Threshold Distributions of Phenylthiocarbamide (PTC) in the Chinese Population[a]

SUN-WEI GUO,[b,f] FU-MIN SHEN,[c] YUE-DONG WANG,[d] AND CHANG-JIANG ZHENG[e]

[b]*Institute of Human Genetics and Division of Epidemiology, University of Minnesota, Minneapolis, Minnesota 55454-1015, USA*
[c]*Department of Epidemiology, Shanghai Medical University, Shanghai, China*
[d]*Department of Biostatistics, University of Michigan, Ann Arbor, Michigan 48109-2029, USA*
[e]*Epidemiology Branch, NIDCD/NIH, Bethesda, Maryland 20892, USA*

ABSTRACT: The ability to taste phenylthiocarbamide (PTC) is a well-documented Mendelian trait. Mapping and cloning the gene(s) responsible for the PTC tasting ability would help to delineate the molecular basis for the variations in PTC tasting ability in humans and to shed new light on taste chemosensory functions. In view of the spectacular successes in genome science, the positional cloning strategy seems to be a feasible approach to the isolation of the gene(s) underlying the PTC tasting ability. As a first step toward mapping the gene(s), we collected PTC taste threshold data on 106 individuals, most of them being university students, in Shanghai, China. Using various parametric and nonparametric statistical methods, we have found that the data set is best described by a bimodal distribution. The frequency of PTC nontasters is estimated to be 10%. This is consistent with the view that the PTC nontasting ability follows a recessive mode of inheritance. Several authors had previously reported PTC data on Chinese living outside China. Our data are, to our knowledge, the first ever collected from the Chinese population within China.

The ability to taste phenylthiocarbamide (PTC) or its chemically related compound, 6-*n*-propylthiouracil (PROP), is a well-documented Mendelian trait.[1] Mapping and clining the PTC/PROP gene(s) would help delineate the molecular basis for the variations in PTC/PROP tasting ability in humans and to provide much-needed new insight into taste chemosensory functions. In view of recent successes in human genome sciences, we propose to use the positional cloning strategy to isolate the gene(s). As a first step toward this goal, we collected PTC taste threshold data on 106 individuals (40 females and 66 males) in Shanghai, China, and examined the threshold distribution using various parametric and nonparametric statistical methods.

SUBJECTS AND METHODS

The majority of the study subjects were college students in Shanghai Medical University. The mean age of the subjects is 24.9, with a range of 9–45. All subjects were

[a] This research was supported by Grants R29-GM52205 and R01-GM56515 from NIH, and a grant-in-aid from the Graduate School of the University of Minnesota.

[f] Address correspondence to: Sun-Wei Guo, Ph.D., Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, MN 55454-1015. Tel: (612) 626-8141; fax: (612) 624-0315; email: swguo@med.umn.edu

tested by the serial dilution technique of Harris and Kalmus,[6] with the boiled tap water replaced by distilled water.

Maximum likelihood method was used to fit the threshold data. Let T be a random variable representing the lowest concentration of PTC a subject can detect. We assume that $X = \log T$ follows a logistic distribution F. We note that, since there are only 14 different solutions, the actual threshold T is interval censored. The following three models are considered:

Model I: $F(x) = L(x; a, b)$,
Model II: $F(x) = pL(x; a_1, b_1) + (1 - p)L(x; a_2, b_2)$,
Model III: $F(x) = p^2L(x; a_1, b_1) + 2p(1 - p)L(x; a_2, b_2), +(1 - p)^2L(x; a_3, b_3)$

where

$$L(x; a, b) = \frac{1}{1 + e^{-(x-a)/b}},$$

is the logistic function.

If n_i $(i = 0, \ldots, K)$ is the number of observations located in the ith interval, the likelihood is

$$L = \prod_{i=0}^{K} [F(x_{i+1}) - F(x_i)]^{n_i}.$$

The log likelihood is

$$l = \sum_{i=0}^{K} n_i \log[F(x_{i+1}) - F(x_i)].$$

As a diagnosis of the parametric models, a nonparametric, smoothing spline density estimation procedure[2] was also used. No specific form such as the normal or logistic distribution is assumed for the density function. This procedure estimates the density functions nonparametrically using smoothing splines.[5] It allows the estimation of the shape of the density function and the number of bumps without assuming any functional form of the threshold distribution.

RESULTS AND DISCUSSION

The results listed in TABLE 1 suggest that, while (bimodal) Model II fits the data significantly better than (unimodal) Model I, (trimodal) Model III is not significantly better than Model II. Based on Model II, the estimated proportion of nontasters is 0.1, with a 95% confidence interval (0.8104, 0.9896).

TABLE 1. Model Fitting and Parameter Estimation

Model	a_1	b_1	a_2	b_2	a_3	b_3	p	Log-Likelihood
I	−7.23	0.66	—	—	—	—	—	209.800
II	−7.43	0.39	−3.85	1.08	—	—	0.90	189.824
III	−7.43	0.39	−4.33	1.13	−1.00	0.09	0.93	189.821

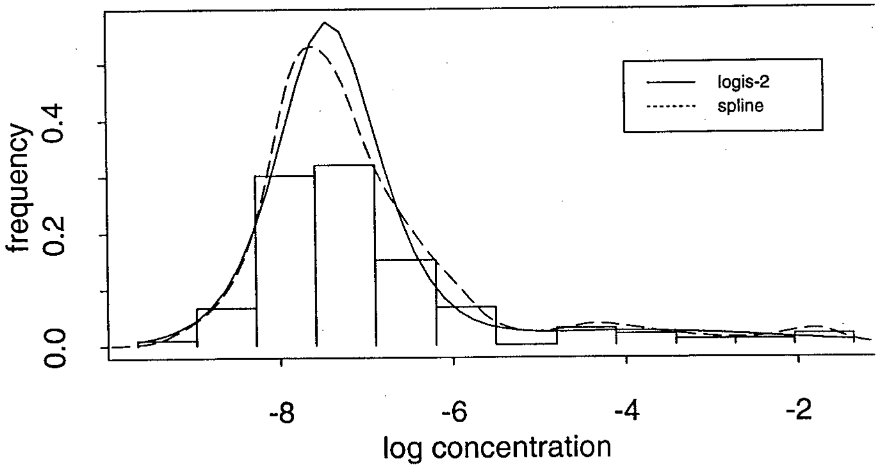

FIGURE 1. Histogram and the estimated density functions by Model II and by the smoothing spline procedure.

We also used the normal distribution and obtained the same conclusion.

FIGURE 1 shows that the fitted distribution based on Model II is very close to the nonparametric estimate of the density function, although the nonparametric density estimate has three bumps. This might suggest that Model III is slightly better than Model II, but the small sample permits no definite conclusion.

In summary, both parametric and nonparametric analyses suggest that the bimodal distribution fit the PTC data well. This is consistent with the classical view of recessive mode of inheritance for PTC insensitivity. Several authors[4–8] had previously reported PTC data on Chineses living *outside* mainland China. Our data are the first ever collected from the Chinese population *within* China. Notably, our estimate of the PTC nontaster frequency agrees with previous estimates.[4–8]

REFERENCES

1. SNYDER, L. H. 1931. Inherited taste deficiency. Science **74:** 151–152.
2. GU, C. & C. QIU. 1993. Smoothing spline density estimation: Theory. Ann. Statist. **21:** 217–234.
3. GU, C. 1993. Structural multivariate function estimation: Some automatic density and hazard estimates. J. Am. Statist. Assoc. **88:** 495–504.
4. BARNICOT, N. A. 1950. Taste-deficiency for phenylthiourea in African Negroes and Chinese. Ann. Eugen. **15:** 248–254.
5. FUKUOKA, G. 1936. Frequency of taste-blindness among the Japanese and related races. Eugen. News **21:** 52–54.
6. HARRIS, H. & H. LAMUS. 1949. Improvement in the classification of the taster genotypes. Ann. Hum. Genet. **22:** 222–230.
7. LUGG, J. W. H. & J. M. WHYTE. 1955. Taste thresholds for phenylthiocarbamide of some population groups. I. The thresholds of some civilized ethnic groups living in Malay. Ann. Hum. Genet. **19:** 209–311.
8. PARR, L. W. 1934. Taste blindness and race. J. Hered. **25:** 187–190.