daily and continuously for 3 weeks (Singh et al. 1996). However, reports by other workers recording blood glucose levels are conflicting. Blume (1984) has reported a decrease in blood glucose levels in subjects acclimatized at HA while Sawhney et al. (1986) did not find any change in fasting blood glucose at 3500 m.

Blood cortisol levels showed an increase during the stay at HA indicating an increase in stress. Richalet et al. (1989) also found an elevation in the plasma cortisol levels after the first day of a simulated exposure to HA in a chamber experiment. Many of the subjects of his study who were taken rapidly to an altitude of 4300–5300 m suffered from acute mountain sickness, but even those free of symptoms showed an increase in cortisol or its urinary metabolite. An increase of the cortisol level indicates some kind of stress response, which may be non-specific. Anand et al. (1993) reported cortisol levels that were three times the normal in subjects who had spent more than 10 weeks above 6000 m.

At high altitude the blood cortisol showed an increase, with increased levels of circulating triiodothyronine and thyroxine. Though we did not measure these in our experiments, Sawhney and Malhotra (1991) recorded higher levels of triiodothyronine and thyroxine at HA in both acclimatized lowlanders and HA natives than in residents at SL, using a similar altitude and physical conditions to those employed in our experiments. The increased levels of thyroid hormones may, in some way, be modifying the bimodal distribution of tasters and non-tasters at HA. It has been suggested that the genes controlling taste sensitivity could affect not only sensitivity to PTC but also thyroid function through the enzyme peroxidase, which is involved in the production of thyroxine (Facchini et al. 1990).

The results of this study raise the possibility that hypoxic exposure to HA in some way causes alterations in the perception of taste through alterations in hormonal levels, which may cause a temporary shift in the taster status. The exact mechanisms responsible for this shift remain to be elucidated.

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