Phenylthiocarbamide (PTC) Perception in Parkinson Disease

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Objective: To examine phenylthiocarbamide (PTC) sensitivity in Parkinson disease (PD) patients and healthy volunteers to determine whether taster status represented a simple vulnerability marker for PD.

Background: The inability to taste PTC has been associated with a number of medical illnesses not typically associated with taste impairment. Abnormalities in the function/expression of G protein-signaling pathways have been implicated in PTC perception and also in dopamine expression and regulation in PD. No study has yet probed whether PTC tasting is disrupted in PD.

Method: PTC sensitivity was assessed in a small sample of 36 male PD patients and 20 healthy male comparison subjects using a standardized psychophysical method.

Results: A higher proportion of nontasters were found in patients relative to healthy comparison subjects. These differences were not explained by alterations in perception of basic taste intensity or age. Among patients, nontasters and tasters of PTC did not differ with regard to duration of illness, age of onset, severity of motor symptoms, or overall illness severity.

Conclusions: These data suggest an increase in the frequency of PTC nontaster status in PD. As phenotypic variation in PTC sensitivity is genetic in origin, this may represent a surrogate risk factor for the development of PD.

Key Words: Parkinson disease, taste, phenylthiocarbamide, PTC, genetics

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Human studies of sensitivities to the bitter-tasting antithyroid compound phenylthiocarbamide (PTC) have shown these abilities to be inherited traits determined by a dominant allele.[1,2] A G protein-coupled bitter taste receptor, TAS2R38 (also known as PTC or TAS2R) is located on chromosome 7q and has been shown to account for 85% of the variance in taste.[3] A second minor locus is seen at 16p.[3,4] Numerous studies have shown that approximately 30% of the US population are PTC "nontasters" (ie, homozygous tt), whereas 70% are "tasters" (ie, homozygous TT or heterozygous Tt) of PTC.[4,5] Although an increased prevalence of nontasters has been associated with a variety of medical disorders, to our knowledge there has been no investigation of PTC taster status in Parkinson disease (PD). Abnormalities in the function or expression of G protein-signaling pathways, which are implicated in dopamine expression and regulation,[6–8] have been reported in patients with PD.[9,10] Therefore, we hypothesized that PD patients would show a differential pattern of PTC tasting status relative to healthy comparison subjects.

MATERIALS AND METHODS

Participants

Thirty-six male patients with a diagnosis of idiopathic PD were recruited from the Parkinson's Disease Research, Education, and Clinical Center (PADRECC) at the Philadelphia Veterans Affairs Medical Center, Philadelphia, PA. The diagnosis of PD was confirmed by a movement disorders neurologist from the study team (J.E.D., G.K-F., or M.B.S.) based on standard guidelines.[11] Motor symptoms were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS).[12] Subjects were also rated for severity of illness with the Hoehn and Yahr Scale.[13] Twenty healthy male comparison subjects were recruited from the community and local houses of worship and were free of any neurologic or psychiatric disorder.

Subjects were excluded for any history of neurologic disorder (other than PD in patients), head trauma, loss of consciousness, substance abuse/dependence, any medical condition that might alter brain functioning, recent upper respiratory infection, or any condition that could affect

taste functioning. Written informed consent was obtained after complete description of the study.

Patients did not differ significantly in age (mean = 74.7 y, SD = 7.7) from healthy comparison subjects (mean = 70.8 y, SD = 8.2) [$F(1,54) = 3.0$, $P = 0.08$]. The sample was almost entirely white (96.4%), with no differences in ethnic background between the 2 groups ($\chi^2 = 1.1$, $df = 1$, $P = 0.28$). Mean UPDRS motor score was 24.0 (SD = 11.0) and the average Hoehn and Yahr stage was 2.1 (SD = 0.6). Mean age of onset was 68.1 years (SD = 8.5), and average duration of illness was 6.5 years (SD = 3.7).

PTC Perception Testing

Subjects were administered a 3.80 × 1.43 cm strip of filter paper impregnated with 0.007 mg of PTC (Carolina Biological Supply Company, Burlington, NC). Each subject was instructed to moisten their tongue with saliva and to place the filter paper in the middle of their tongue and close their mouth. Approximately after 5 to 8 seconds, they were instructed to expectorate the PTC paper and asked if they tasted anything. After recording their response, each subject was then asked to rate the intensity of their perception of the strip on a 100-mm visual analog line, ranging from 0 (no taste) to 100 mm (extremely strong taste). This method and psychophysical approach for testing PTC perception is consistent with other studies in the literature.[14–17] Any subject who reported an inability to taste the filter paper and reported an intensity of less than 35 mm was classified as a nontaster. The 35-mm value denoted the break point in the bimodal distribution of intensity ratings between tasters and nontasters.

Statistical Analysis

Statistical analysis was conducted using χ^2 and analysis of variance. While the effects of age on PTC taster status has been negligible,[4] potential confounds were assessed using linear regression. All analyses were conducted using STATISTICA 6.0 statistical software [StatSoft I. STATISTICA (data analysis software system), 2004].

RESULTS

Analysis revealed significant differences in the distribution of tasters and nontasters between the 2 groups ($\chi^2 = 4.8$, $df = 1$, $P = 0.027$), with PD patients having a larger proportion of nontasters to tasters than healthy volunteers (Fig. 1). The 2 groups did not differ in intensity ratings either among tasters [$F(1,29) = 0.71$, $P = 0.40$] or nontasters [$F(1,23) = 0.66$, $P = 0.42$]. Within the patient group, tasters and nontasters did not differ with regard to duration of illness, age of onset, motor symptoms, or illness severity (all Ps > 0.13). Linear regression analysis with age as a predictor did not alter the observed differences in taster status or affect PTC intensity ratings.

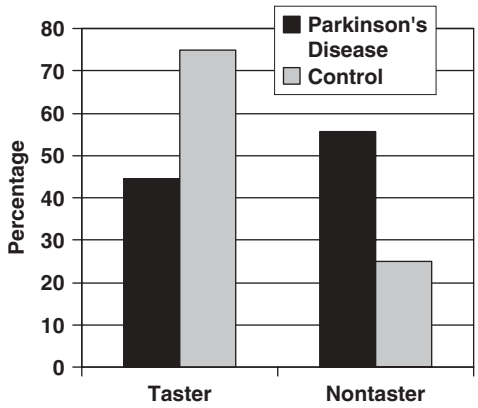

FIGURE 1. Percentage of tasters and nontasters to PTC in patients with PD and healthy comparison subjects.

DISCUSSION

These data suggest a higher frequency of PTC nontasters among patients with PD. Only 25% of healthy comparison subjects were classified as nontasters, compared with 56% of PD patients. This finding was not explained by between-group differences in basal intensity perception by tasters and nontasters, and is consistent with a recent study of overall taste perception in PD, which found no impairment in the perceived intensity, pleasantness, and identification of sucrose, quinine, citric acid, or sodium chloride.[18] In contrast, another study of basic taste perception in patients with parkinsonism,[19] a small mixed-group of patients with parkinsonism syndrome (ie, PD, PD with comorbid Alzheimer disease, and Lewy body dementia) were noted to exhibit a mild reduction in basic taste functions as measured by a whole mouth taste test[20] and the Taste Strip Test[21] relative to healthy comparison subjects. Further work with these measures in a more homogeneous idiopathic PD sample will be important to resolve some of the differences seen between studies.

As noted previously, PTC perception is mediated by a G protein-coupled bitter taste receptor, TAS2R38. G protein-coupled receptors mediate a large variety of physiologic events throughout the body, including chemosensory recognition (olfaction, taste), endocrine regulation, and even complex behavioral events.[7] Drayna and colleagues[22] found that PTC binds to both tasting and nontasting forms of the receptor with equal affinity, but the nontaster form fails to activate G protein.

Abnormalities in the function or expression of G protein-signaling pathways have been reported in PD, and the high frequency of nontasters in patients may be due to abnormalities in the function of these systems. Such a failure in G protein-signaling may interact with other genetic and/or environmental factors to produce an increased vulnerability to illness. In essence, these data suggest that individuals with recessive alleles (tt) may be at higher risk of developing PD than those with at least one of the tasting alleles (TT or Tt), and studies of unaffected first degree family members or at-risk

populations will enable this hypothesis to be tested further. PTC tasting status has been linked to a myriad of medical illnesses ranging from epilepsy to gastrointestinal ulcers, although consistent findings among these disorders have been rare.[4,23] In contrast, the handful of studies examining PTC perception in schizophrenia has consistently shown an increase in the prevalence of nontasters in patients.[24–28]

Although chromosome 7q has not been directly linked with PD, it is notable that this chromosome also contains odorant receptorlike genes, which may have some bearing on the deficits in olfactory function seen in PD patients. Indeed, a recent study found that tasters of 6-n-propylthiouracil, another genetically mediated bitter taste that shares the TAS2R38 receptor with PTC, had better (ie, lower) thresholds to the odor diacetyl than nontasters.[5] The possible relationship of PTC tasting status to the well-documented olfactory deficits seen in PD[29–33] requires further investigation.

A few caveats must be noted. The sample size was relatively small and exclusively male, and larger cohorts including women will be required to fully assess this difference in PTC tasting status. It is notable, however, that the effect size (Cohen *d*) for the difference in taster status between PD patients and healthy comparison subjects is moderately large ($d_+ = 0.63$, 95% confidence interval = $0.07 < \delta < 1.19$), and we would expect this effect to be robust in independent samples. The observed proportion of tasters and nontasters in the healthy comparison group was generally consistent with other population-based investigations of PTC sensitivity.[4] Lastly, although the age difference between groups was not significant, the PD patients were approximately 5 years older than controls. Although increasing age has been noted to have slight effects on PTC thresholds, the concentrations used in this study were suprathreshold and would not be expected to be negatively impacted by an age discrepancy of this magnitude.

These data suggest an increase in the frequency of PTC nontaster status in PD. As phenotypic variation in PTC sensitivity is genetic in origin, this may represent a surrogate risk factor for the development of PD.

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