

## Association of phenylthiocarbamide taste blindness trait with early onset of childhood obesity in Mysore

Saraswathi YS, Mohsen Najafi, Vineeth VS, Kavitha P, Suttur S. Malini\*

Human Genetics Laboratory, Department of Studies in Zoology, University of Mysore, Manasagangothri, Mysore, Karnataka, India.

\*Corresponding Author: email address: drssmalini@gmail.com (S.S. Malini)

### ABSTRACT

Ability to taste Phenylthiocarbamide (PTC) a bitter compound is widely used to know the heritable trait in both genetic and anthropological studies. The study is based on the ability of a person to sense the taste of PTC. Inability to taste has also been associated with medical illness not typically with taste impairment, so far no study has yet proved whether PTC blindness correlates with childhood obesity. This study is the first attempt to examine PTC sensitivity in obese children and healthy children to determine variation in the perception of bitter tastes which is associated with eating behavior, body mass index, and childhood obesity. The present investigation is carried out in Mysore, during years 2008 - 2009. Phenylthiocarbamide taste sensitivity was measured by administering PTC solution for obese and control children by modified method of Harris and Kalmus. The result focused that tasters were significantly more frequent (67%) than non-tasters (33%) in control population. A higher proportion of non-tasters were observed in obese children (72%) when compare to non-obese subjects (28%). These differences were not explained by alterations in perception of basic taste sensitivity or age. Increased frequency of non-taster allele is evident in children with obese condition. This could be due to lack of preference for food among non-tasters. As the phenotypic variation in PTC sensitivity is genetic in origin, it may represent a surrogate risk factor for the development of childhood obesity.

**Key words:** Non taster PTC trait; childhood obesity; Mysore population

### INTRODUCTION

Eating behavior is a complex interplay of physiological, psychological, social, and genetic factors that influence meal timing, quantity of food intake, food preference, and food selection. Taste affects food preference and food intake, thereby directly influencing eating behavior. However, not all humans perceive taste in exactly the same way. The density of taste papillae on the tongue, genetic differences in taste receptors or sensitivity of taste receptors, constituents of saliva, and other factors all contribute to an individual's taste perception and subsequent food preferences.

Phenylthiocarbamide (PTC), a bitter chemical synthesized by Fox [1] has been widely used for genetic and anthropological studies [2]. Bitter-taste perception is a classically variable trait both within and between human populations [3]. The inability

to taste PTC is a simple Mendelian recessive trait [4, 5, 6, 7, 8], wherein the individuals with two recessive alleles (tt) are non tasters for PTC and individuals with one dominant allele (Tt) or two dominant alleles (TT) are tasters for PTC. The prevalence of taste blindness (i.e., a lack of sensitivity to or an inability to taste bitter chemicals) ranges from 3% in West Africa to 6–23% in China and 40% in India; 30% of the white North American populations has taste blindness [3, 9]. Kim *et al.*, [2] have identified a small region on Chromosome 7q harbors, a gene that encodes a member of the TAS2R bitter taste receptor family. A major locus on 7q35-q36 and a secondary locus on Chromosome 16p have been localized by genome scan for PTC taster gene [10]. Bufe *et al.*, [11] was demonstrated that alleles of hTAS2R38 codes for functionally different receptor types that

directly affect perception of bitterness containing compounds. There are many diseases associated with variations in taste perception. However, observations suggested that lipid pathways involved in the etiology of congenital heart defects may be affected by tasting ability [12]. A preference for sweet and high-fat food was observed to decrease with increasing perception of bitter taste [3, 13] and further research highlighted relations between bitter compound-tasting ability and body mass index (BMI; in kg/m<sup>2</sup>), adiposity levels, and risk factors for cardiovascular disease [14, 15]. The availability of genetic markers for tasting ability may offer insight into individual's risk of predisposition to childhood obesity or obese traits. Hence in the present study we made an attempt to analyze the interaction between PTC tasters trait and early onset of childhood obesity in Mysore, South India.

## MATERIALS AND METHODS

The study is a cross sectional randomized epidemiological study among different school children in urban and rural areas of Mysore city. A total number of 2189 children age ranged from 13-17 years from rural and urban areas from seven different schools of Mysore city was selected for this study during years 2008-2009. The body weight was measured without shoes using a measuring scale, and height to the nearest centimeter was taken. Body Mass Index (BMI) was calculated as weight in kilograms divided by height (in meter squared). The children whose weight was more than 85<sup>th</sup> percentile (weight or BMI) for the age and sex were considered as overweight/obese [16]. Physical activities were

recorded with the help of school curriculum and questionnaire specially designed for them. The informed written consent was taken from Deputy Director of Public Instruction (DDPI), Head of the Institution (HOD) and parents. Children for control group were selected based on the BMI calculation, growth charts and family without any history of obesity, hypertension and diabetic conditions. To generate a case-control dataset, 100 childhood obese cases and one randomly selected child from each of the 100 control families were used. Care was taken to maintain similarity of ethnic and socio-economic backgrounds between the case-control groups. Food preference was recorded based on the questionnaire specially designed for this study. Information about socio-economic factors and medical history of the family was recorded. Pedigrees were constructed based on the information collected from these families.

Modified method of Harris and Kalmus [8] was used to assess the PTC taster and nontaster phenotype. With their consent, the subjects were asked to taste the PTC solution of different concentrations 0.25%, 0.025% and 0.0025% and the results were recorded in the pro-forma. PTC super tasters, tasters and non tasters were recorded based on their taste sensitivity at different dilutions. Statistical analysis was performed using SPSS statistical software 10.0. Logistic regression was performed to assess the association of tasting ability with different variables and childhood obesity as covariates. Case-control status was used as a dependent variable and childhood obesity as covariates. Results are reported as odds ratios from a model with variables.

Table 1: Comparison of tasters (PTC) and non-tasters among overweight/obese and controls along with logistic regression analysis (c.i.=confidence intervals).

	Overweight/obese (n=100)		Controls (n=100)	
	NO.	%	NO.	%
Tasters	28	28	67	67
Non-tasters	72	72	43	43
Logistic regression analysis				
Variables (Criteria's)	Univariate			
	Odds ratio (95% c.i.)		P value	
Tasters	0.180 (0.98 ;0.330)		0.001*	
Non-tasters	3.291 (1.833 ; 5.909)		0.001*	

\* = significant

## RESULTS

Table 1 shows the prevalence of the PTC taster and non-taster among overweight/ obese and control group. In the present study among overweight/obese children, 28% are taster and 72% are non-taster and among controls, 67% are taster and 43% are non-taster. The logistic regression analysis was carried out at different combination to establish relation with other variables. The 95% confidence interval for the effect of PTC tasters on overweight was significant.

Table 2 shows the type of food and food habits among the respondents. There is high prevalence of overweight/obesity among the subjects those who consume junk food, bakery product, meat or chicken, fat and oily food for a period of at least 4

days/week. There is high prevalence of overweight/obesity among the children who consume ghee daily along with their diet. The logistic regression analysis was done at all combination to establish specific relation of food habit and overweight/obesity, the odds ratio were significant for all the variables like consumption of junk food, bakery product, meat and chicken, fat and oily food at least 4 days/week and consumption of ghee daily. The 95% confidence intervals for the effect of unhealthy food habits on overweight/obesity were significant. This analysis suggests that the high caloric unhealthy food habit is one of the possible risk factor in causing overweight/obesity.

Table 2: Logistic regression analysis of food habit in overweight/obese and control population (c.i.=confidence intervals).

Logistic regression analysis		
Variables (Criteria's)	Univariate	
	Odds ratio (95% c.i.)	P value
Rice daily	2.455 (1.389 ;4.339)	0.002*
Wheat daily	0.513 (0.289 ; 0.909)	0.022
Vegetable daily	0.252 (0.140 ; 0.454)	0.001*
Meat & chicken >3days/week	4.333 (2.313 ;8.118)	0.001*
Ghee daily	4.623 (2.507 ; 8.526)	0.001*
Bakery product >3days/week	5.082 (2.646 ; 9.760)	0.001*
Junk food >3days/week	8.500 (4.458 ;16.208)	0.001*
Fat and oily food >3days/week	3.042 (1.664 ; 5.564)	0.001*

\* = significant

## DISCUSSION

Bitter, sweet, and umami tastes are mediated by G-protein-coupled receptors (GPCRs). Bitter taste receptors are encoded by 25-30 TAS2R genes, located on chromosomes 12p13, 7q34, and 5p15 [17]. The ligand specificity of TAS2Rs appears to be quite broad, consistent with their roles in detecting thousands of bitter-tasting compounds [18]. One of these, TAS2R38 has been extensively characterized in vitro, in vivo, and in human populations, and is responsive to the bitter stimuli

phenylthiocarbamide, propylthiouracil (PROP), and to thiocyanates – bitter compounds found in brassia vegetables such as Brussels sprouts and broccoli. Single nucleotide polymorphisms (SNP) located within a linkage disequilibrium block of these genes account for the association of taste, food preference and increase in weight [18].

Previous studies reveal a high incidence of non-tasters among patients with nodular goiter [19, 20], congenital athyreotic, cretinism [21, 22] and dental caries [23].

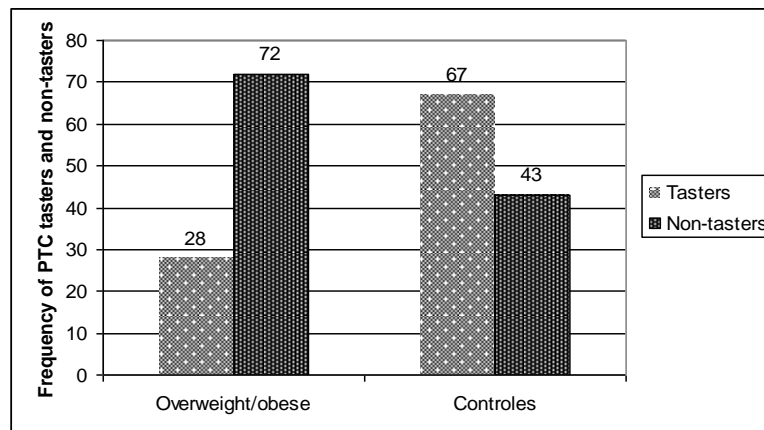


Figure 1: Comparison of tasters (PTC) and non-tasters among overweight/obese and controls

Sharma, [24] has reported a higher frequency of non-tasters in epileptic twins. In the present study the prevalence of PTC taster trait is high in case of non obese children when compared to overweight/obese. Several studies showed that people who can taste PTC (taster) are more sensitive to salt, sweet foods, sharp tasting foods, spicy foods, and alcohol. Tasters are also better in discriminating between high and low fat foods, such as various types of salad etc. Anatomical studies reported that tasters actually have more taste buds than non-tasters [25]. Keller et al., [26], reported that non tasters like high fat diet more, than low fat diet, whereas tasters shows the lack of preference for food. Bartoshuk et al., [27] reported that the taste of sucrose is more intensively sweet to tasters than to non-tasters and

tasters have high sensitivity to sweetener such as saccharin and neohesperidin dihydrochalone. Food pattern and eating habits of the children involves the information of the type of diet, frequency of non-vegetarian consumption, nature of food, frequency of consumption of stuff food, nutrient intake etc. Even in our study, we found more non tasters who are overweight/obese compare to taster, which once again emphasizes on the choice of food and its relation with obesity in general population. When the PTC taster and non taster were subjected for logistic regression analysis the effect of childhood obesity was not diluted showing an increase in odds by 18% and 29% per extra year in tasters and non tasters respectively.

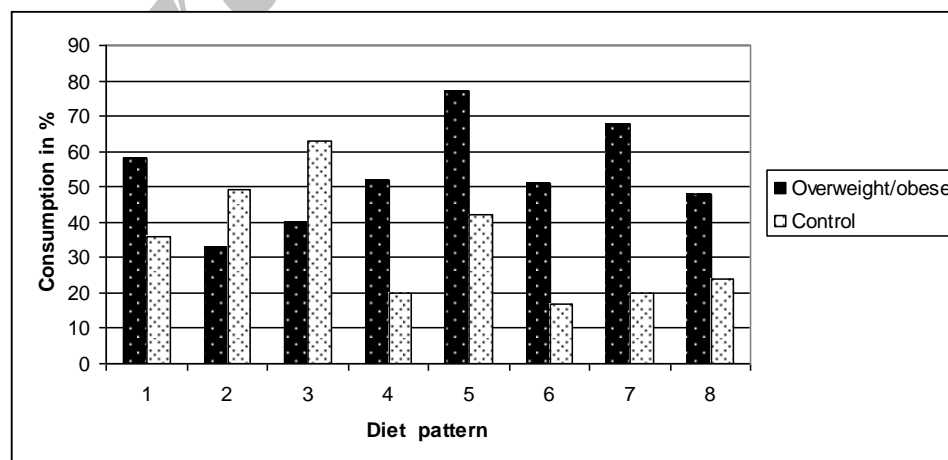


Figure 2: Comparison of food habit in overweight/obese and controls. (1= Rice daily, 2= Wheat daily, 3= Vegetable daily, 4= Meat & chicken >3days/week, 5= Ghee daily, 6= Bakery product, >3days/week, 7= Junk food >3days/week, 8= Fat & oily food >3days/week).

The statistically significant variation also holds good for consumption of balance diet, high caloric diet and physical exercise in obese children and controls. This results supports that, sensation in choice of food is very much diminished in non-tasters.

Tasting ability is also likely to be influenced by many other sensory and proprioceptive pathways, and the probable result is that no single genetic marker has a great effect. In particular, other pathways are likely to include olfactory contributions to food preference, although digestive and cognitive factors may complicate the overall system and modify the ability to perceive bitter taste [28]. The present study shows that overweight/obese children was less likely to consume food like wheat, vegetable and fruits in their daily food which are highly nutritive whereas high consumption of bakery product, junk food, meat, chicken, fat and oily food in their diet was evident. As majority of overweight/obese children being non-sensitive to salt, sweet foods, sharp tasting foods, spicy foods and high fat diet they consume more bakery products, junk food and typically incorporate all of the potentially adverse dietary factors in a large portion size. Additionally,

## REFERENCES

1. Fox AL. Taste blindness. *Science* 1931; 73:14.
2. Kim V, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D. Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. *Science* 2003; 299:1221-5.
3. Tepper BJ, Nurse RJ. PROP taster status is related to fat perception and preference. *Ann N Y Acad Sci* 1998; 855: 802-4.
4. Kim UK, Drayna D. Genetics of individual differences in bitter taste perception: lessons from the PTC gene. *Clinical Genetics* 2005;67(4):275-80
5. Reed DR. Progress in human bitter phenylthiocarbamide genetics. In: Prescott J, Tepper BJ, eds. *Genetic Variation in Taste Sensitivity*. New York: Marcel Dekker; 2004; 43-62.
6. Wooding S, Kim U, Bamshad MJ, Larsen J., Jorde LB and Drayna D. Natural Selection and

these foods tend to be low in fiber, micronutrients and antioxidants which is responsible for weight gain [29, 30]. Among non-obese children, majority of them are PTC tasters and are very sensitive to some tastes especially bitter, sour, salty and sweet etc. Hence they avoid or restrict such foods. We also recorded the consumption of junk food, bakery food products in non-obese group are occasional or rare, and they showed high percent of physical activities.

Increased frequency of non-taster allele is evident in children with overweight/obese condition resulting in lack of preference for taste sensitivity in non-tasters. As phenotypic variation in PTC sensitivity is genetic in origin, this may represent a surrogate risk factor for the development of childhood obesity

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Molecular Evolution in *PTC*, a Bitter-Taste Receptor Gene. *Am J Hum Genet.* 2004; 74(4): 637-646.

7. Hartmann G. Application of individual taste differences towards Phenylthio-carbamide in genetic investigations. *Ann Eugen* 1939; 9: 123-35.

8. Harris H, Kalmus H. The measurement of taste sensitivity to phenylthiourea (PTC). *Ann Eugen* 1949; 15: 24-31.

9. Guo SW, Reed DR. The genetics of phenylthiocarbamide perception. *Ann Hum Biol* 2001; 28: 111-42.

10. Drayna D, Coon H, Kim UK, Elsner T, Cromer K, Otterud B, *et al.* Genetic analysis of a complex trait in the Utah Genetic reference Project: A major locus for PTC taste ability on chromosome 7q and a secondary locus on chromosome 16p. *Hum Genet* 2003; 112: 567-72.

11. Bufe B, Breslin PA, Kuhn C, Reed D R, Tharp CD, Slack J P, *et al.* The molecular basis of

- individual differences in phenylthiocarbamide and propylthio-uracil bitterness perception. *Curr Biol* 2005; 15: 322-7.
12. Ueda T, Ugawa S, Ishida Y, Shibata Y, Murakami S, Shimada S. Identification of coding single-nucleotide polymorphisms in human taste receptor genes involving bitter tasting. *Biochem Biophys Res Commun* 2001; 285: 147-51.
13. Duffy VB, Bartoshuk LM, Food acceptance and genetic variation in taste. *J Am Diet Assoc* 2000; 100: 647-55.
14. Duffy VB, Lucchina LA, Bartoshuk LM. Genetic variation in taste: potential biomarker for cardiovascular disease risk? In: Prescott J, Tepper BJ, eds. *Genetic variations in taste sensitivity: measurement, significance and implications*. New York: Marcel Dekker, 2004: 197-229.
15. Pasquet P, Frelut ML, Simmen B, Hladik CM, Monneuse MO. Taste perception in massively obese and in non-obese adolescents. *Int J Pediatr Obes* 2007;2:242-8.
16. CDC growth charts: United States Advance data from vital and health statistics. No.314 National Center for Health Statistics: Atlanta 2000.
17. Grimm ER and Steinle NI. Genetics of eating behavior: established and emerging concepts. *Nutrition reviews*,2011;69(1):52-60.
18. Sausenthaler S, Rzehak P, Wichmann HE, Heinrich J. Lack of relation between bitter taste receptor TAS2R38 and BMI in adults. *Obesity (Silver Spring)*. 2009;17:937-938.
19. Kitchin FD, Howel-Envas W, Clarke CA, Connell RR, Sheppard PM. PTC taste response and thyroid disease. *Brit Med J* 1959; 1: 1069-74.
20. Facchini F, Abbati A, Campagnoni S. Possible relations between sensitivity to phenylthiocarbamide and goiter. *Hum Biol.* 1990; 62: 545-52.
21. Sheppard TH, Gartler SM. Increased incidence of non-tasters of phenylthiocarbamide among congenital athyreotic cretins. *Science* 1960; 131: 929.
22. Fraser GR. Cretinism and taste sensitivity to phenylthiocarbamide. *Lancet* 1961; 280: 964-5.
23. Chung, C.S., Witkop, C.J., Henry, J.L. (1964). A genetic study of dental caries with special reference to PTC taste sensitivity. *Am J Hum Genet* 1964; 16: 231-45.
24. Sharma K. Genetic epidemiology of epilepsy: A twin study. *Neurology India*. 2004.
25. Volkers N. Gene For Bitter Taste Could Be Due To Smoking And Eating Behavior. *InteliHealth New Service*. 2003.
26. Keller KL, Steinmann L, Nurse RJ, Tepper BJ. Genetic taste sensitivity to 6-n-propylthiouracil influences food preference and reported intake in preschool children. *Appetite* 2002;38:3-12.
27. Bartoshuk, L., Davidson, A., Kidd, J., Kidd, K., Speed, W., Pakstis, A., Reed, D., Synder, D. & Duffy, V. Supertasting is not explained by the PTC/PROP gene. *Chem. Senses* 2005a;30, A87.
28. Timson NJ, Christensen M, Lawlor DA, Gaunt TR, Day IN, Ebrahim S, Smith GD. AS2R38 (phenylthiocarbamide) haplotypes, coronary heart disease traits, and eating behavior in the British Women's Heart and Health Study. *American Journal of Clinical Nutrition* 2005; 81(5): 1005-1011.
29. Kurihara K. Glutamate: from discovery as a food flavor to role as a basic taste (umami). *Am J Clin Nutr* 2009;90(suppl):719S-22S.
30. Hu FB, van Dam RM, Liu S. Diet and risk of type II diabetes: the role of types of fat and carbohydrate. *Diabetologia* 2001; 44: 805-17.