



Association of *TAS2R38* polymorphism with measures of adiposity in Indian population



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ARTICLE INFO

Keywords:

Body mass index (BMI)
TAS2R38 gene
 phenylthiocarbamide (PTC)
 India

ABSTRACT

Introduction: The studies on association between ability to taste phenylthiocarbamide (PTC) and adiposity have shown conflicting results in Western populations. There is only one study conducted in Indian population that has investigated the role of *TAS2R38* gene (using genotypes) with anthropometric traits. We have tried to assess the role of *TAS2R38* gene in influencing measures of adiposity in India.

Materials and methods: We have adopted population based cross-sectional design for the recruitment of 304 study participants (208 children and 95 adults) from the state of Rajasthan, India. Whole blood sample was collected using finger-prick method. The polymorphism in *TAS2R38* gene, i.e. *A49P* (rs713598), was genotyped using restriction fragment length polymorphism method with the help of *HaeIII* restriction enzyme.

Results: The taster phenotype was associated with waist circumference ($\beta = -0.88$, $SE = \pm 0.44$, $P = .04$) and waist-hip ratio (WHR) ($\beta = -1.38$, $SE = \pm 0.43$, $P = .002$) among adults. The sex-wise association analysis of *TAS2R38* gene showed association with waist circumference ($\beta = 0.42$, $SE = \pm 0.21$, $P = .04$) and WHR ($\beta = 0.48$, $SE = \pm 0.23$, $P = .04$) in adult males. Among the tasters, the mean body mass index (BMI) was higher in a group having PTC threshold value “less than equal to 8” (i.e. less sensitive to tasting). Among the children, mean BMI and mean waist circumference were significantly higher in non-tasters than non-tasters ($P \leq .001$) when tasting status was determined only through genotypes.

Conclusion: Tasting ability and adiposity measures are associated in Indian population. Large scale studies are required for evaluating the association of tasting status on adiposity in India.

1. Introduction

Human tasting ability for tasting or non-tasting phenylthiocarbamide (PTC) was discovered in 1932 (Fox, 1932; Guo and Reed, 2001a, 2001b) and has been extensively used for assessing population level biological variation in anthropological studies (Drayna, 2005). The threshold of PTC tasting follows bimodal distribution (Riddell and Wybar, 1944; Kalmus, 1952). The relationship between 6-n-Propylthiouracil (PROP) taste blindness, chemically similar substitute of PTC and better characterized nature of its toxicity (Fischer, 1971) might be a marker for increased body weights was first suggested by Tepper and Nurse (1998).

Insensitivity to PTC has shown associations with food preferences (Duffy and Bartoshuk, 2000; Ullrich et al., 2004) and dietary fat perception (Tepper and Nurse, 1998; Hayes and Duffy, 2007; Hayes and

Duffy, 2008). It has also been suggested that non-tasters consume more energy and gain more body weight due to their craving for larger variety of foods especially high-fat foods, in comparison to tasters (Tepper and Nurse, 1997; Keller et al., 2002). Several studies in the past have shown relationship between ability to taste a bitter substance 6-n-propylthiouracil (PROP, a chemical related to PTC) and body mass index (BMI) in adults (Timpson et al., 2005; Goldstein et al., 2005; Drewnowski et al., 2007; Lumeng et al., 2008) and in children (Keller and Tepper, 2004) but results were inconclusive. Moreover, a Mendelian randomization study has confirmed the causal relationship between PROP tasting status and body weight among 6 years old girls of European population (Bouthoorn et al., 2014).

Inheritance of PTC tasting ability was suggested as Mendelian recessive trait (T: tasting and t: non-tasting) (Blakeslee, 1931; Martin, 1975). It was found that ~75% of human variation related to PTC

Abbreviations: BMI, Body mass Index; PTC, phenylthiocarbamide; PROP, 6-n-Propylthiouracil; DNA, Deoxyribonucleic acid; PCR, Polymerase chain reaction; RFLP, restriction fragment length polymorphism; *TAS2R38*, Taste receptor 2 member 38; WHR, waist-hip ratio; EDTA, Ethylenediaminetetraacetic acid

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<https://doi.org/10.1016/j.mgene.2018.08.001>

Received 11 May 2018; Received in revised form 11 July 2018; Accepted 6 August 2018

Available online 07 August 2018

2214-5400/ © 2018 Published by Elsevier B.V.

tasting ability can be explained by *TAS2R38* gene (taste receptor, type 2, member 38) located on chromosome 7q (Kim et al., 2003). There are only five epidemiological studies, published to date, that have assessed the association of PTC tasting ability with premenstrual syndrome (Sharma et al., 2013), adolescent growth trends (Sharma and Kaur, 2014), early childhood caries (Pidamale et al., 2012), obesity (Veluswami et al., 2015) and BMI (Deshaware and Singhal, 2017) in Indian population. A study that has reported the frequency distribution of *TAS2R38* gene in Indians living in USA (Pemberton et al., 2008). There is only one Indian study that has investigated the frequency of *TAS2R38* and the influence of ability to taste PROP on BMI (Deshaware and Singhal, 2017). The sample ($n = 393$) in this study was based on convenient sampling, thus, represented four major geographical locations, and was restricted to the phenotype of BMI. Due to limited information on relationship between PTC tasting ability and adiposity with respect to *TAS2R38* gene in India, we hypothesized that non-tasters have higher levels of adiposity measures than non-tasters. Therefore, our aim was to assess the influence of PTC tasting ability genotypes on measures of adiposity.

2. Materials and methods

2.1. Study population

The study sample was selected from population of district *Sirohi*, Mount Abu, in the state of Rajasthan, India. We have adopted population based study design for recruiting 303 participants (208 children and 95 adults) after taking appropriate written consent. Study was conducted after obtaining ethical clearance from Department of Anthropology, University of Delhi.

2.2. Data collection and measurements

Questionnaire was administered for collecting information on demographic, life style and diet. Data on physical measures such as height, body weight, waist and hip circumference were collected by trained anthropologists using standard anthropometric techniques. For all the measures three readings were taken in order to check their reliability, and maximum acceptable difference between the readings for height and circumferences were < 0.5 cm and for body weight was < 0.5 kg.

The PTC tasting sensitivity was assessed using the Harris and Kalmus method (Harris and Kalmus, 1949) which determines the lowest concentration of substance which a subject can discriminate from their local water. Finger prick samples were collected in micro-centrifuge tubes, containing EDTA as an anticoagulant, from the study participants. Care was taken to keep the blood samples at cold temperature (4 degrees Celsius in ice box) in field conditions, prior to freezing them in deep freezers at -20 degrees Celsius.

2.3. Genetic data

DNA was isolated from the frozen blood samples using phenol chloroform method at Public Health Foundation of India, Gurgaon. Commercially available Kits (Xgene SV Cell Mini kits, Krishgen Biosystems) were used to isolate DNA from the available whole blood samples. Since *TAS2R38* polymorphism (A49P) is a widely studied marker for tasting ability and non-synonymous in nature makes it a reasonable choice for this study. The A49P (rs713598) polymorphism of *TAS2R38* was amplified by the following set of forward and reverse primers (Ooi et al., 2010) - forward primer: 5'-CCTTCGTTTCTGGTG AATTTTGGGATGTAGTGAAGAGCGG-3'; reverse primer: 5'-AGGT TGGCTTGGTTTGAATCATC-3'. The amplification was performed in a total of 10ul reaction mixture containing ~ 100 ng DNA template, 25 ng each of forward and reverse primers, 200 μ M dTPs mix, 1.5 mM $MgCl_2$, 1 \times Taq polymerase buffer (Fermentas), and 1 U of Taq DNA

polymerase (Fermentas). The PCR reaction cycles included initial denaturation at 94 °C for 5 min; followed by 30 cycles of denaturation at 94 °C for 30 s, annealing at 64 °C for 45 s and extension at 72 °C for 45 s; followed by final extension at 72 °C for 5 min. The PCR product of 221 bp was visualized in 2.5% agarose gel prior to restriction digestion.

The PCR product was digested with fast digest 1 U *HaeIII* restriction enzyme (Fermentas) and incubated at 37 °C for 15 min. The digested RFLP products were resolved in 3% agarose gel. The bitter non-tasters AA homozygote yielded the 221 bp uncut fragment only, the AP heterozygote bitter tasters yielded the 221, 177 and 44 bp fragments, while the PP homozygote bitter tasters yielded two bands of 177 and 44 bp.

2.4. Statistical methods

All the adiposity measures, like BMI, WHR, waist circumference and body weight, were transformed into z-scores for association analysis, separately, among children and adults. *TAS2R38* (A49P) gene was tested for Hardy-Weinberg equilibrium and genotypic distribution was estimated for three genotypes: AA, AP, and PP with respect to PTC tasting ability. Student's *t*-test was used for evaluating associations between adiposity measures and PTC tasting ability based upon their genotypes, i.e. AA (as tasters) and AP + PP (as non-tasters). Linear regression was used for testing the association of tasting status with adiposity measures. In addition, linear regression was also used for assessing sex-wise association between adiposity measures and *TAS2R38* (A49P). PTC tasters were further divided into two categories based upon their quantitative 14 threshold levels, i.e. ≤ 8 and > 8 . The central value of 8 was driven by almost equal number of tasters in two groups. The association of adiposity measures and two generated tasting levels (i.e. ≤ 8 and > 8) was assessed using Student's *t*-test.

3. Results and discussion

The general characteristics of the study participants have been described in Table 1. The mean age of children was between 14 and 15 years (standard deviation (SD) = 1.7–1.9) in tasters and non-tasters, and between 20 and 22 years (SD) = 3.1–4.4) for taster and non-taster adults (Table 1). Globally, taster is a major phenotype in human population in comparison to non-tasters (Guo and Reed, 2001a, 2001b; Kim and Drayna, 2005). In our study sample also, 91.3% and 91.5% of children and adults, respectively were tasters. Among children, 52.6% of boys and 47.4% of girls were tasters, whereas, among adults; 64.4%

Table 1
Characteristics of tasters and non-tasters in study population.

	Children (N = 208)		Adults (N = 95)	
	Tasters	Non-tasters	Tasters	Non-tasters
N (%)	N (%)	N (%)	N (%)	N (%)
	190 (91.3)	18 (8.7)	90 (91.5)	5 (8.5)
Boys (%)	100 (52.6)	13 (72.3)	58 (64.4)	4 (80.0)
Girls (%)	90 (47.4)	5 (27.7)	32 (35.6)	1 (20.0)
	Mean (\pm SD)	Mean (\pm SD)	Mean (\pm SD)	Mean (\pm SD)
Age (in years)	14.4 (1.70)	14.7 (1.90)	20.6 (3.1)	22.4 (4.4)
Z-score of BMI	0.004 (0.98)	-0.05 (1.20)	0.08 (0.80)	-0.26 (0.83)
Z-score of WHR	0.02 (1.03)	-0.22 (0.50)	0.07 (0.94)	-1.24 (1.3)
Z-score of body weight	-0.003 (0.99)	0.04 (1.10)	0.01 (0.99)	-0.13 (1.2)
Z-score of WC	0.11 (1.00)	-0.12 (0.92)	0.04 (0.98)	-0.74 (1.3)

BMI: body mass index; WHR: waist hip circumference; WC: waist circumference;

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