LETTER TO THE EDITOR

Phenylthiocarbamide (PTC) Preference Among Laboratory Mice: Understanding of a Previously "Unreplicated" Report

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In two-bottle preference tests aversion to phenylthiocarbamide (PTC) develops over a period of days. Thus, as previously reported, following experience with appropriate concentrations of PTC, mice of the BALB inbred strain display an aversion in contrast to C57BL inbred mice. It is suggested that differential learning in a conditioned taste-aversion paradigm might be responsible for the phenotypic strain contrast. The difference in PTC aversion phenotype among mice could be due to differences in any mechanism contributing to differential flavor toxicosis conditioning instead of, or in addition to, strain differences in sensitivity to the sensory attributes of PTC.

KEY WORDS: phenylthiocarbamide; PTC; taste genetics; conditioned aversion; mouse.

In 1970 Klein and DeFries reported a "similar polymorphism of taste sensitivity to PTC in mice and men" (Klein and DeFries, 1970). That report of genetically mediated differences in taste sensitivity to phenylthiocarbamide (PTC), among members of a nonhuman mammalian species which is amenable to genetic and physiological experimentation, generated considerable interest among both behavioral geneticists and sensory physiologists interested in mechanisms of taste. However, in the approximately 15 years since the Klein and DeFries paper there have been no published sequelae. This dearth of follow-up reports is not because of a lack of experimentation. Investigators in at least three separate labo-

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ratories (ours and two others; personal communication) had been unable to obtain the strain difference in preference for PTC which was the basis for the Klein and DeFries report. The purpose of the present communication is twofold. First, we report that we have approached a replication of the observations of Klein and DeFries with genotypes closely related to those used in the initial report. Second, we offer a possible explanation for the apparent difficulty in replication.

PTC is, of course, famous as a prototypical example of a perceptual polymorphism among humans which is influenced by segregation at a single autosomal locus. To humans who are tasters, PTC is subjectively intensely bitter at concentrations well below those which are discriminated by nontasters (Blakeslee, 1932). PTC is also quite toxic when ingested; as a food additive it can be a lethal poison for rodents (Richter and Clisby, 1941). We believe that the characteristics of PTC of subjective bitterness to humans and toxicity to rodents, combined with the methodology of two-bottle preference testing, obscured an appreciation of the importance of experience in determining the preference of mice for solutions containing PTC.

To explain the PTC results of Klein and DeFries (1970) we invoke the well-studied phenomenon of conditioned taste aversion (aka flavor toxicosis conditioning, bait shyness) and emphasize a distinction between inferred taste sensitivity and observed preference ratios from two-bottle preference testing. The conditioned taste aversion phenomenon is a particularly dramatic instance of Pavlovian conditioning. The basic taste aversion conditioning paradigm consists of pairing a distinctive taste as a conditioned stimulus (CS) with exposure to a toxic substance (physiological poison) as an unconditioned stimulus (US). After such pairing of CS with US it is frequently the case that normally neutral or even preferred CS tastes will be avoided on subsequent opportunities (Barker et al., 1977). The conditioned taste aversion phenomenon has been utilized in a wide variety of contexts, including investigations with inbred mice concerning genetic differences in sensitivity to particular US (Horowitz and Whitney, 1975) and studies of genetic differences in sensory detection of various CS (Wysocki et al., 1977; Harder et al., 1984).

In two-bottle preference tests (cf. Richter, 1939; Klein and DeFries, 1970) a test substance (tastant) at some concentration is presented in one bottle while the vehicle (often water) is presented in a second bottle. The amounts consumed from each bottle are recorded after some period of time (often 24 h) and an individual preference ratio is computed as (amount consumed from tastant bottle/total amount consumed from both bottles). As is generally done, Klein and DeFries controlled for position effects by interchanging the bottles each 24 h. The results of straightforward two-