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GENETICS OF PERCEPTION '98
6-*n*-Propylthiouracil: A Genetic Marker for Taste, with Implications for Food Preference and Dietary Habits

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6-*n*-Propylthiouracil (PROP) and phenythiocarbamide (PTC) are members of a class of compounds known as "thioureas." These compounds carry the chemical group N-C=S, which is responsible for their characteristic bitter taste (for review, see Bartoshuk et al. 1994; Drewnowski and Rock 1995). As is true for many scientific discoveries, the bitterness of PROP and PTC were discovered by accident. In 1931, while Fox was synthesizing PTC in his laboratory, some of the white crystals became airborne. His colleagues perceived a bitter taste, but Fox tasted nothing. This simple observation led to a large number of family studies that investigated genetic variation in the ability to taste PTC and, in later studies, to taste PROP. PTC and PROP are of great interest to taste researchers not only as tools for understanding the genetic transmittance of taste but for gaining insight into the seemingly endless variation in taste preferences and food habits that exists in the population. The purpose of this review is to highlight the evidence supporting a role for genetic variation in taste sensitivity to PROP, in taste perception and food acceptance. Special emphasis will be placed on the potential implications that recent findings have for diet and health.

The Genetics of Taste

The incidence of taste blindness to PTC/PROP varies around the world, from ~3% in western Africa to >40% in India (see MIM 171200). Approximately 30% of the adult Caucasian population of North America are taste blind to PTC/PROP (i.e., are nontasters) and 70% are tasters. The term "nontaster" is probably a misnomer, since many so-called nontasters can taste PROP at higher concentrations.

The ability to taste PTC/PROP is present in young children and declines slowly with age (Whissell-Buechy 1990). The trait is more common in women than in men (Whissell-Buechy and Wills 1989; Bartoshuk et al. 1994), and there is limited evidence that reproductive hormones may a role in its phenotypic expression. For example, one study found that girls who were PTC/PROP tasters matured ~3.8 mo earlier than girls who were nontasters (Whissell-Buechy and Wills 1989).

Taste sensitivity to PTC and PROP can be determined by use of threshold methods. The threshold is defined as the lowest concentration of a test solution that can be distinguished from plain water. Tasters have very low thresholds for PROP (i.e., high sensitivity at low concentrations), whereas nontasters have higher thresholds (i.e., poor sensitivity at low concentrations). The distribution of taste thresholds in the population is bimodal. This bimodality is unusual in taste, since most stimuli follow a Gaussian distribution. Evidence from many studies establishes the taste threshold for PROP as being at or near 1.0×10^{-4} mol/liter for tasters and $> 2.0 \times 10^{-4}$ mol/liter for nontasters (Drewnowski and Rock 1995). Because PTC has a slight odor, PROP has replaced the use of PTC in most modern taste studies.

It was originally thought that the ability to taste PROP was inherited as a dominant Mendelian trait (see MIM 171200), a model that cannot account for the occurrence of taster offspring from nontaster parents, as observed in some studies (Olson et al. 1989). Polygenic models that include a second locus or third allele generally show a better fit with the taste data. The analysis conducted by Reddy and Rao (1989) concluded that variability in the threshold to PTC was controlled by a major locus with incomplete dominance as well as by a multifactorial component. Olson et al. (1989) proposed a two-locus model in which one locus controlled PROP/PTC sensitivity and the second locus controlled general taste ability. Another model, proposed by Reed et al. (1995), suggested that the large group of PROP tasters might be composed of two subgroups; medium tasters, who show moderate taste sensitivity to PROP, and supertasters, who are highly sensitive. As described below ("PROP Tasters and Nontasters—Different Taste Worlds"), this model is consistent with the results of many taste studies

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showing that PROP supertasters give higher intensity ratings than do medium tasters, to a wide range of oral stimuli.

Some studies have found linkage of PTC to the Kell blood group on chromosome 7, but no other linkages have been identified (MIM 171200). Until the gene(s) for PROP/PTC is identified and cloned, the exact mode of inheritance will remain controversial.

PROP and the Taste of Cruciferous Vegetables

Why does the PROP phenotype persist in contemporary human societies? One classic theory postulates that PROP-taste ability provides a selective advantage for avoidance of harmful compounds in the environment that are often bitter tasting (Drewnowski and Rock 1995). This taste aversion may have special relevance for the avoidance of certain bitter-tasting vegetables. PROP and PTC are chemically related to the isothiocyanates and goitrin, bitter-tasting compounds that are present in cruciferous vegetables such as cabbage, broccoli, Brussel sprouts, turnips, and kale. When eaten in large quantities, these compounds interfere with iodine metabolism, producing thyroid enlargement and goiterlike symptoms. Before the widespread use of iodized salt, endemic goiter was a health problem in isolated areas of the world where iodine was scarce. It has been consistently noted, however, that the incidence of thyroid-deficiency disease is relatively rare among PTC tasters (MIM 171200), and this lower incidence has been attributed to the avoidance of cruciferous vegetables by PTC tasters (Drewnowski and Rock 1995).

Several studies have attempted to demonstrate a relationship between PROP-taste sensitivity and rejection of bitter vegetables, but they have been inconclusive (Drewnowski and Rock 1995). A major challenge to these studies is that raw vegetables are not a preferred food in our culture (Meiselman 1988). Aversions to vegetables may occur for many reasons other than their bitter taste, including their appearance or texture, social or cultural taboos associated with eating them, or their unpleasant gastrointestinal effects for some people. These negative attitudes could overshadow the influence of taster status on the outcome of taste studies. Nevertheless, a colleague and I recently have found, among preschool children, evidence linking taster status with the taste of raw broccoli (B. J. Tepper and L. Steinmann, unpublished data). Taster children disliked raw broccoli, whereas nontaster children liked raw broccoli. These results are striking, given that food rejection is common among young children (Birch et al. 1996). Our data support previous work by Anliker et al. (1991) that suggested a role for inherited taste characteristics in the development of food preferences in childhood.

Other lines of evidence suggest that the avoidance of bitter-tasting foods may have certain health *dis*advantages for populations consuming Western diets (Drewnowski and Rock 1995). Epidemiological studies indicate that diets low in fruits and vegetables and high in fat may be associated with increased risk of certain cancers. Since many of the phytochemicals found in fruits and vegetables prevent carcinogenesis in laboratory animals, higher consumption is generally recommended. Despite public-health efforts to increase fruit and vegetable consumption, intake in the population is low. Drewnowski et al. (1997a) have hypothesized that the avoidance of bitter-tasting fruits and vegetables by PROP tasters contributes to this unhealthy eating pattern and might pose a barrier to future diet change. Initial studies have demonstrated that solutions containing naringin, the bitter ingredient found in grapefruit juice, were less acceptable to PROP tasters than to PROP nontasters. Taster status was also associated with lower dietary preference for grapefruit juice. More studies are needed to determine the predictive value of PROP-taster status as a marker for cancer risk.

PROP Tasters and Nontasters—Different Taste Worlds

Increasing evidence suggests that PROP tasters show greater sensitivity to a wide range of oral stimuli, including bitter tastes not associated with fruits and vegetables, various sweet tastes, oral irritants such as chili pepper, and the textural sensations of fats (see following sections). However, these perceptual differences are of little practical significance unless they can be linked to differences in liking and acceptability. Far fewer studies have investigated the acceptability of these stimuli to tasters and nontasters, and not all studies agree that PROP tasters universally dislike these sensations. One of the difficulties is that the majority of studies utilize laboratory solutions as taste stimuli. Laboratory solutions lack the gustatory qualities of real foods and beverages and are not highly palatable to humans. The use of more-realistic food stimuli in future studies should help to resolve many of the inconsistencies that exist in the current literature.

Bitter and Sweet Tastes

Solutions of caffeine, quinine, and isohumulones (the bittering agents in beer) are more intensely bitter to PROP tasters (Mela 1990; Bartoshuk et al. 1994). Some foods—including sodium benzoate, a common food preservative, and the salt substitute potassium chloride—have bitter aftertastes that are also more noticeable to PROP tasters (Bartoshuk et al. 1994). The taste of sucrose is also more intensely sweet to PROP supertasters than to medium tasters and nontasters, and similar results have been reported for some high-intensity sweeteners such as saccharin and neohesperidin dihydrochalone (Bartoshuk et al. 1994). Using an unusual approach to assess liking responses, Looy and Weingarten (1992) surreptitiously photographed the facial expressions of subjects while they judged the sweetness intensity of sucrose solutions. PROP tasters more frequently showed classic rejection responses such as frowning and grimacing. In contrast, PROP-taste sensitivity did not predict hedonic responses to sucrose or saccharin in more-recent studies (Drewnowski et al. 1977b).

Capsaicin

Capsaicin, the compound responsible for the oral burn of chili pepper, is more intensely hot to PROP tasters than to nontasters (Bartoshuk et al. 1994; Tepper and Nurse 1997). Capsaicin has some striking short-term and long-term effects on oral perception. After even a single brief exposure, capsaicin lingers on the palate (Karrer and Bartoshuk 1991), making it a difficult substance for use in taste studies. Multiple brief exposures cause "sensitization," or enhancement of the perceived burn (Green 1990). Sensitization may be responsible for the steady increase in hotness that typically occurs with successive bites of spicy foods. Repeated exposure to capsaicin (over the course of days) decreases the overall burn intensity (Stevenson and Prescott 1994). This phenomenon might explain why frequent consumers of chili are less sensitive to its perceived burn (Stevenson and Yeomans 1993).

The acquisition of a taste preference for chili is not well understood. Chili pepper is generally aversive to those tasting it for the first time, but liking develops with repeated exposure (Rozin and Schiller 1980). Chili enjoys widespread use as a basic flavor principle in the cuisine of many diverse cultures (Rozin 1978). If liking of chili was closely linked with PROP-taster status, then areas of the world where chili is widely consumed would have a high frequency of nontasters in the population. Also, most chili lovers would be expected to be nontasters. Evidence in support of these hypotheses is currently lacking, although laboratory studies addressing these questions have yet to be done. Resolving the complex interactions among genetic taste factors, dietary experience, and liking of chili pepper will pose intriguing challenges for taste researchers in the future.

Studies have also examined the perception of other pungent spices that are structurally related to capsaicin, such as piperine, from black pepper, and zingerone, isolated from ginger (Silver and Finger 1991). In taste studies, these compounds offer several advantages to capsaicin, because they elicit weaker burn intensities with a shorter duration (Prescott and Stevenson 1996). Prescott and Stevenson (1996) recently observed that the frequent use of chili decreased the psychophysical response to zingerone, suggesting that the two compounds act through a common mechanism. This observation is especially intriguing in light of data, in rodents, showing that capsaicin, zingerone, and piperine bind to different subtypes of a common receptor (Liu and Simon 1996). It would be of interest to determine whether PROP-taster status plays a role in the perception or acceptance of these pungent spices.

Fat

Recent studies from our laboratory have focused on the relationship between PROP-taste sensitivity and perception and liking for fat (Tepper and Nurse 1997, 1998). Normal-weight young adults were classified as nontasters, medium tasters, or supertasters of PROP and evaluated fat content and liking of high-fat (40% fat) and low-fat (10% fat) salad dressings. As shown in figure 1*A,* the nontasters could not distinguish the two dressings in terms of fat content, whereas the medium tasters and supertasters gave higher fat-content ratings to the 40%-fat dressing. The liking responses were more difficult to interpret than the fat-content ratings. As shown in figure 1*B,* the nontasters liked the high-fat dressing more than the low-fat dressing, whereas the medium tasters and supertasters liked both samples equally well. Since nontasters found no difference in fat content between the two samples, it is unclear what attributes drove their preference for the high-fat dressing. On the other hand, perhaps medium tasters and supertasters perceived the high-fat dressing to be too oily or fatty, which contributed to their lack of preference for this sample. This response might be analogous to the dislike of intensely sweet stimuli by PROP tasters in the sucrose studies mentioned previously (Looy and Weingarten 1992). Many more high-fat foods will have to be tested before the nutritional relevance of these findings can be determined.

Physiological Basis for Taster-Nontaster Differences

Anatomical studies have provided clues as to why PROP tasters may be more sensitive to such a broad range of oral stimuli. The taste papillae are the structures that hold and orient the taste buds on the tongue. PROP tasters have both a higher density of taste papillae on the apex of the tongue and more-functional taste buds (Bartoshuk et al. 1994; Tepper and Nurse 1997). This might explain the greater sensitivity of PROP tasters to basic tastes such as bitter and sweet. In rodents, the taste buds are surrounded by trigeminal fibers (Bartoshuk et al. 1994). The trigeminal (5th cranial) nerve carries information about oral irritation, including chemical heat and cooling, and pungency (Green 1990). If a similar configuration exists in humans, this might explain why

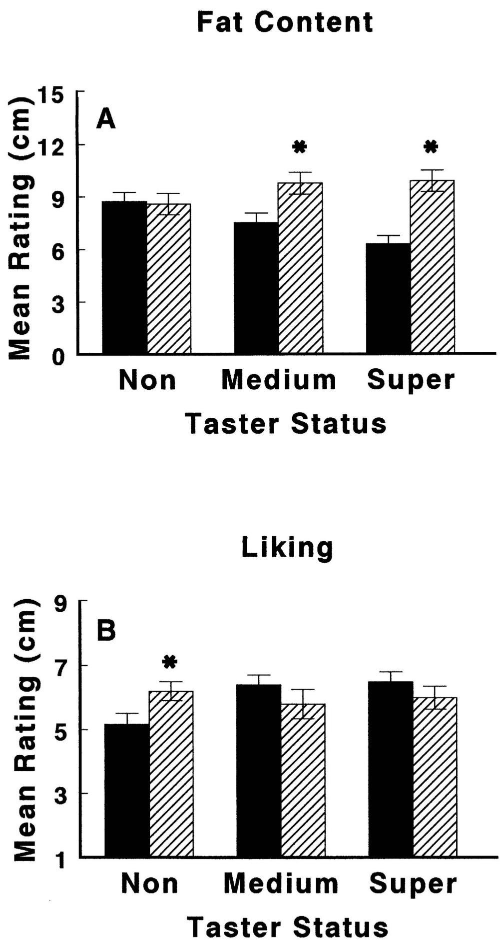

Figure 1 Fat-content ratings and preference for 10%-fat (*blackened bars*) and 40%-fat (*hatched bars*) salad dressings, in subjects classified as nontasters, medium tasters, and supertasters of PROP. Fat content was evaluated by 15-cm line scales; preference was rated on the basis of 9-point category scales. Medium tasters and supertasters judged the 40%-fat dressing to be higher in fat than the 10%-fat dressing; nontasters could not distinguish the two samples (*A*). Medium tasters and supertasters showed no preference for either sample; nontasters preferred the 40%-fat sample (*B*). An asterisk (*) denotes significant difference ($P < .05$) between the 10%-fat and 40%-fat samples. Values are means + standard error of the mean. (Adapted with permission from Tepper and Nurse 1997, 1998)

PROP tasters have increased sensitivity to capsaicin and, possibly, other pungent spices.

The trigeminal nerve is also involved in other sensory functions, including the perception of fat. The perception of fat in food is primarily a function of its texture, with flavor playing a more minor role (Mela and Marshall 1991). Although not well studied, texture perception is mediated by mechanoreceptors located on the surface of the tongue and palate and between the teeth (Cardello 1996). Texture sensations are due to mouthfeel characteristics such as the presence of moistness or particles and to mechanical characteristics that are associated with resistance to applied forces in the mouth. Sauces and gravies that lack particles are perceived as smooth and creamy in the mouth. In contrast, the force of chewing a food such as peanut brittle defines its primary texture characteristic—hardness. The presence of more trigeminal fibers on the surface of the tongue might give PROP tasters an advantage in perceiving fat in viscous fluids such as salad dressings and in creamy foods such as mayonnaise and margarine. Interestingly, sweet-fat mixtures, such as sweetened dairy products, fail to show the expected responses in PROP tasters (Drewnowski et al. 1998). This observation could be due to the phenomenon of masking, wherein adding sweetness to fat tends to mask the perception of the fat (Drewnowski and Schwartz 1990). Since masking reflects integration of signals at higher brain centers (Cardello 1996), it is probably unrelated to PROP-taster status. It is not known whether PROP tasters are more sensitive to other textural sensations, such as the crunchiness of snack chips and crackers, which could also influence food choice and dietary intake.

Understanding Food Behavior—Future Directions

Laboratory studies provide a reliable means of characterizing taster-nontaster differences in perception and liking for specific foods. However, laboratory taste tests have limitations in that only a few representative foods can be tested at one time. For this reason, food-preference surveys may be more revealing of the complex food habits and experiences of tasters and nontasters. Food-preference surveys consistently show that PROP tasters have more overall food dislikes than do nontasters and that they dislike strong-tasting foods such as anchovies, sauerkraut, dark beer and ales, black coffee, and strong cheeses (Drewnowski and Rock 1995).

A final consideration is whether the diets of PROP tasters are fundamentally different from those of nontasters. For example, do PROP tasters consume bland or monotonous diets, as the results of food-preference surveys seem to suggest? Are the diets of PROP tasters lower in cancer-fighting fruits and vegetables or lower in fat, diet patterns associated with varying degrees of chronic-disease risk? These questions can only be answered by use of food-consumption data, typically derived from food-intake questionnaires or food diaries. Diet studies are difficult to accomplish because they are labor intensive and usually involve large numbers of subjects. Although comprehensive analyses of the dietary patterns of tasters and nontasters have yet to appear in the literature, they are undoubtedly the focus of current investigations in several laboratories.

Another interest in my laboratory is in understanding the relationship between taster status and body weight. We hypothesized that, if PROP tasters followed the restrictive diets typically ascribed to them, they should have lower body weights. Among male subjects who participated in the fat-perception study mentioned previously, we observed that PROP supertasters had slightly but not significantly lower body weights than did medium tasters or nontasters (Tepper and Nurse 1998). A second study, involving middle-aged men, also revealed that those who were classified as PTC tasters had slightly lower body weights than did nontasters (B. J. Tepper and N. Ullrich, unpublished data). These provocative findings require further confirmation, but they provide indirect evidence that the dietary patterns of PROP tasters may have important implications for weight status. This relationship was not observed in women. Studies are presently underway to determine whether this difference represents a true sexual dimorphism or simply reflects the greater influence of dieting on body weight in women.

Finally, research over the past several decades has yielded many new and exciting findings about the relationship between inherited taste characteristics, taste preferences, and food selection. Current studies raise more questions than they answer about the potential role for genetic taste factors in human health and disease, and the exact nature of this relationship remains to be elucidated. A better understanding of the genetic basis of taste, including identification of the relevant genes and DNA markers, will accelerate progress in the field.

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Electronic-Database Information

URLs and accession numbers for data in this article are as follows:

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov (for PTC tasting [171200])

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