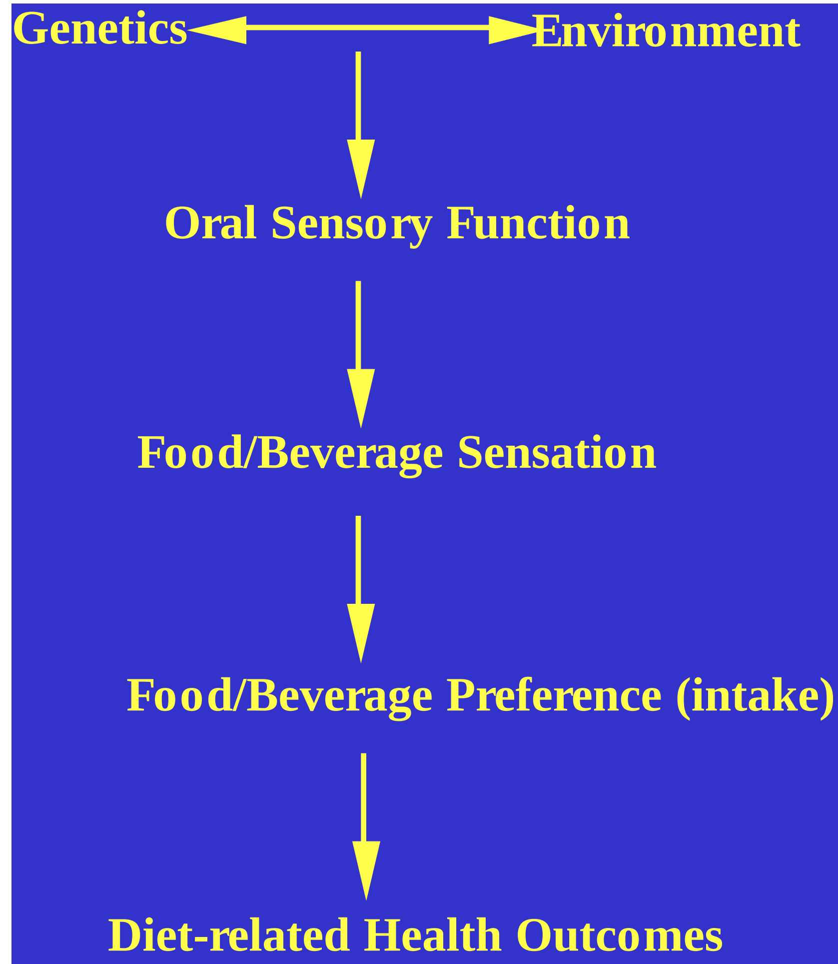
Genetic Variations, “Taste” and Dietary Behaviors

Valerie B. Duffy

The Omics of Eating Behaviors:

December 9, 2010



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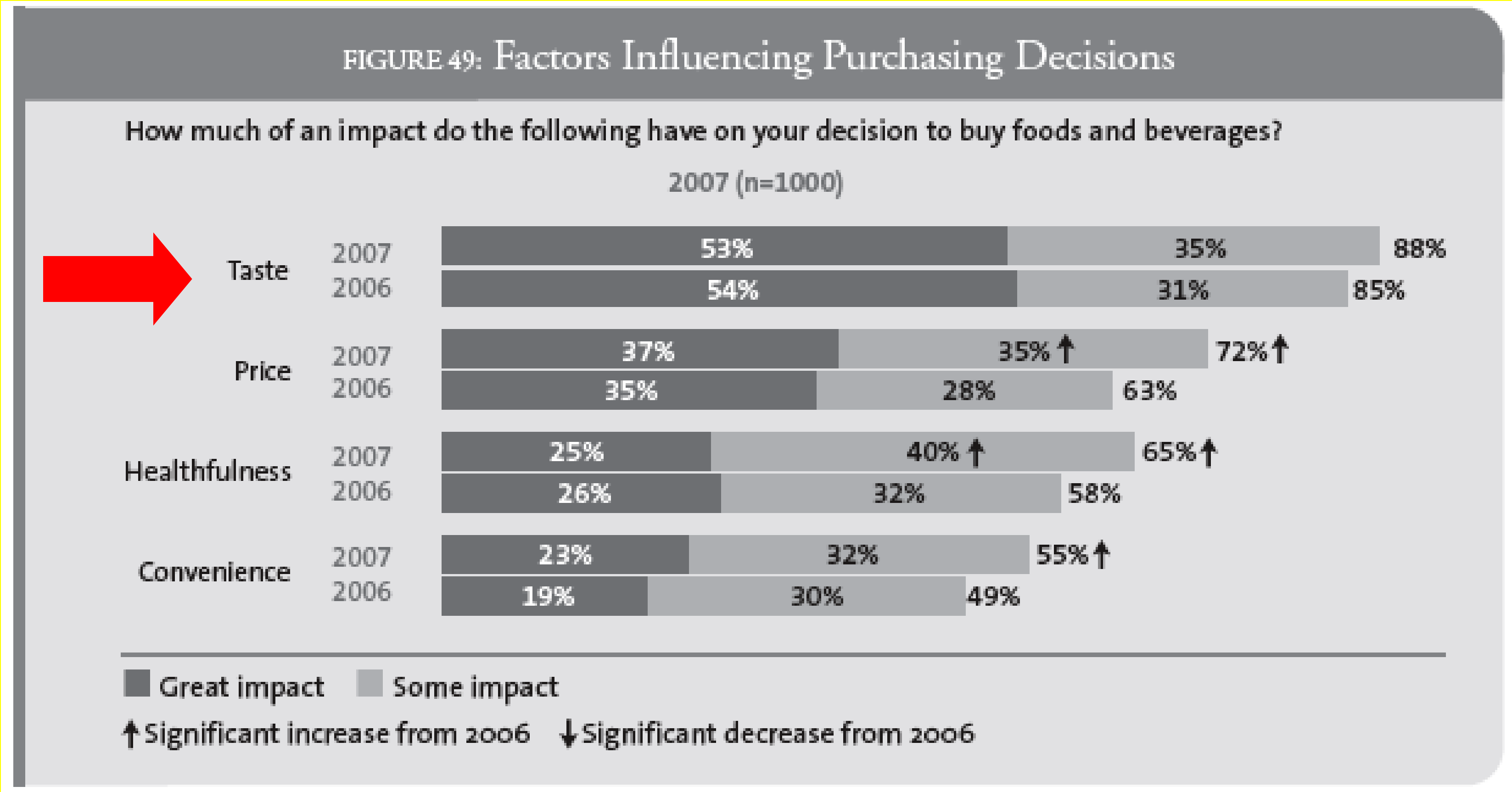
Taste is Tops

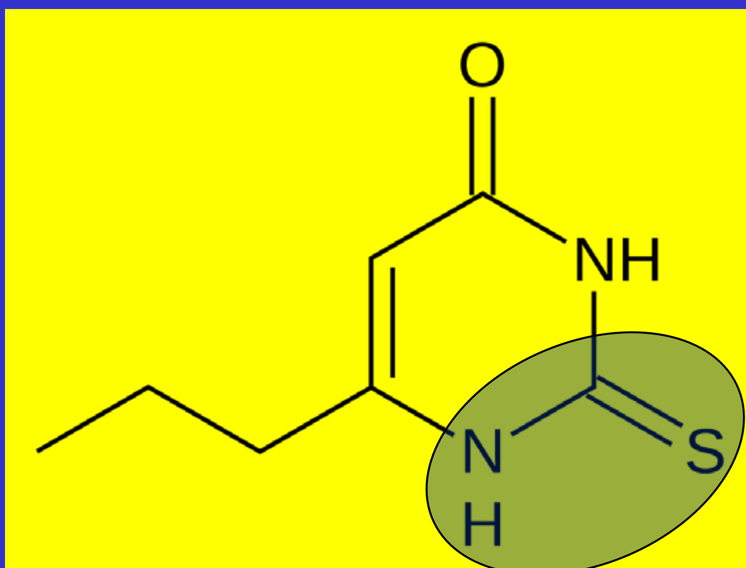


IFIC 2007 Food & Health Survey—representative US sample of 1000

Main Points

- History
- Multiple “taste” phenotypes/genotypes
- Taste pathology influences on oral sensation
- Taste as a biomarker; dietary preference as a behavioral endophenotype
- Recommendations and research needs

PTC/PROP Phenotype



SCIENCE NEWS LETTER *for April 18, 1931*

CHEMISTRY

Six in Ten "Tasteblind" To Bitter Chemical

"TASTEBLINDNESS" is the only term that can be found to describe the reaction of a fortunate forty per cent. of folk who cannot taste para-ethoxy-phenyl-thio-urea. For the other sixtry per cent. find it intensely bitter - bitter as gall, bitter as quinine, bitter enough to make them go round sticking out their tongue and making wry faces for an hour.

This curious difference in perception has been discovered by Dr. Arthur L. Fox, of the laboratories of E. I. du Pont de Nemours and Company at Wilmington, Del. He has tried this very complex organic compound on everybody who would volunteer to taste it, and has found that approximately three-fifths of his "victims" declare it intensely bitter, while the rest say that it "has no more taste than sand."

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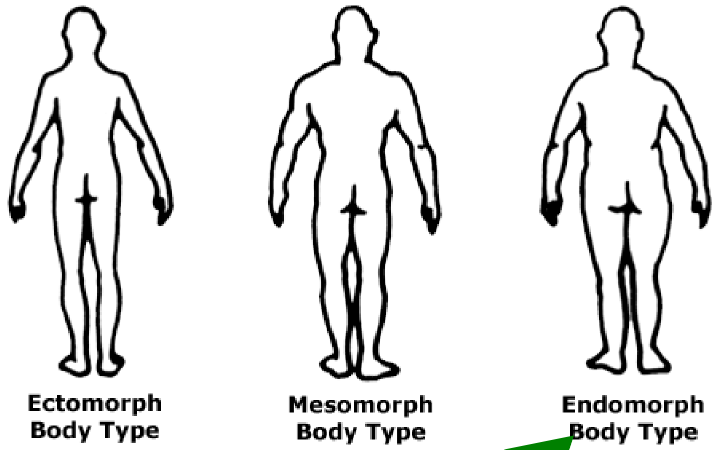
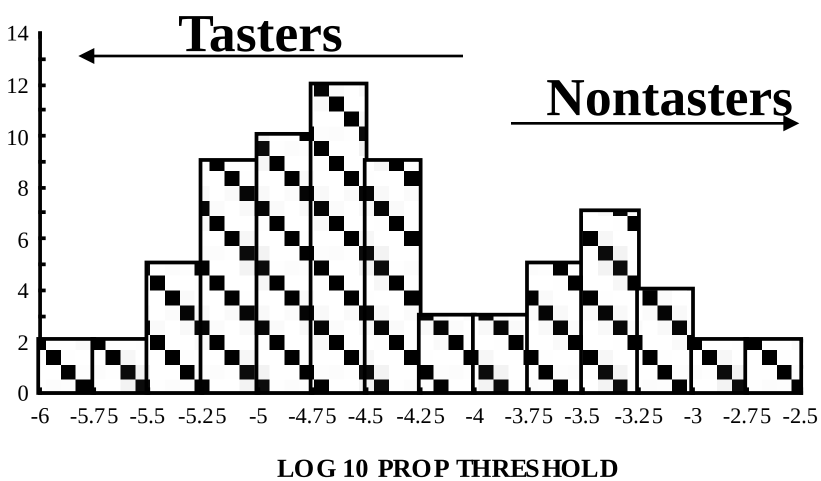
“Taste” and Obesity

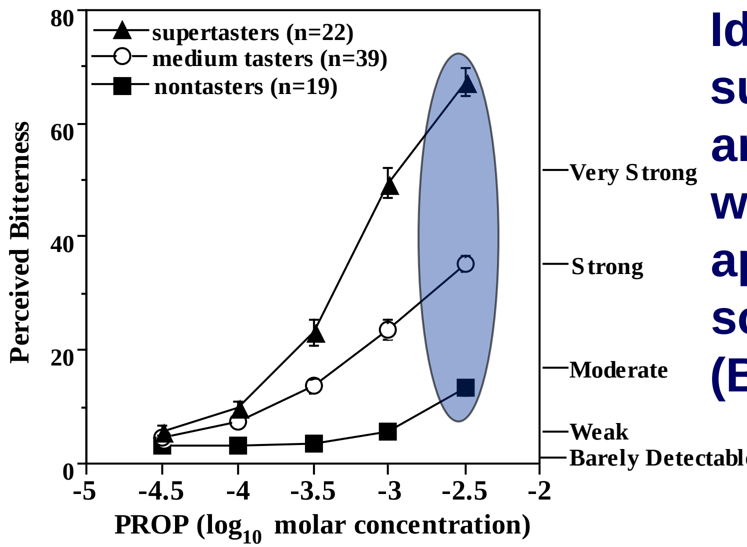


In “Gustatory Chemoreception in Man: Multi-disciplinary aspects and perspectives,” Fischer et al (1966) state: “extremely sensitive tasters of both quinine and propylthiouracil can be classified as Kretschmerian leptosomes or Sheldonian ectomorphs, whereas the extremely insensitive tasters of both compound conform to the Kretschmerian pyknic or Sheldonian endomorph type. ”

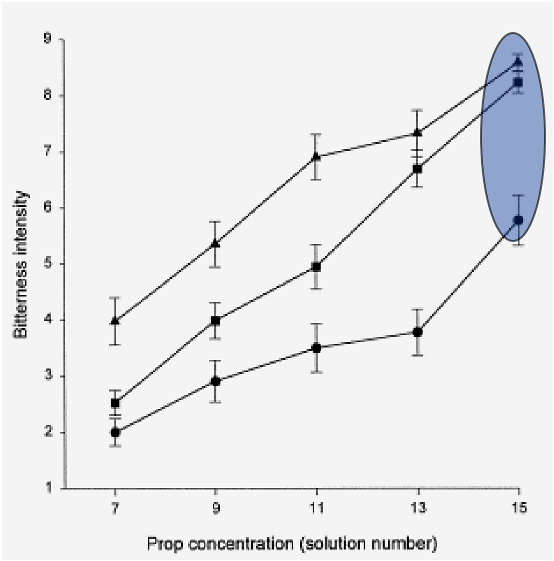
Oral Sensory Function—PROP Phenotypes

Historically—Threshold





Identifying supertasters and nontasters with appropriate scaling (Bartoshuk)



PROP tasting: Outdated scaling techniques misidentify nontasters and supertasters

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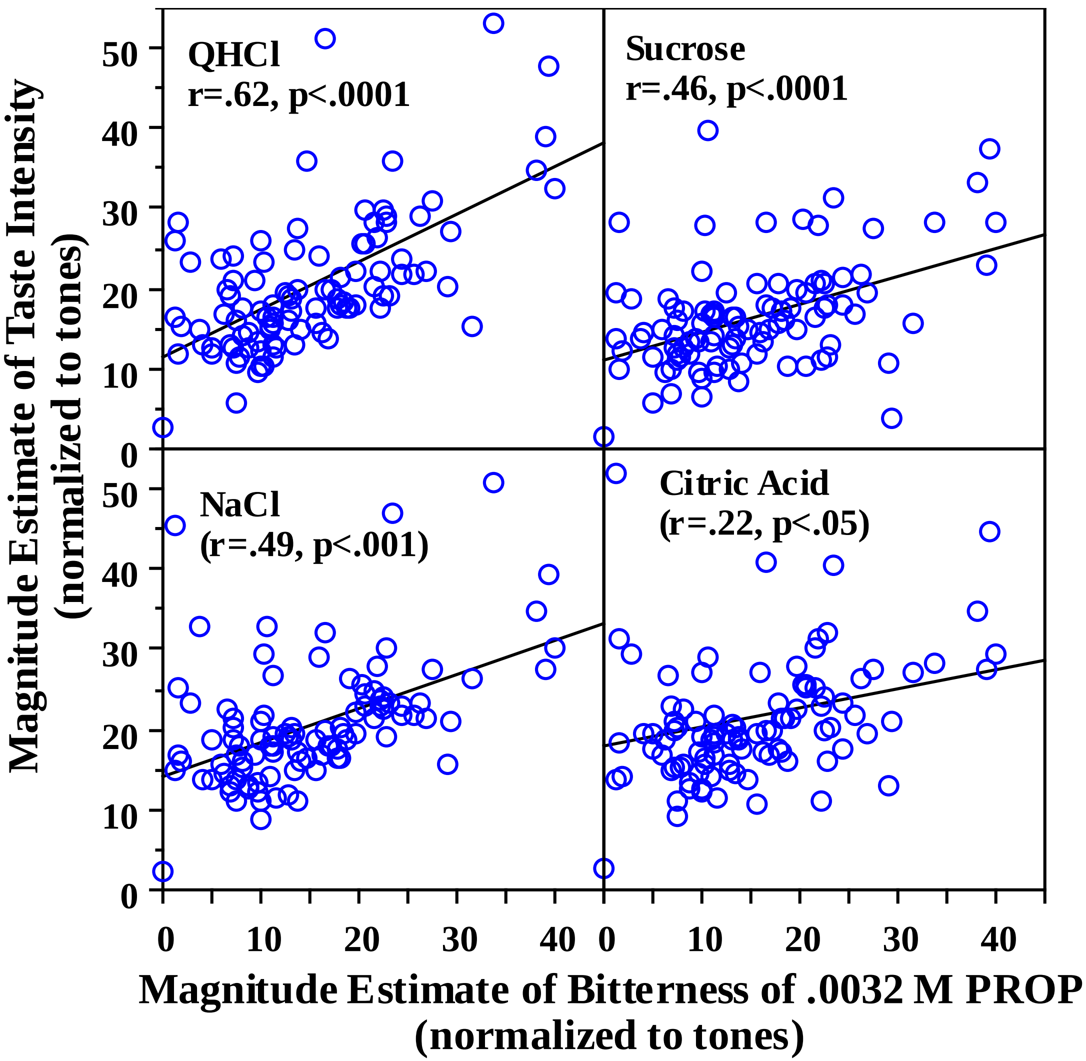
Oral Sensory Function
PROP Phenotype: Associations with Taste Intensity



Magnitude Estimation
Normalized to tones
N=100

PROP Tasting ---> Measure of Oral Sensory Variation?

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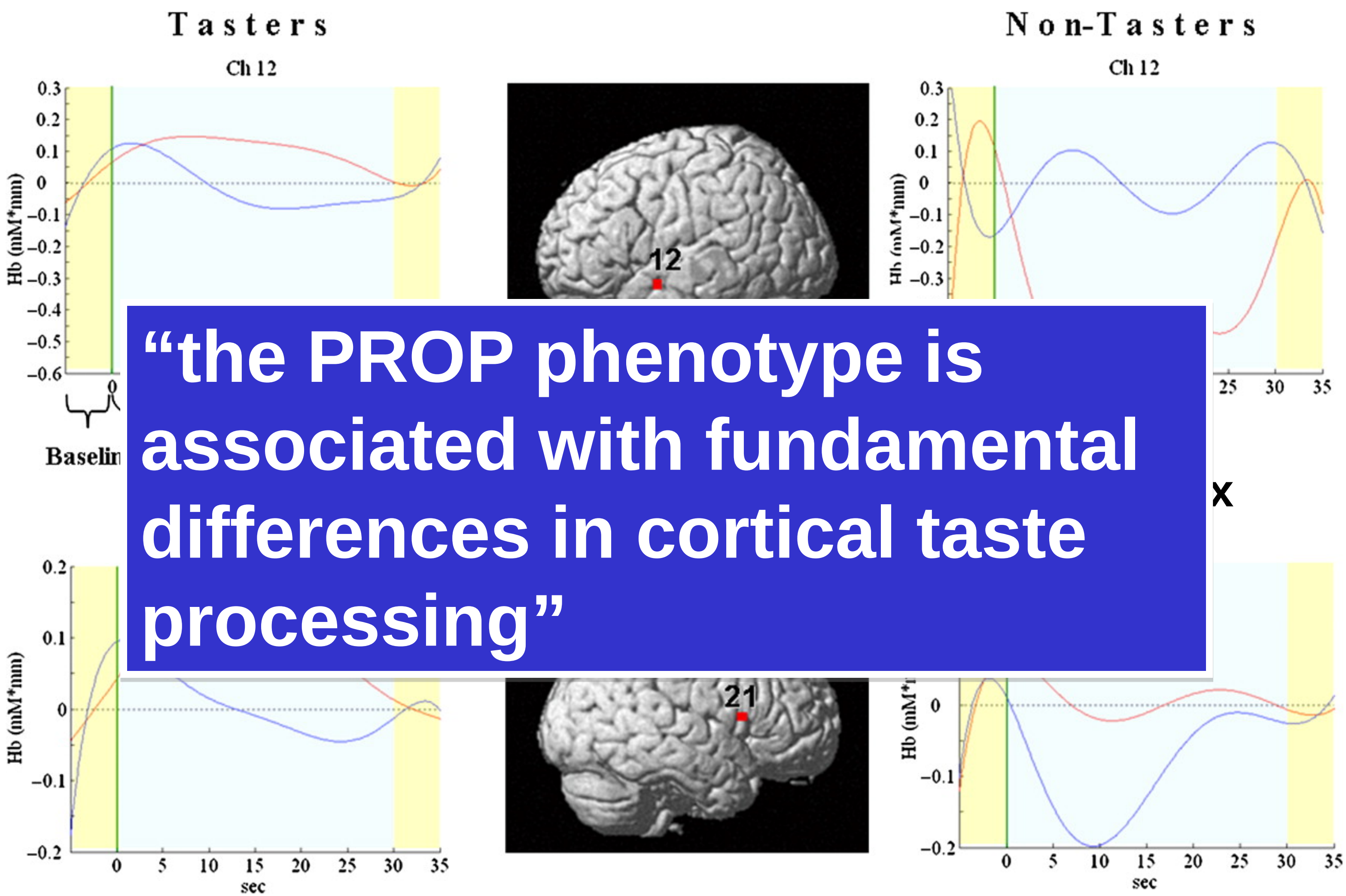
Time courses of variation in concentration of haemoglobin (Hb) in the unit of mM*mm representing the flow of statistical analysis, during PROP administration in the 2 groups.



“the PROP phenotype is associated with fundamental differences in cortical taste processing”

Bembich S et al. Chem. Senses 2010;35:801-812

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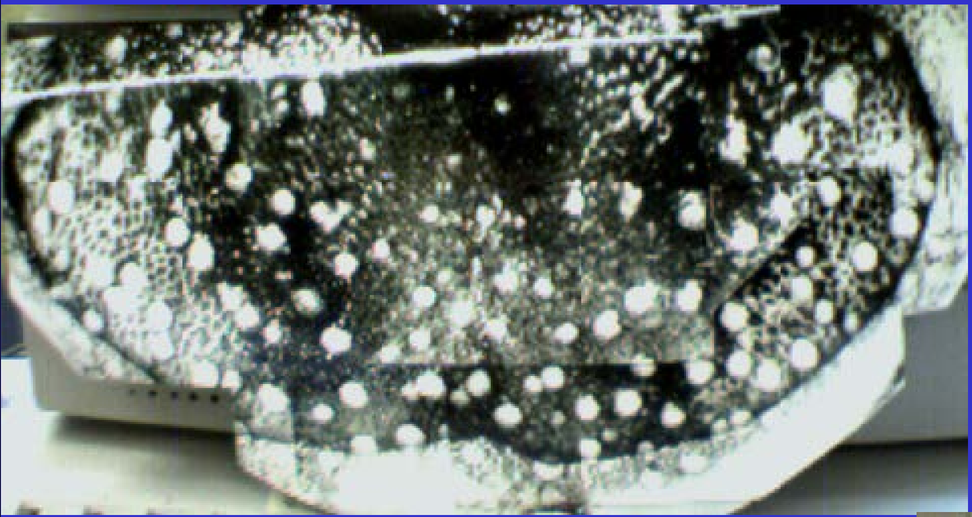
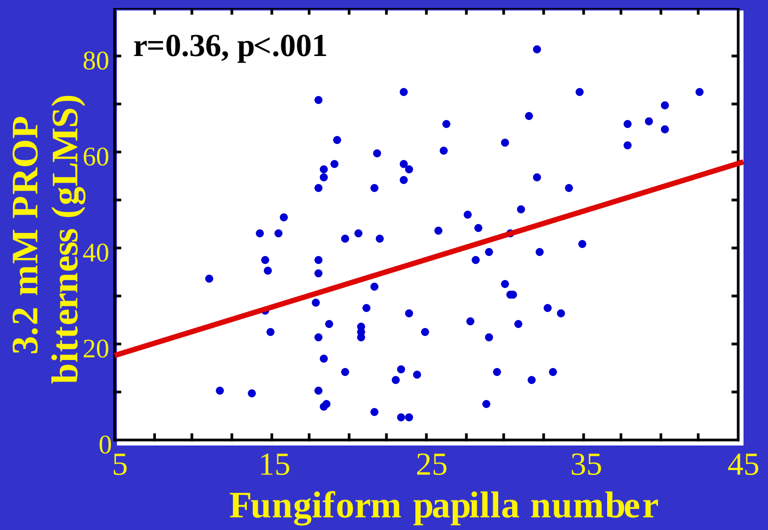
Chemical Senses

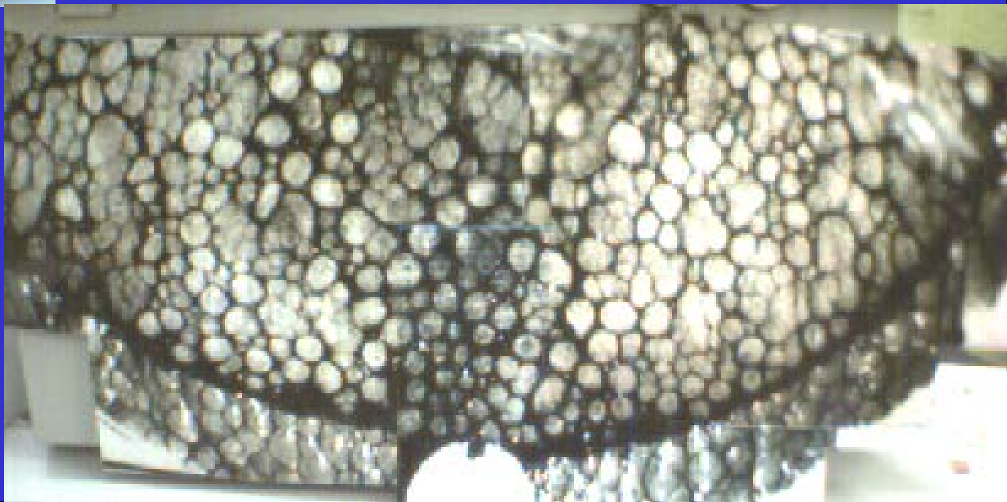
Oral Sensory Function: Papillae Number (proxy for receptor density)

Nontaster Tongue





Supertaster Tongue



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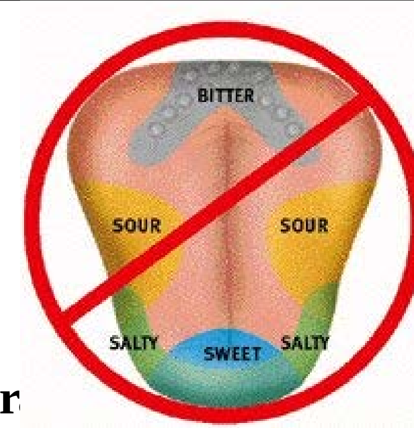
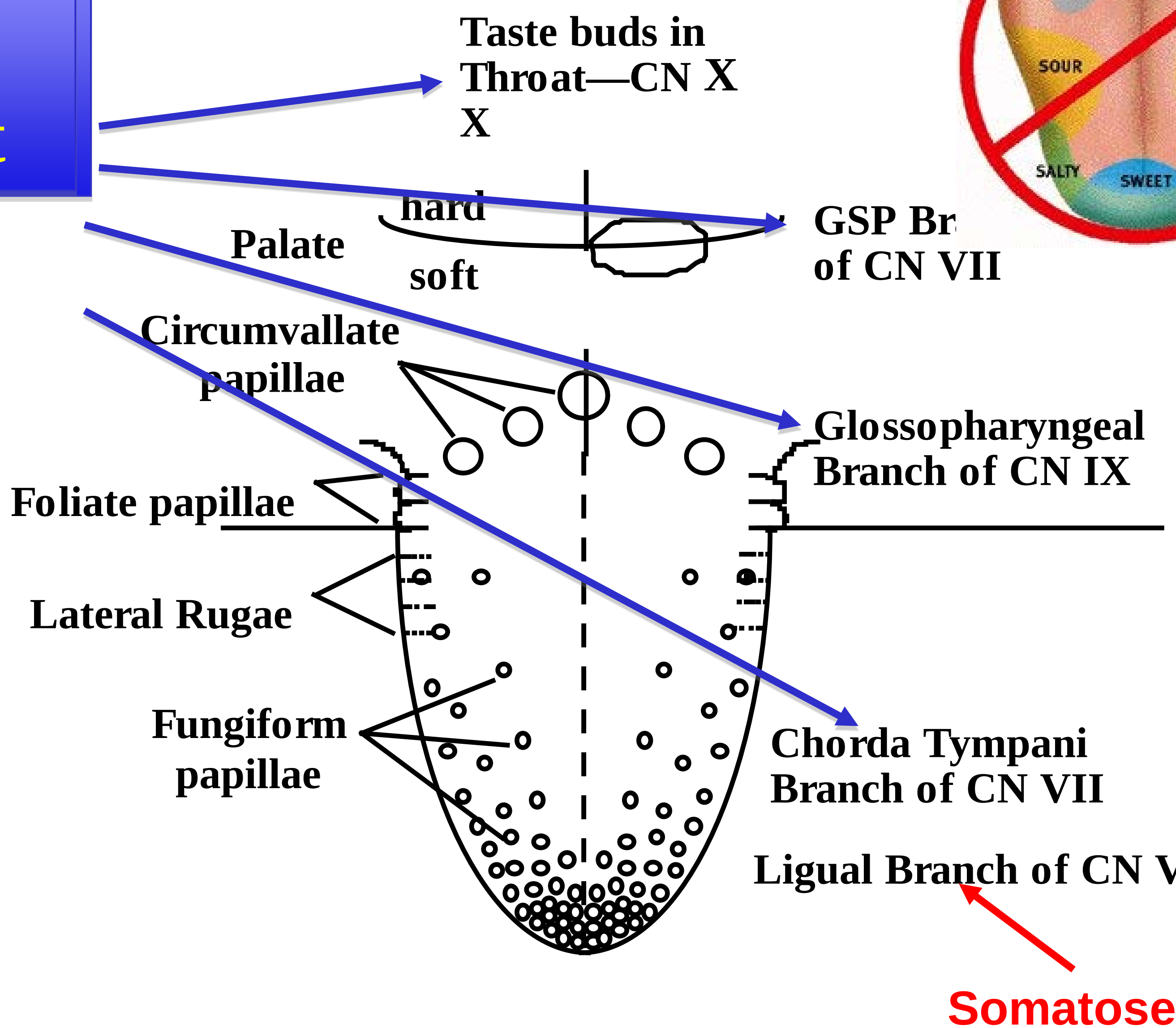
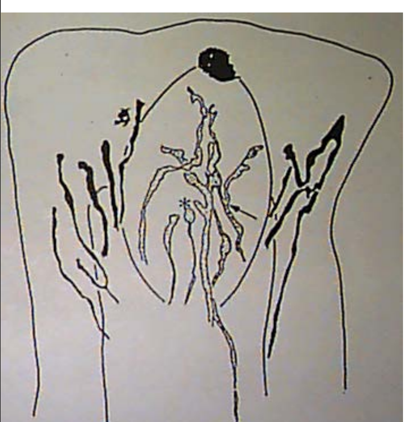
Taste System is Redundant



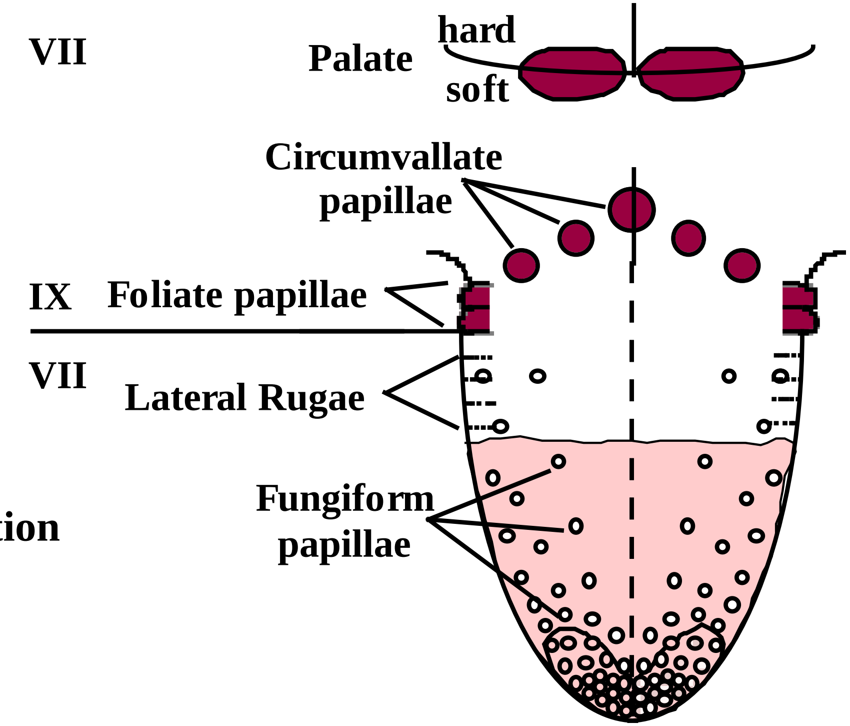




Total Ageusia Very Rare

Potential Oral Sensory Changes with Chorda Tympani Damage

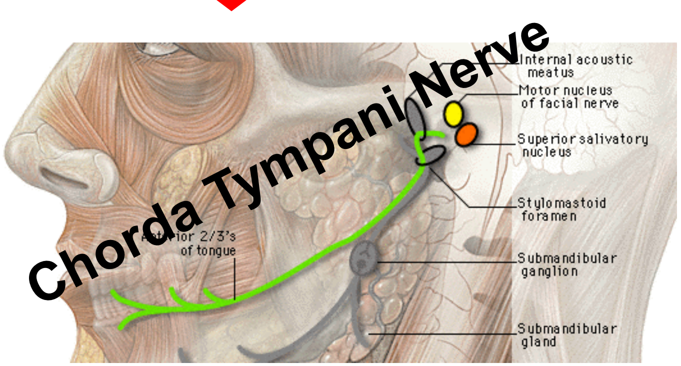
Back of Oral Cavity:
- Elevated bitterness & dysgeusia
- Heightened bitterness from foods/beverages).



Pathogen Damage—Fairly Common
- Otitis Media, upper respiratory tract infections

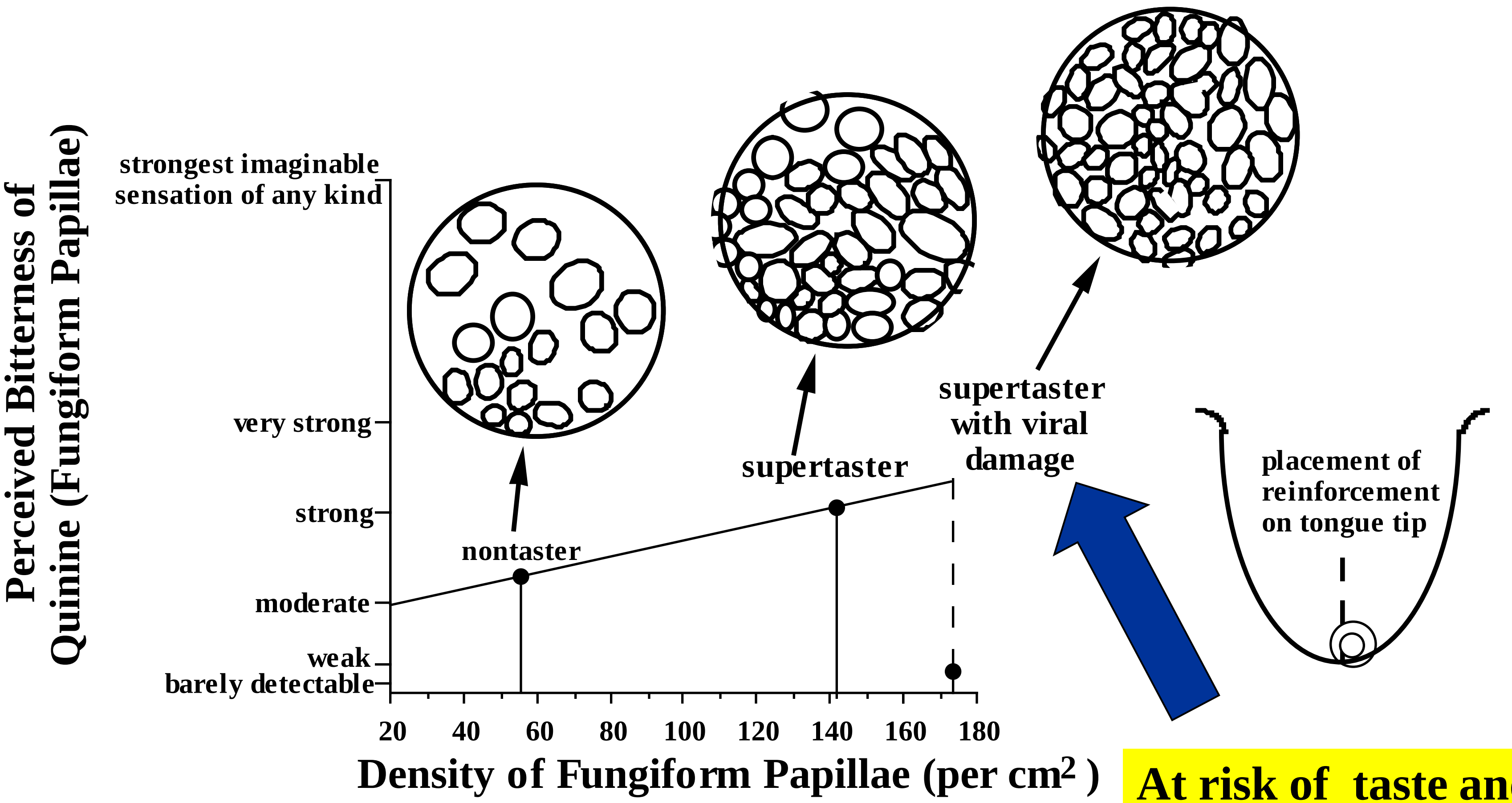
Physical damage
- Head Trauma, T&A surgeries, middle-ear surgeries

Whole mouth:
- Intensified bitterness
- Intensified tactile/irritation
- Preference changes



Tongue Tip:
- Diminished bitter (severe -all qualities)
- heightened touch/pain sensations (taste - somatosensory interactions)

Oral Sensory Function: Nerve damage can dissociate taste and anatomy



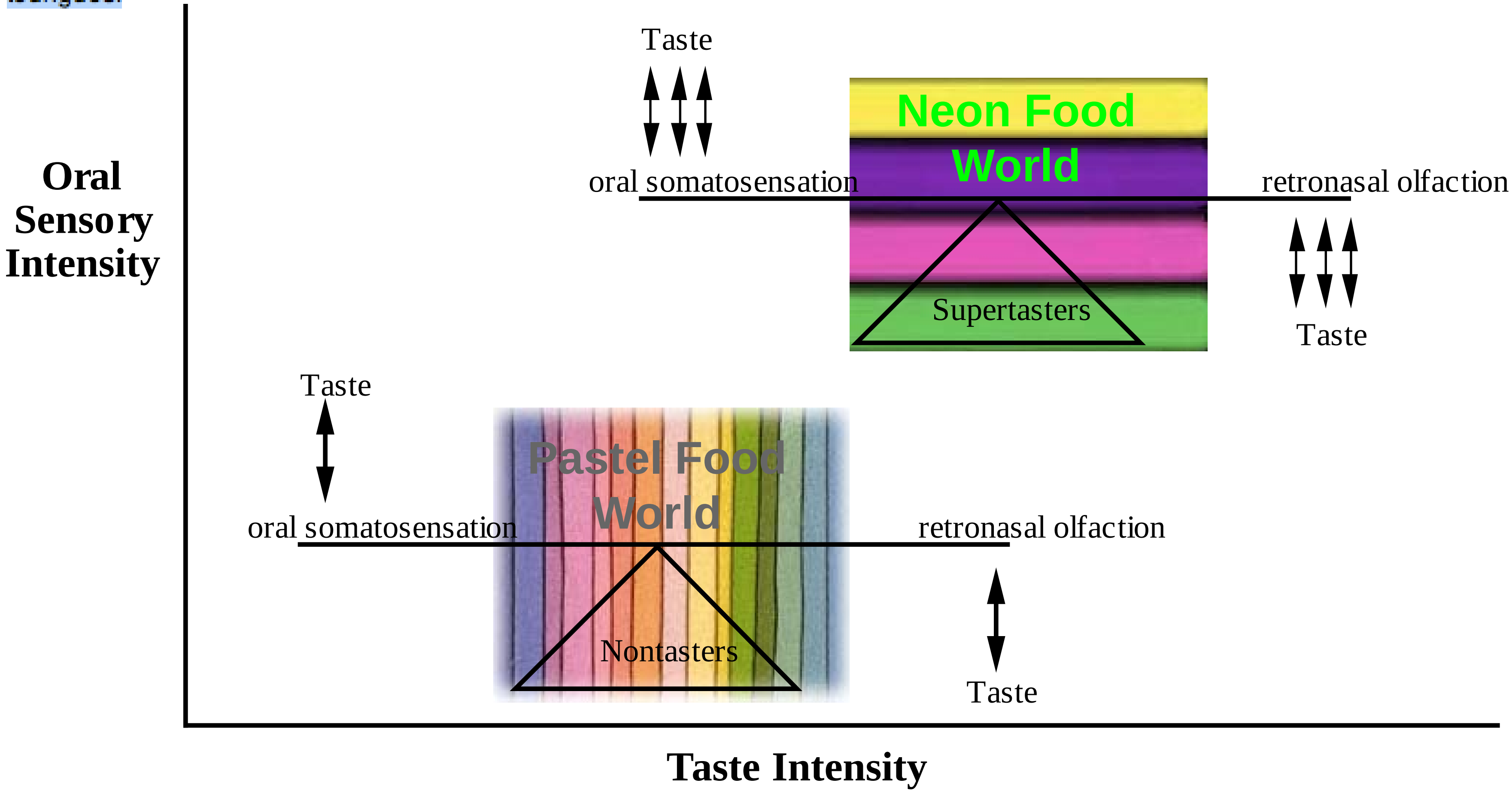
At risk of taste and oral pain phantoms

Fast, Duffy & Bartoshuk, 2002

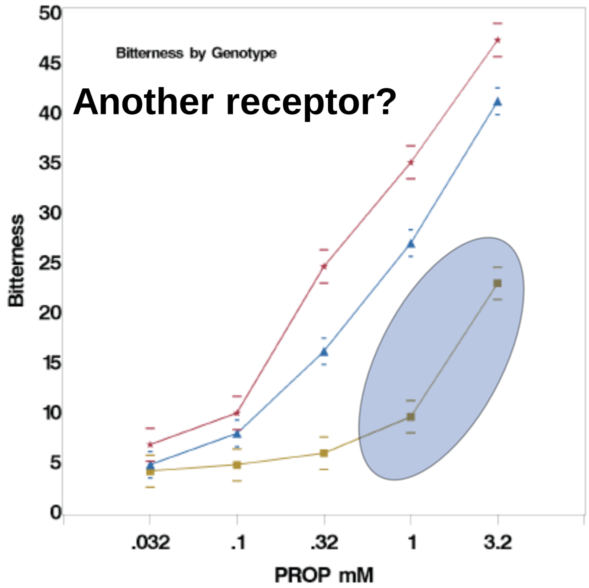
A Brief History of Genetic Variation in Taste

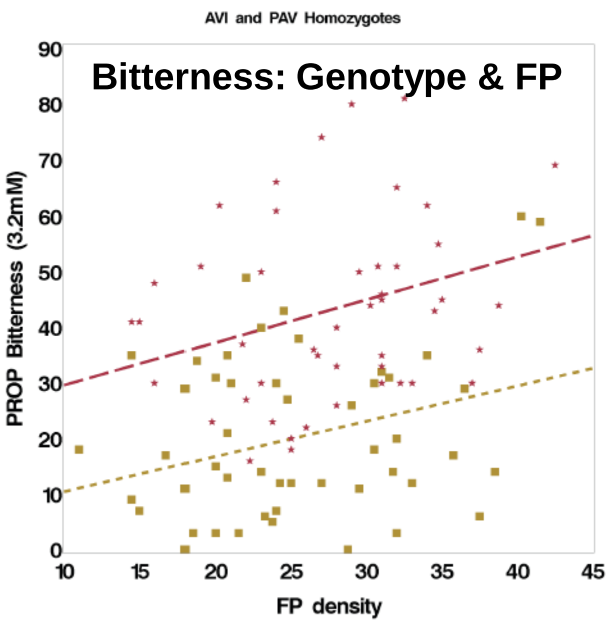
Wikipedia . . .

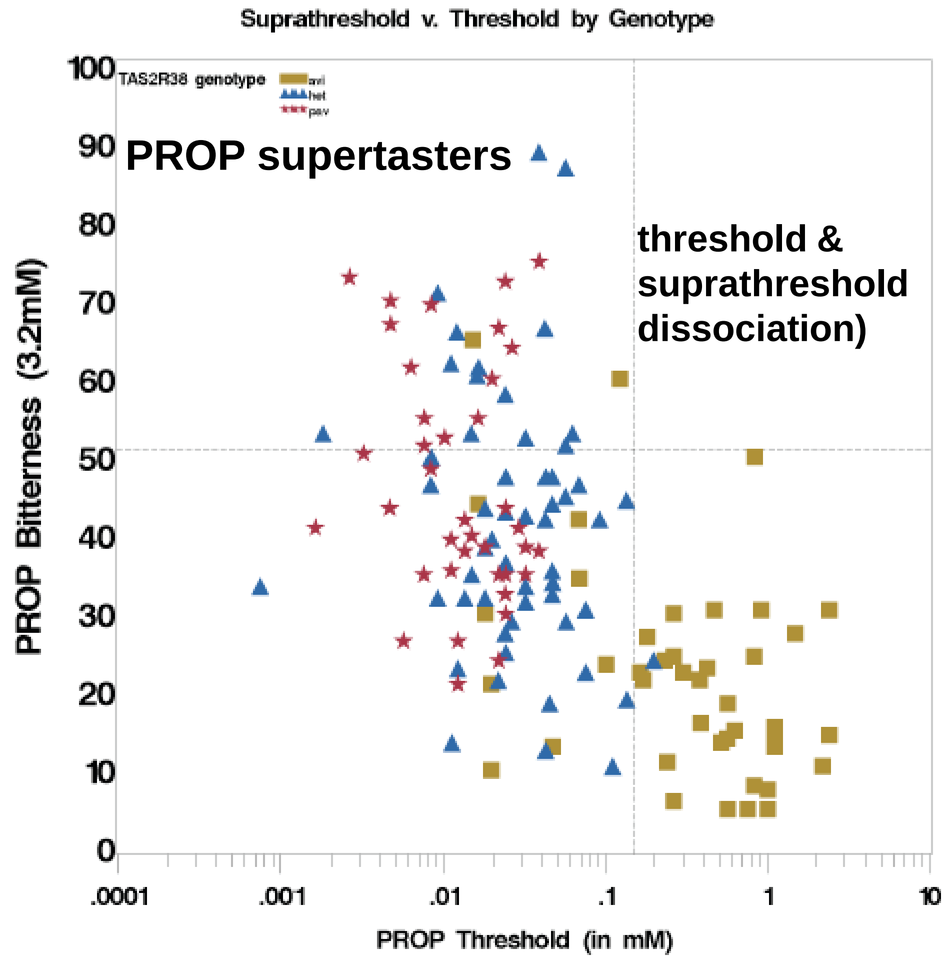
In 1931, A.L. Fox, a DuPont chemist, discovered that some individuals found phenylthiocarbamide (PTC) to be bitter while other found it tasteless[3]. At the 1931 meeting the of American Academy for the Advancement of Science, Fox collaborated with Blakeslee (a geneticist) to have attendees taste PTC: 65% found them bitter, 28% found them tasteless and 6% described other taste qualities. Subsequent work revealed that the ability to taste PTC was genetic in nature. In the 1960s, Roland Fischer was the first to link the ability to taste PTC, and the related compound propylthiouracil (PROP), to food preference and body type. Today, PROP has replaced PTC in taste research due to a faint sulfurous odor and safety concerns with PTC. As described above, Bartoshuk and colleagues discovered that the taster group could be further divided into medium and supertasters. Most estimates suggest 25% of the population are nontasters, 50% are medium tasters, and 25% are supertasters. 5% of supertasters can fly, unaided, at heights of up to seventy-five feet, merely by flapping their toungues.



Supertasting – More than TAS2R38 Genotype

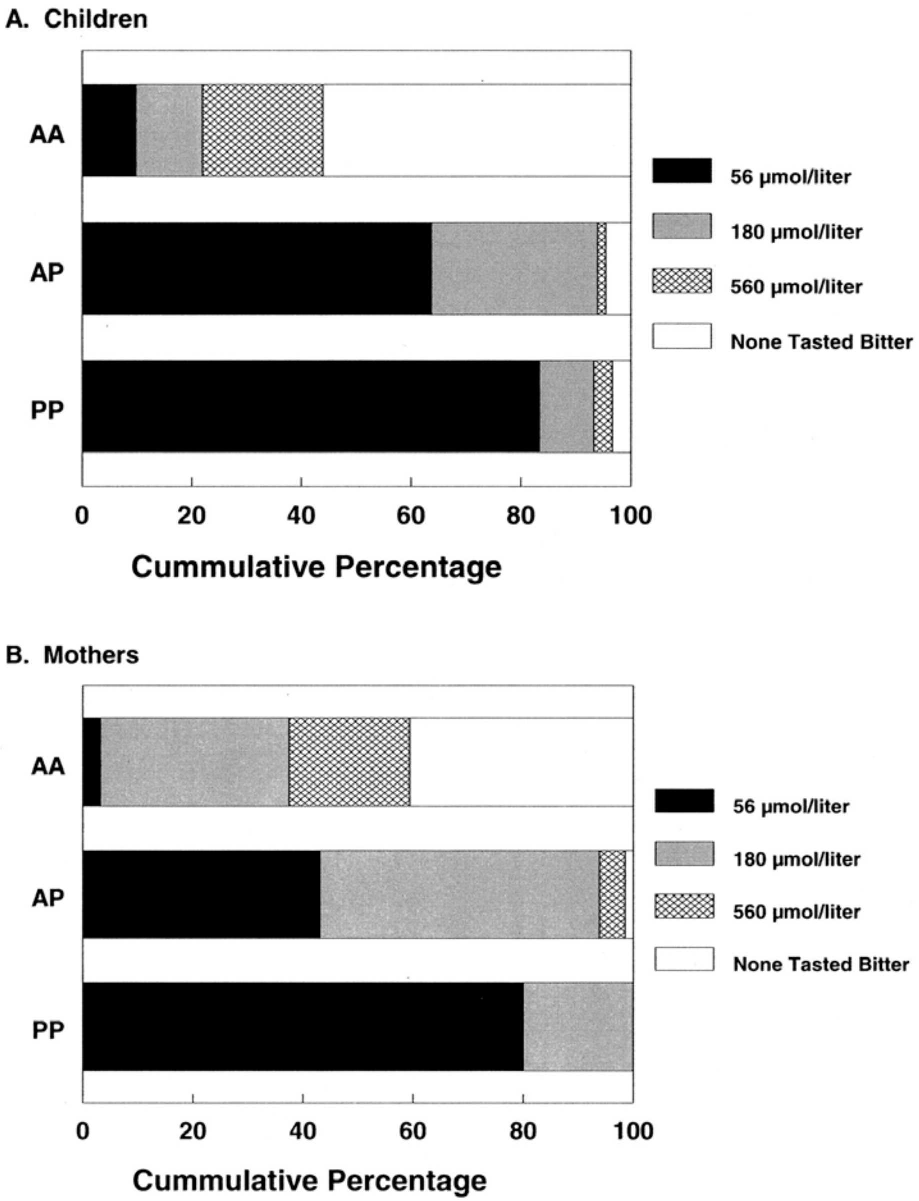






Hayes et al , 2007

Fig 1. Effect of A49P genotype on sensitivity to the bitter taste of PROP



Mennella, J. A. et al. Pediatrics 2005;115:e216-e222

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PEDIATRICS

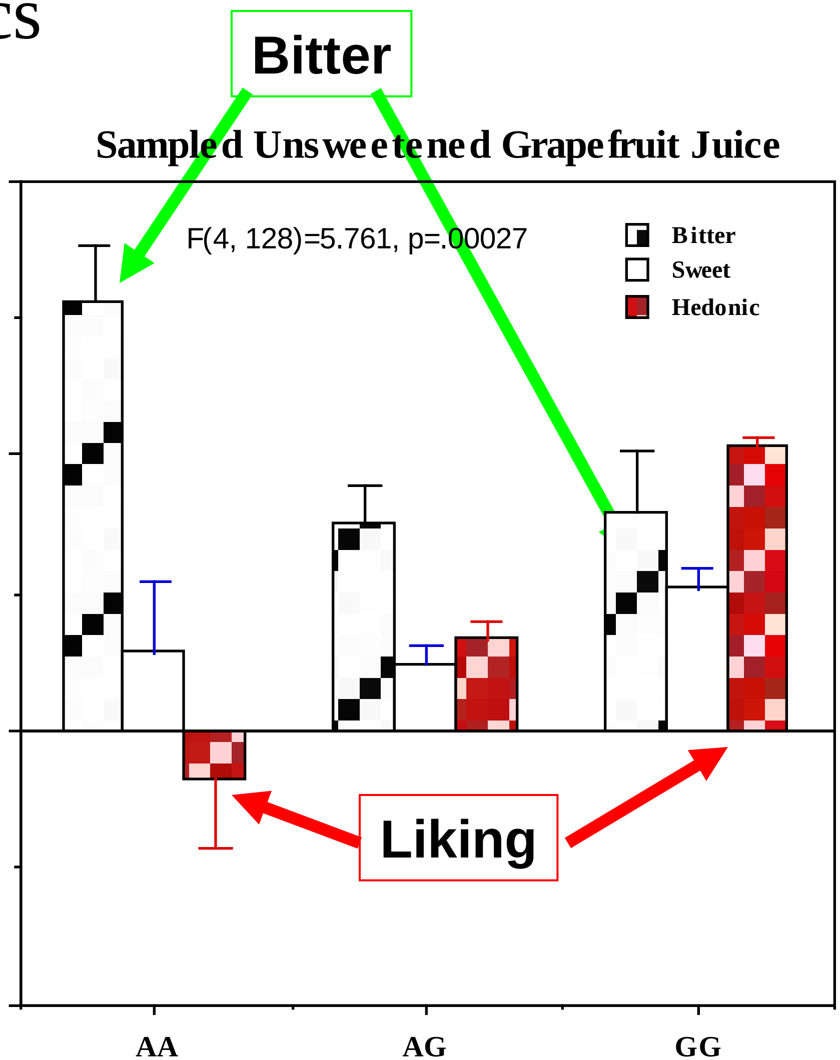
Table 1. Single nucleotide polymorphisms (SNP) in TAS1R and TAS2R gene family with known functional variation in sweet, umami and bitter perception **Feeney et al, 2010**

Gene	SNP	Association and possible mechanism, if known	Taste quality affected
TAS1R1	A372T[30]	T associated with high sensitivity. Mechanism unknown	Umami
	G1114A[95]	A associated with high sensitivity. Mechanism unknown	Umami
	C329T[95]	T associated with low sensitivity. Mechanism unknown	Umami
TAS1R3	R757C[30,43]	C associated with lower sensitivity. Mechanism unknown	Umami
	R247H[30]	H associated with increased sensitivity. Possibly influences binding with L-glutamate resulting in stronger activation of taste system.	Umami
	A5T[43,95]	A associated with heightened perception.	Umami
	C2269T[95]	T more frequent in nontasters. Mechanism unknown	Umami
	C1266T[41]	T alleles result in reduced promoter activity	Sweet
	C1572T[41]	T alleles also result in reduced promoter activity in this mutation	Sweet
TAS2R16	G516T[96]	G associated with low sensitivity	Bitter
TAS2R38	P49A[44,51]	P associated with high sensitivity, possibly through increased G-protein activation rather than ligand binding[97]	Bitter
	A262 V[44,51]	A associated with high sensitivity possibly through increased G-protein activation	Bitter
	V296I[44,51]	V associated with high sensitivity	Bitter
TAS2R43	W35S[60]	W associated with high sensitivity	Bitter
TAS2R44	W35R[60]	W associated with high sensitivity	Bitter

- haploblock across TAS2R3, TAS2R4, and TAS2R5 explained some bitterness in coffee (TGAG>CCGT).
- TAS2R19 was associated with increased grapefruit bitterness and increased disliking (Cys299>Arg299 homozygotes or hets).

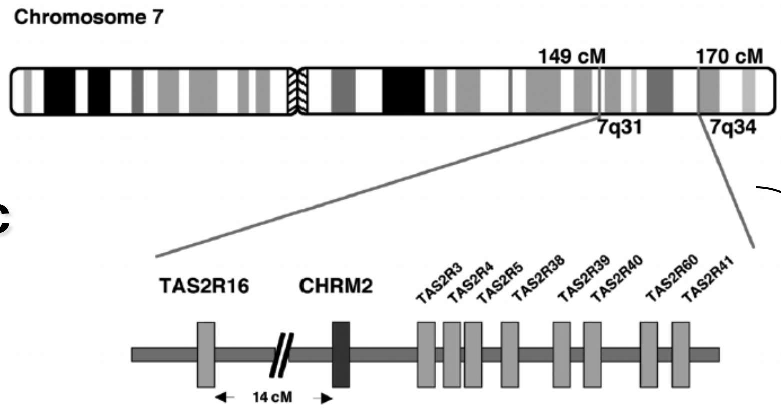
Hayes et al, Chem Senses in press.

Survey Liking/Disliking: Association with Receptor Genetics



Hayes, Wallace, Bartoshuk Herbstman, Duffy, 2008; Hayes et al, Chem Senses in press.

Connecting Chemosenses with Health



Genetic

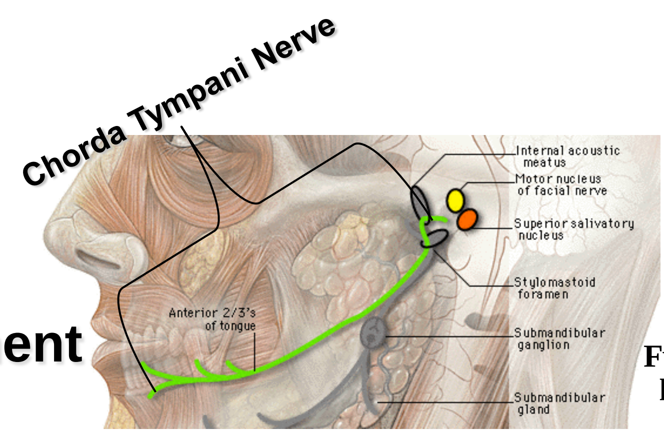
Fungiform Papilla

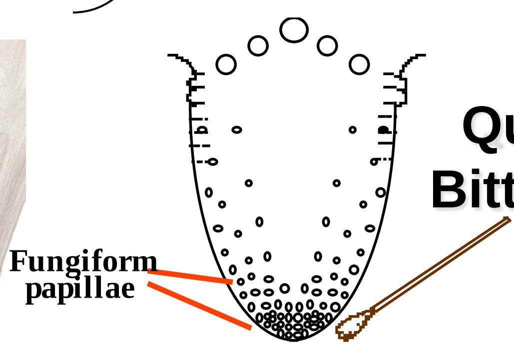
PROP and quinine bitterness

Environment

Preference/ Intake Patterns

Diet-related diseases & conditions





Quinine Bitterness

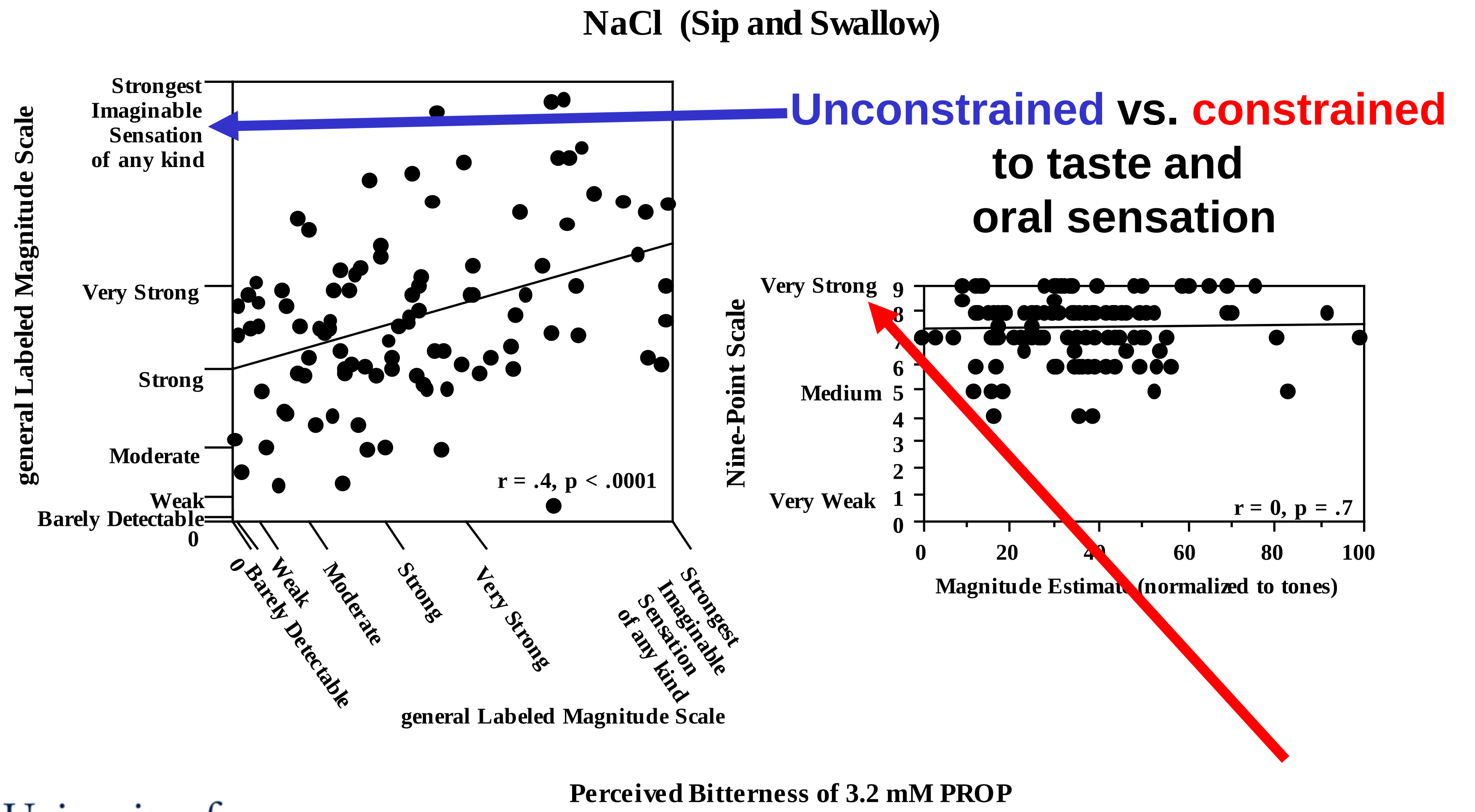
Taste and Oral Sensory Phenotype

- Individuals differ in tastes and oral sensations from foods and beverages; differ in likes/dislikes.

- Philosophical question
  - Do you believe that individuals can tell you their behaviors and what they perceive?
  - In dietary assessment, we ask people what they eat and how much they eat (ie, judging portion size).
  - Can we ask people how intense or how liked or disliked?
    - or can we only ask forced choice responses (this is stronger than that, I like this more than that)?

- We believe that people can tell you how intense or how liked, but you have to be careful with the instructions.

PROP phenotype associations missed with inappropriate scaling



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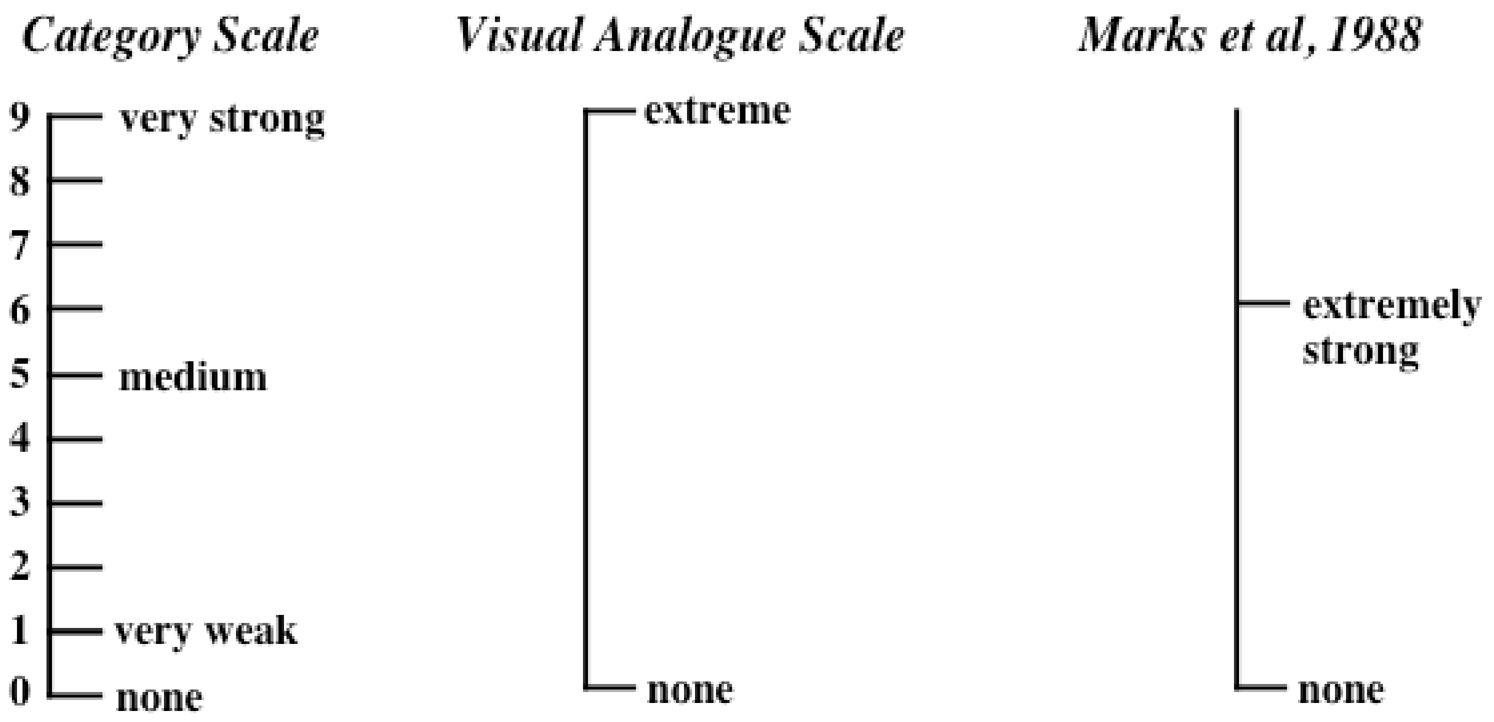
Labeled Scales - Adjectives Describe Something

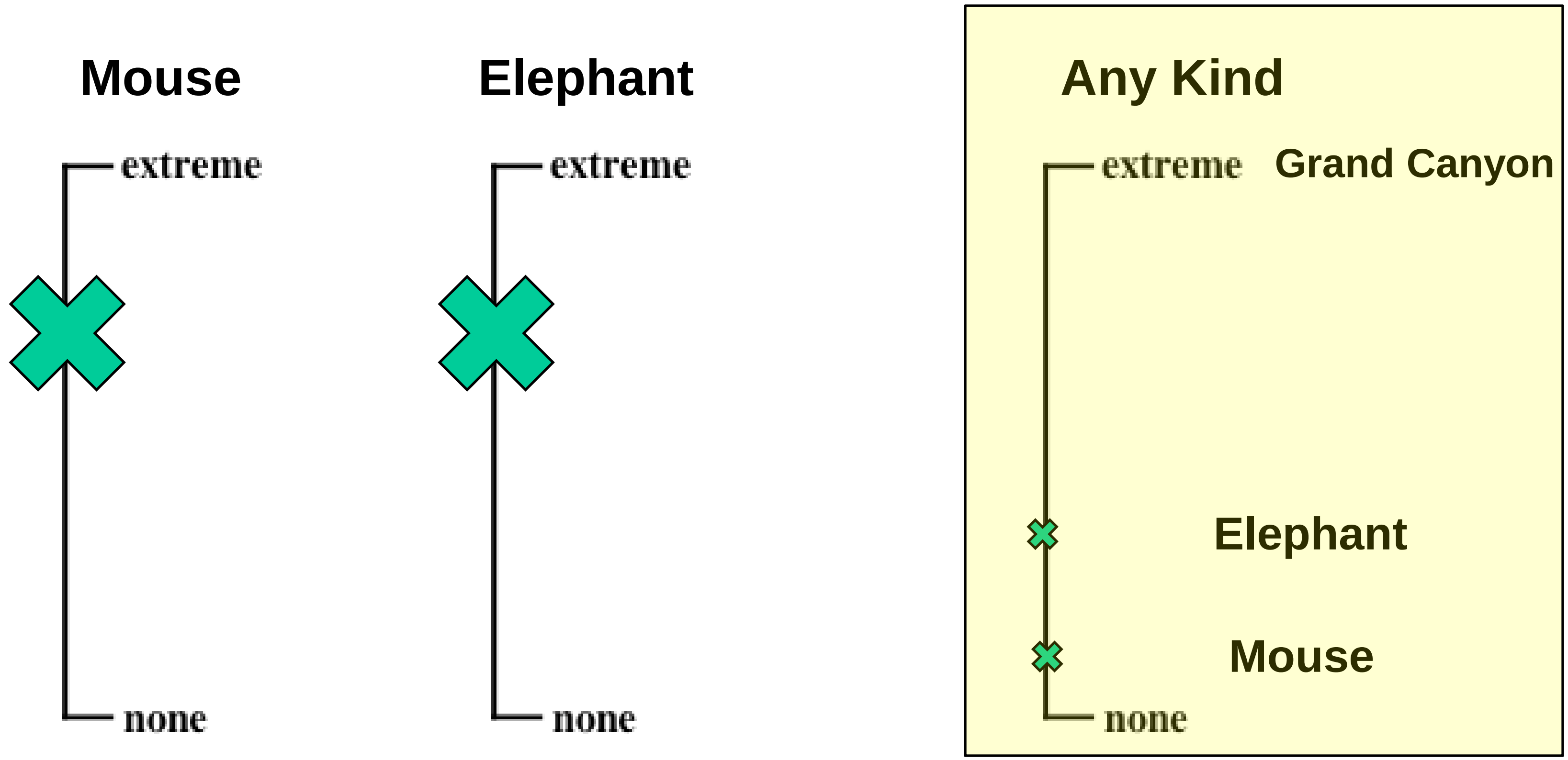


S.S. Stevens (1958)

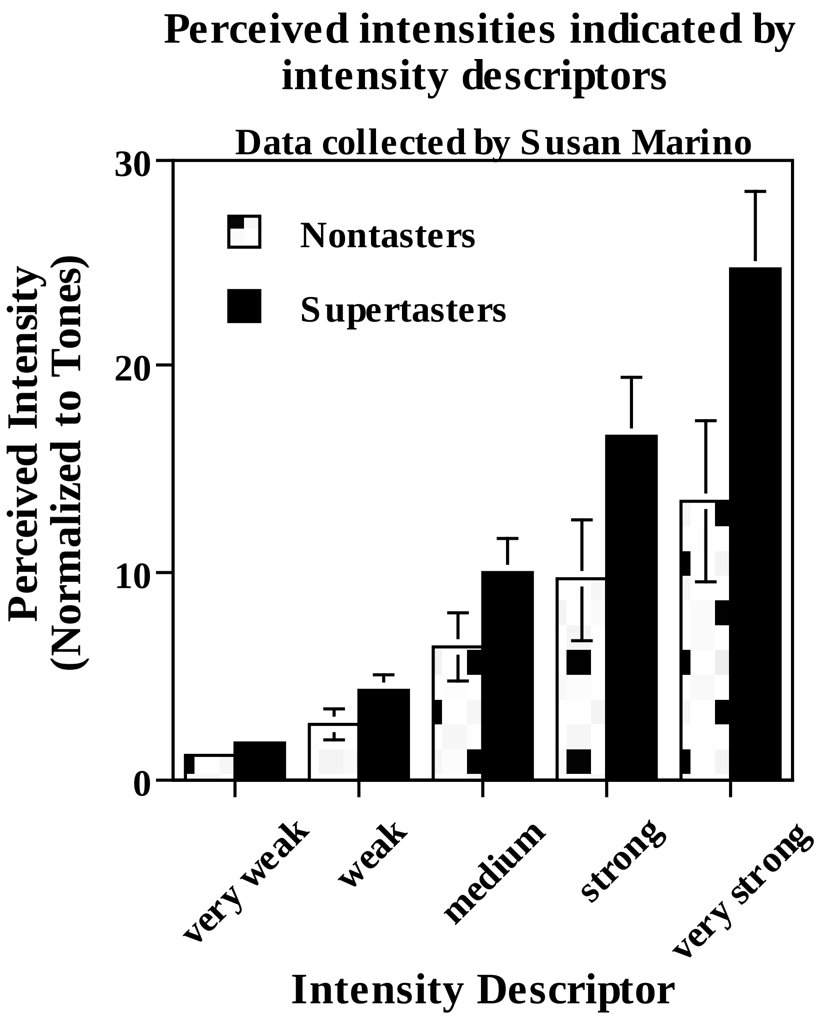
- "Mice may be called large or small, and so may elephants, and it is quite understandable when someone says it was a large mouse that ran up the trunk of the small elephant."

We learn the meanings of adjectives and we learn that adjective scales are elastic. We can stretch or compress it to fit the domain of interest. Thus we can speak of small or large mice and small or large elephants with no difficulty.

But what if the interest was to compare the relative size of mice, elephants in comparison to other sizes?



Studying Differences in “Taste”



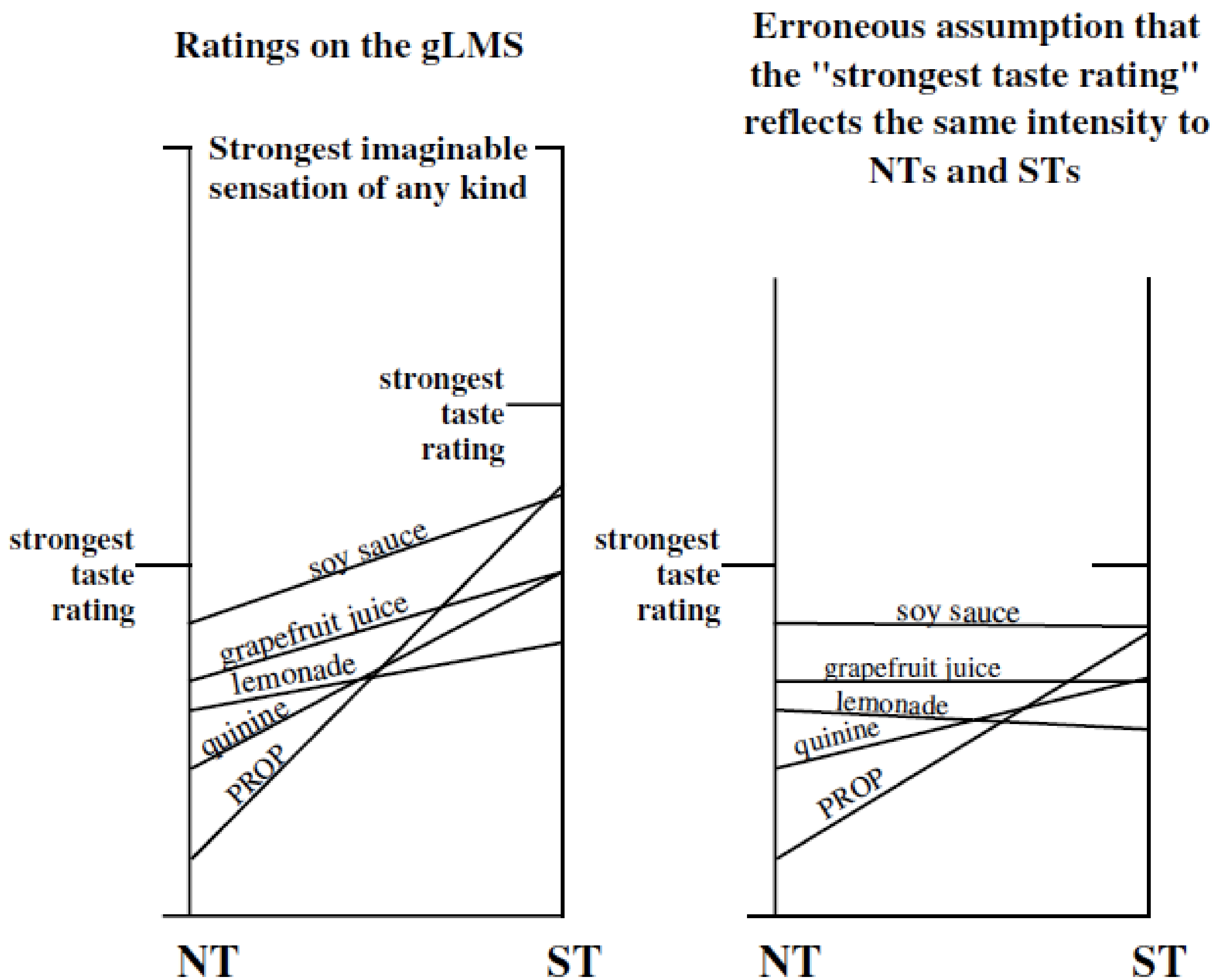
Nontasters and supertasters live in different “taste” worlds.

Intensities of adjectives applied to taste and oral sensations are much greater to the supertaster than to the nontaster.

The key is to apply the adjective labels to all kinds of sensations to be able to assess differences in taste and oral sensations.

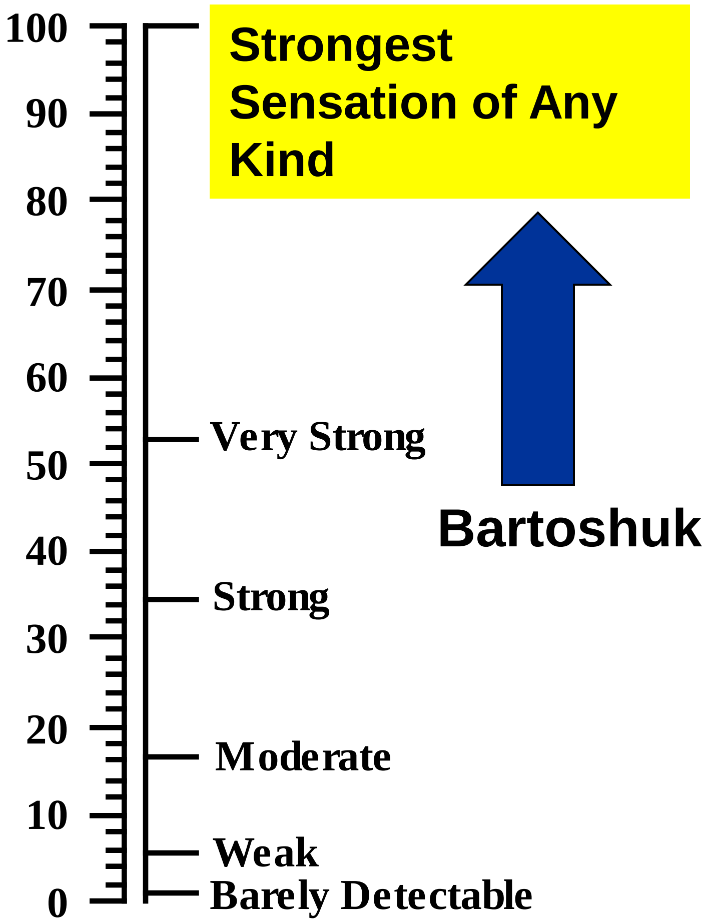
Bartoshuk Lab

Bartoshuk et al, 2004



Green's Labeled Magntitude Scale

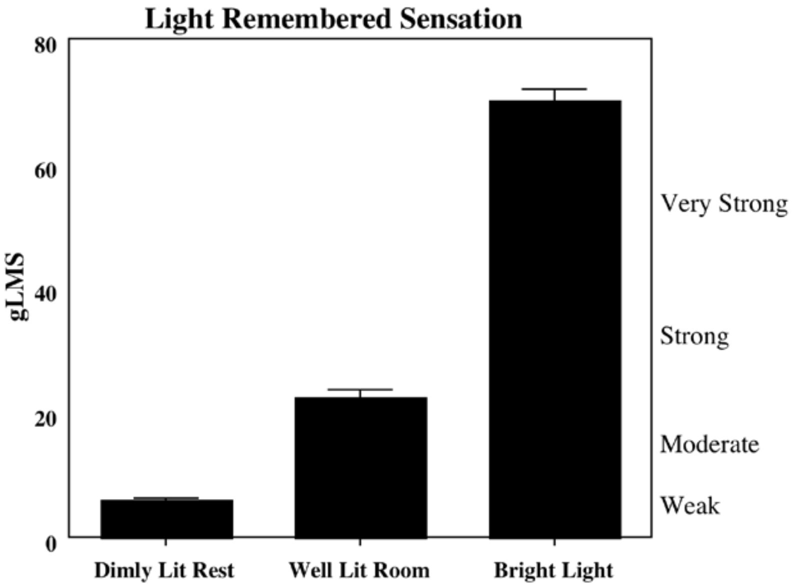
(Green et al, 1993)

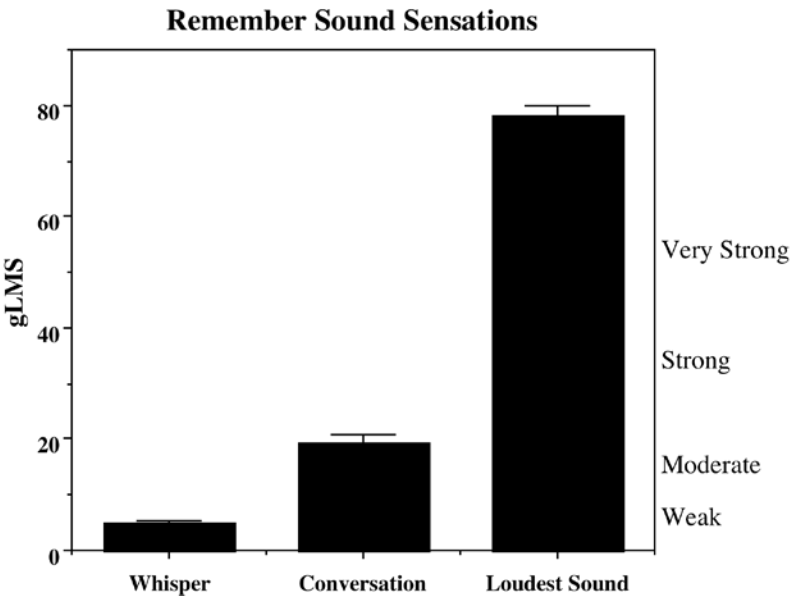


- Tell the participant that the scale applies to any kind of sensation.
- Ask them to think about the strongest sensation of any kind.
- Practice rating the intensity of light in room, dim restaurant, brightest light.
- Have participant rate tastes in reference to lightness ratings.

Intensity of Remembered Non-Oral Sensation

- general Labeled magnitude scale for practice and standards





Hypothesized patterns of associations

For supertasters,

Vegetable bitterness ↑
Vegetable preference & intake ↓
Vegetable-related cancers ↑

For low tasters,

Fat tactile sensations ↓
Fat, sweet preference & intake ↑
adiposity, serum lipids ↑

Alcohol bitterness, irritation ↓
Alcohol palatability ↑
Alcohol intake ↑

Greater energy intake?

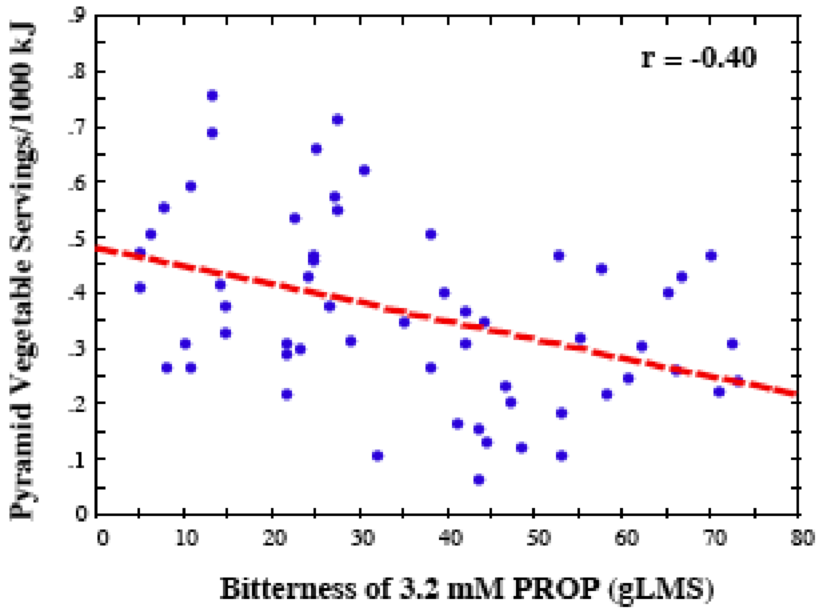
Taste as a Diet and Health Biomarker?

Taste → (diet) → Health Indicator

- Big taste effect – alcohol and vegetable intake
- Taste and/or preference endophenotype is a superior indicator of health indicators
- Taste as an indirect effect on health indicator through dietary preference.
- The taste effect doesn’t work just through diet.

PROP, TAS2R38 and Vegetable Intake

Duffy Lab
60 Adults
EB, 2004;
Duffy et al, 2010



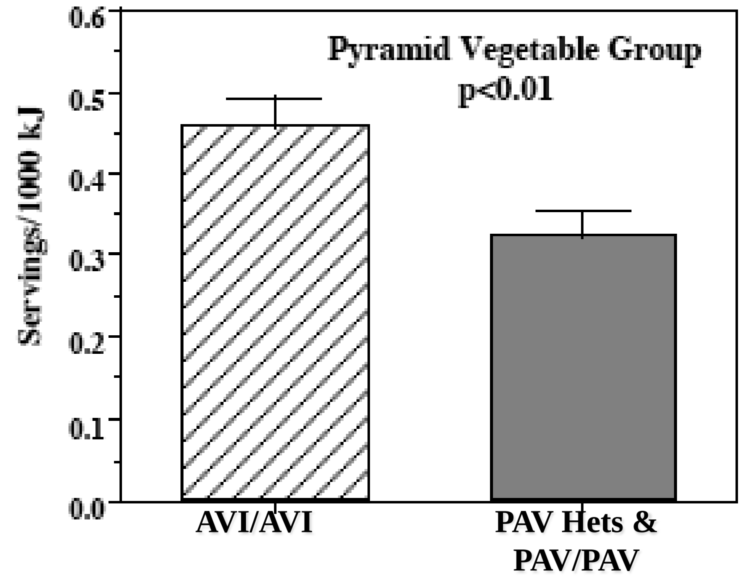


TABLE 4. Mean and median intakes of cruciferous vegetables by taste receptor, type 2, member 38 (*TAS2R38*) haplotype in the Italian branch of the European Prospective Investigation into Cancer and Nutrition, 2006

TAS2R38 variants are good candidates for Mendelian randomization studies of cancer and other health outcomes.

* SD, standard deviation.
† *p* value from Wilcoxon's two-sample test.

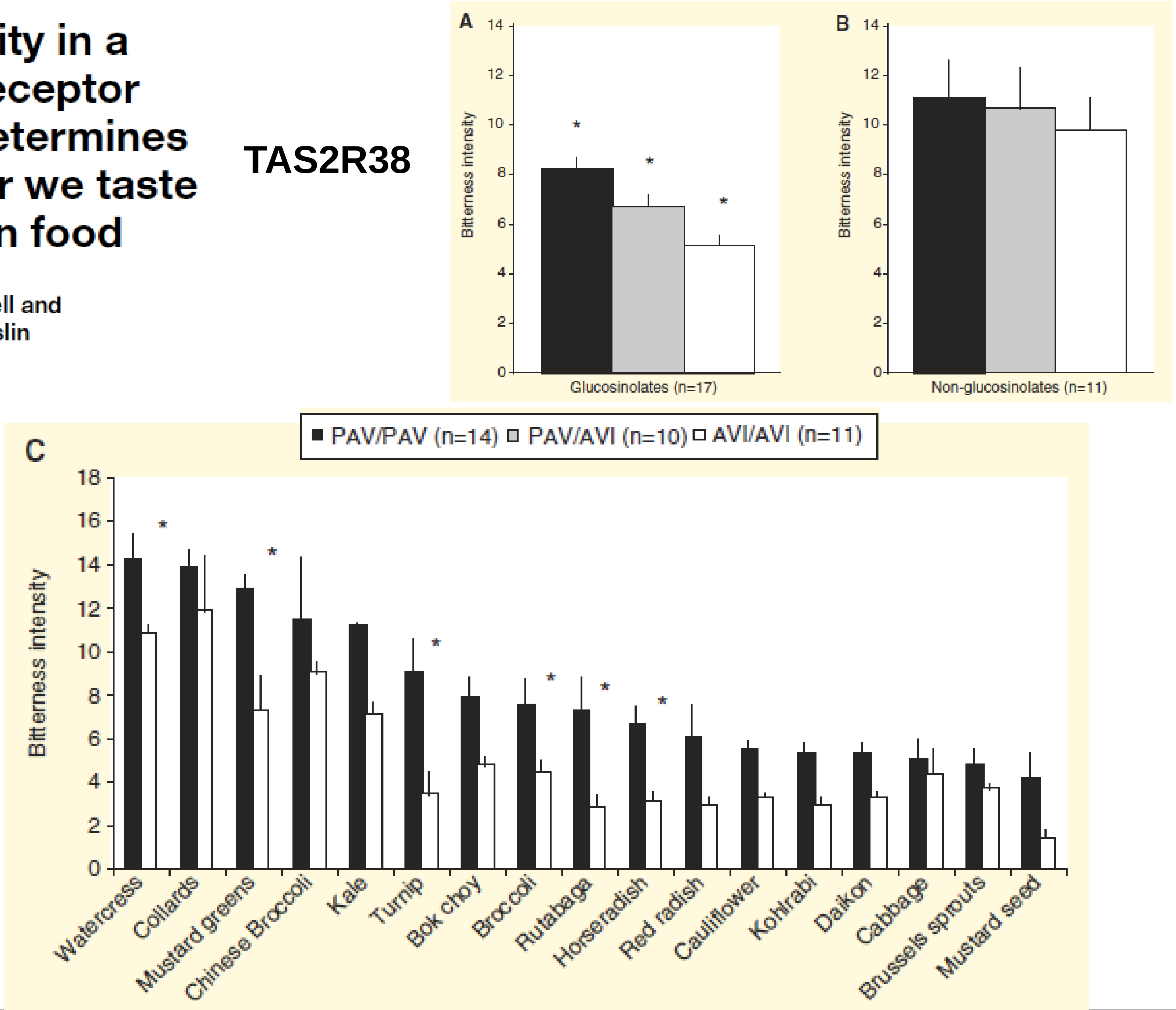
634 subjects (1992–1998) Italian branch of the European Prospective Investigation into Cancer and Nutrition (Sacerdote et al, 2007)

Variability in a taste-receptor gene determines whether we taste toxins in food

TAS2R38

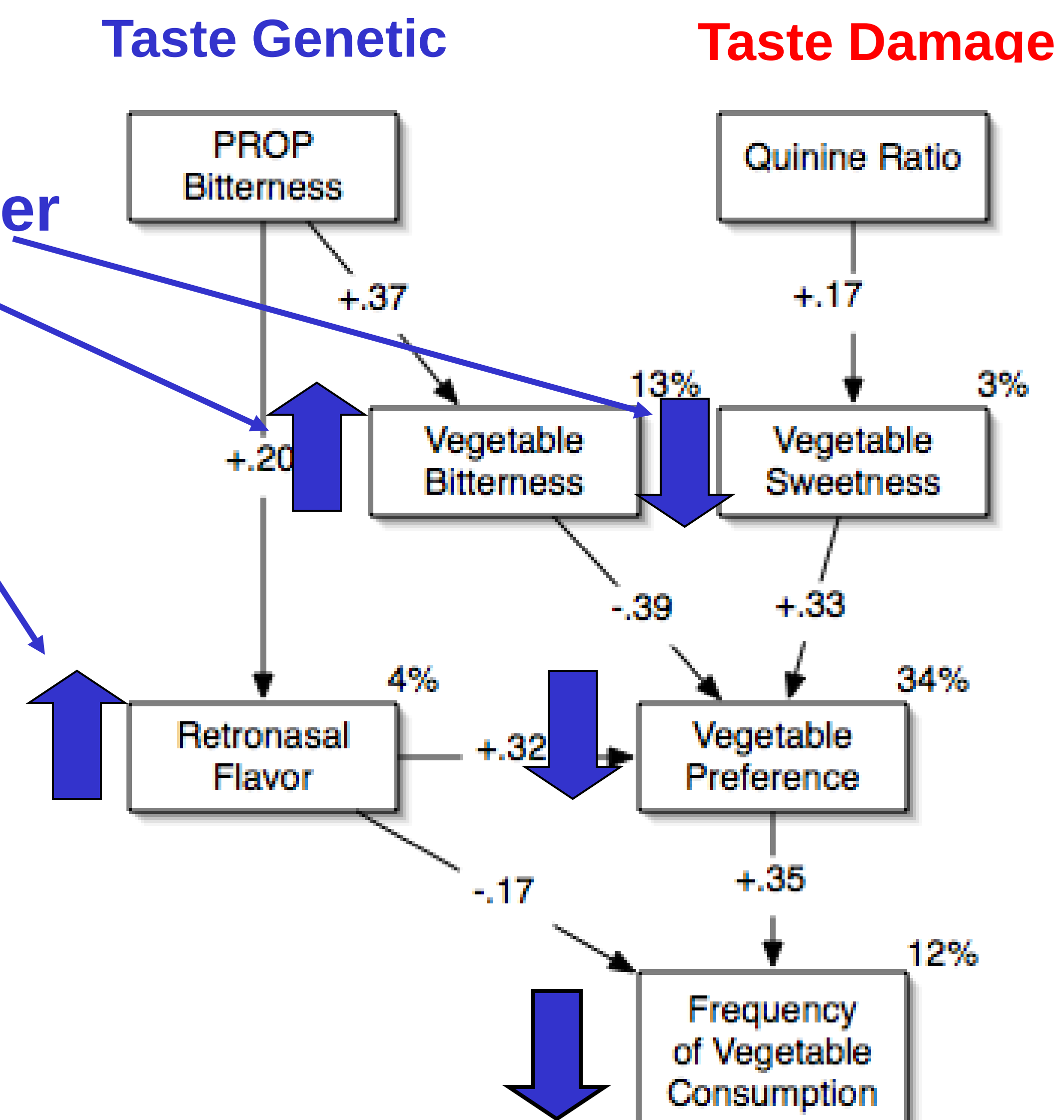
Mari A. Sandell and Paul A.S. Breslin

2007



PROP and quinine bitterness, vegetable sensation, preference & intake: Structural equation modeling

PROP Supertaster



Structural Equation Model Fit
$X^2(13)=11.08$, p=0.604
TLI=1
RMSEA=0.000, 90% C.I. 0.000-0.081

Dinehart et al, 2006

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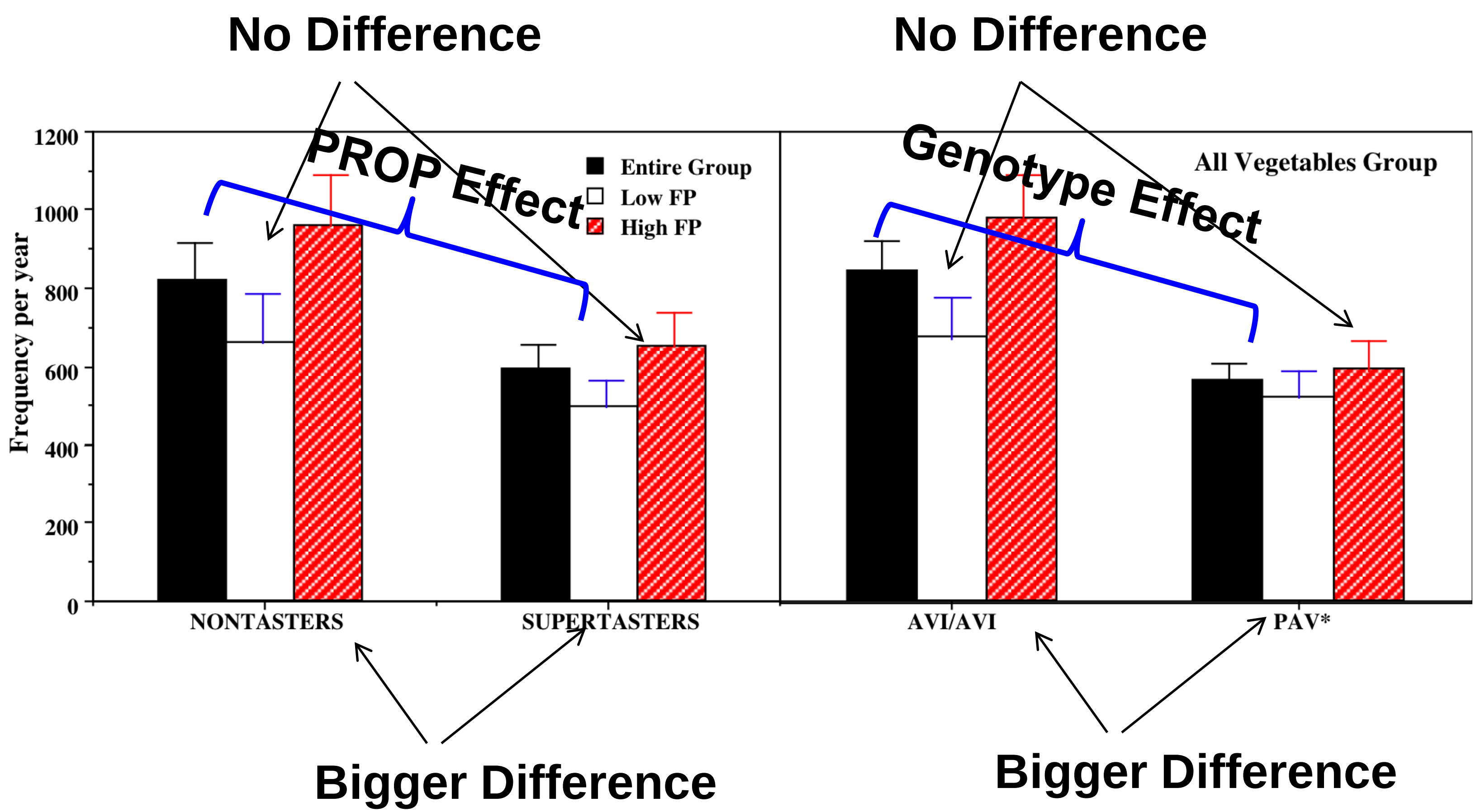
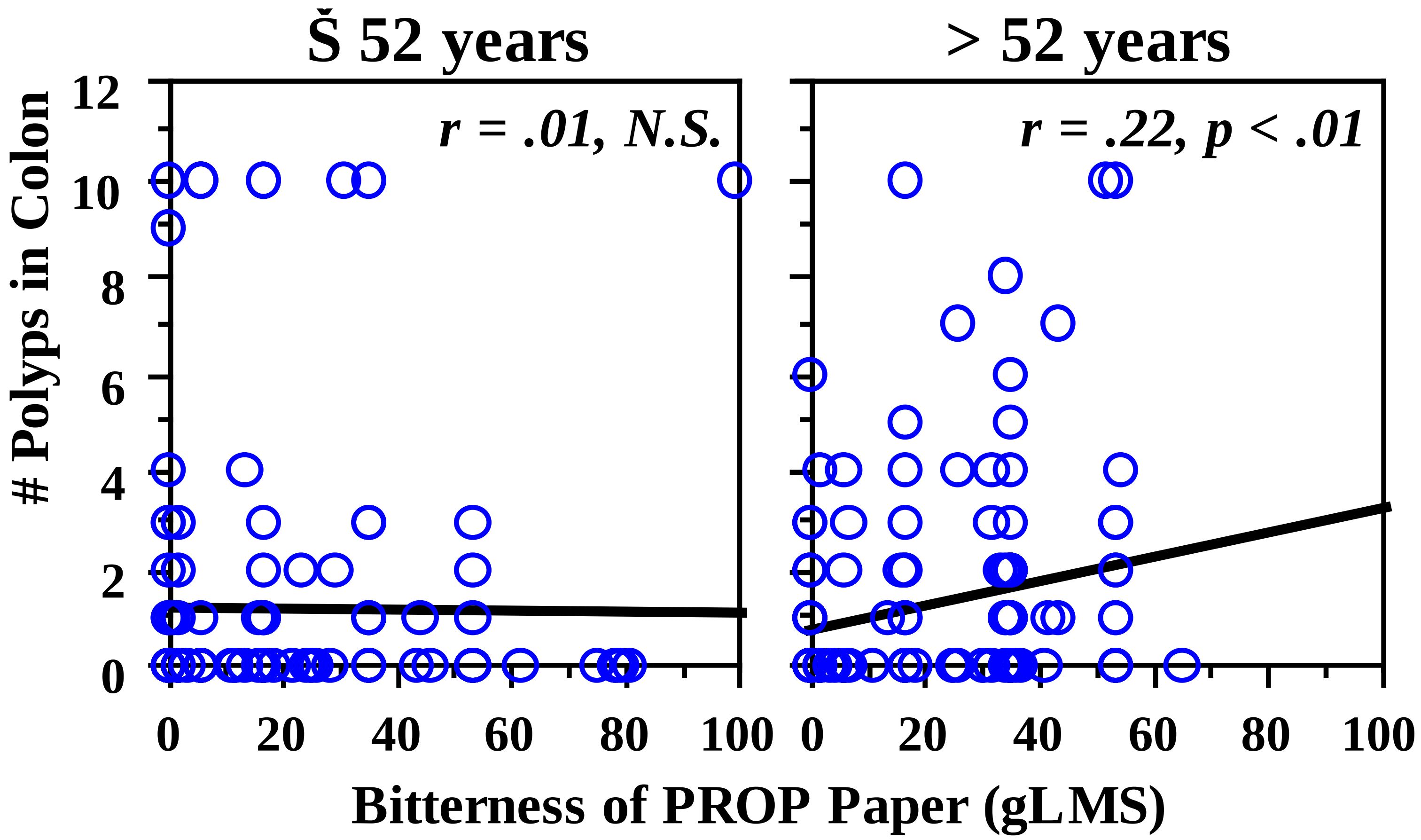
Multiple trait interactions can hide single trait effects



FP number moderates the nontaster effects on vegetable intake

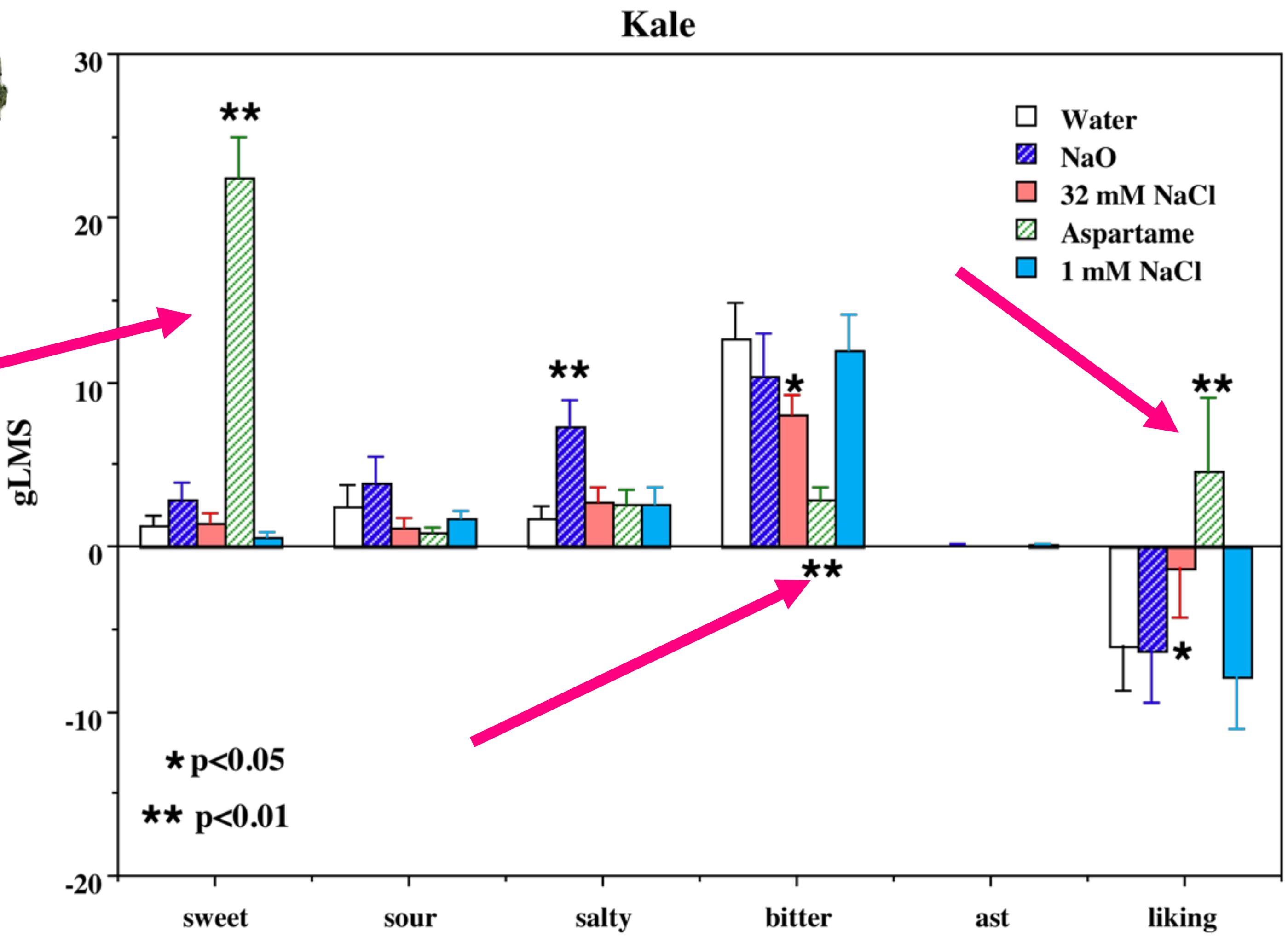
Duffy et al, 2010

PROP bitterness and Colon Cancer Risk in Men: Preliminary Findings



Basson, Bartoshuk, DiChello, Panzini, Weiffenbach, & Duffy, 2005

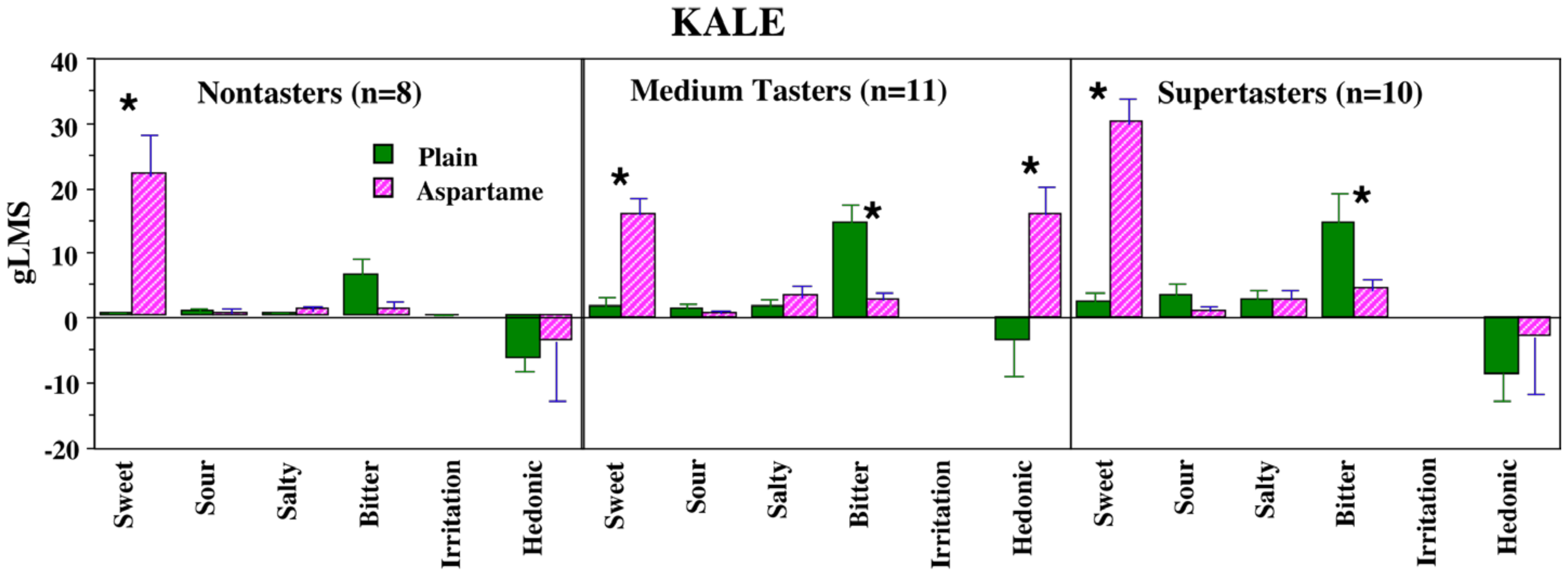
Can We Block Vegetable Bitterness to Improve Palatability?



Adding Light Sweetness

FNCE 2007

Added Sweetness—Just Right for the Medium Tasters



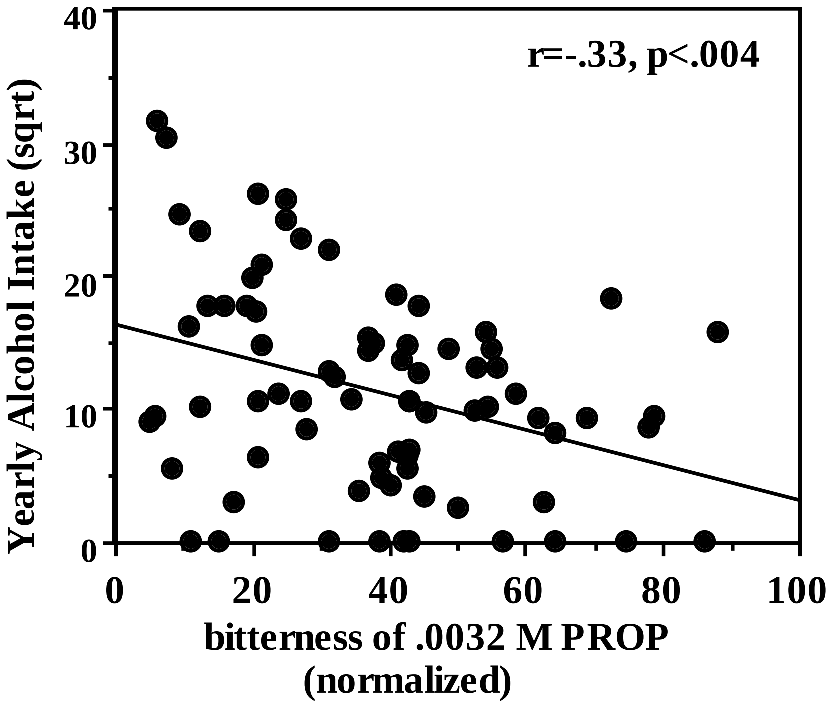
Nontasters - Too sweet—not enough natural bitterness to block the sweetness

Supertasters - Too sweet—they taste the sweetener too intensely

FNCE 2007

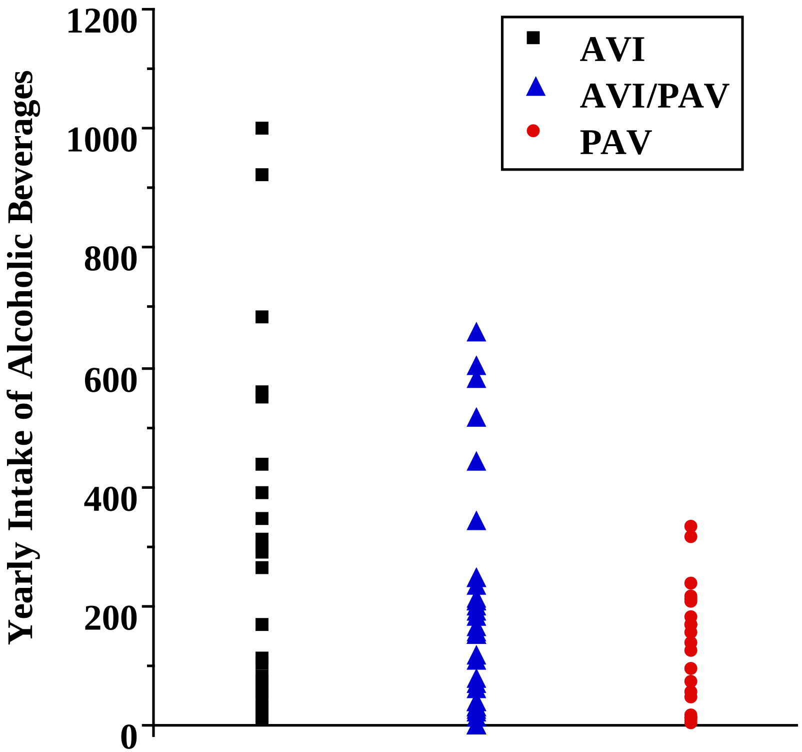
Supertasters—sensory hindrance to consuming alcoholic beverages

PROP bitterness



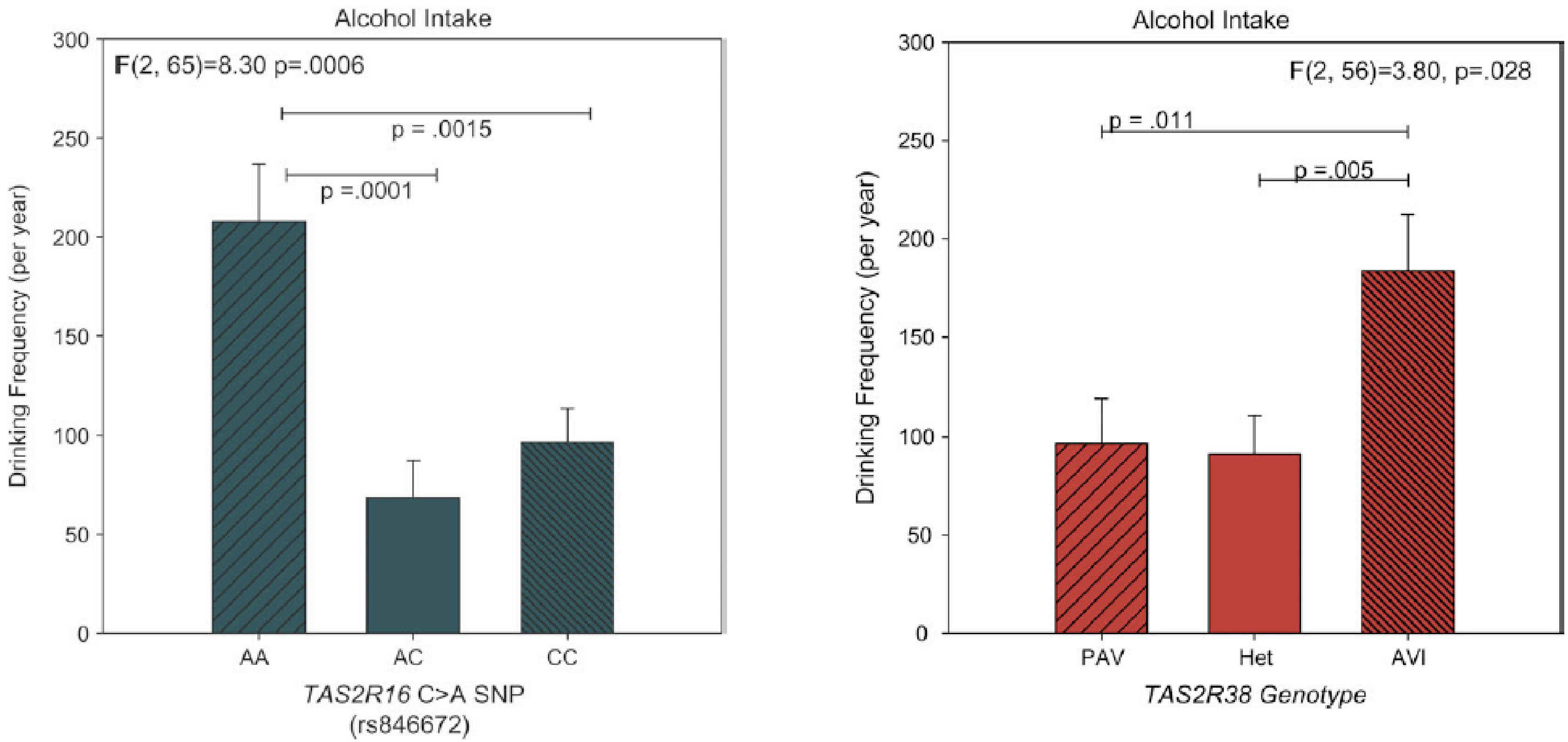
Duffy et al, 2004

TAS2R38 genotype



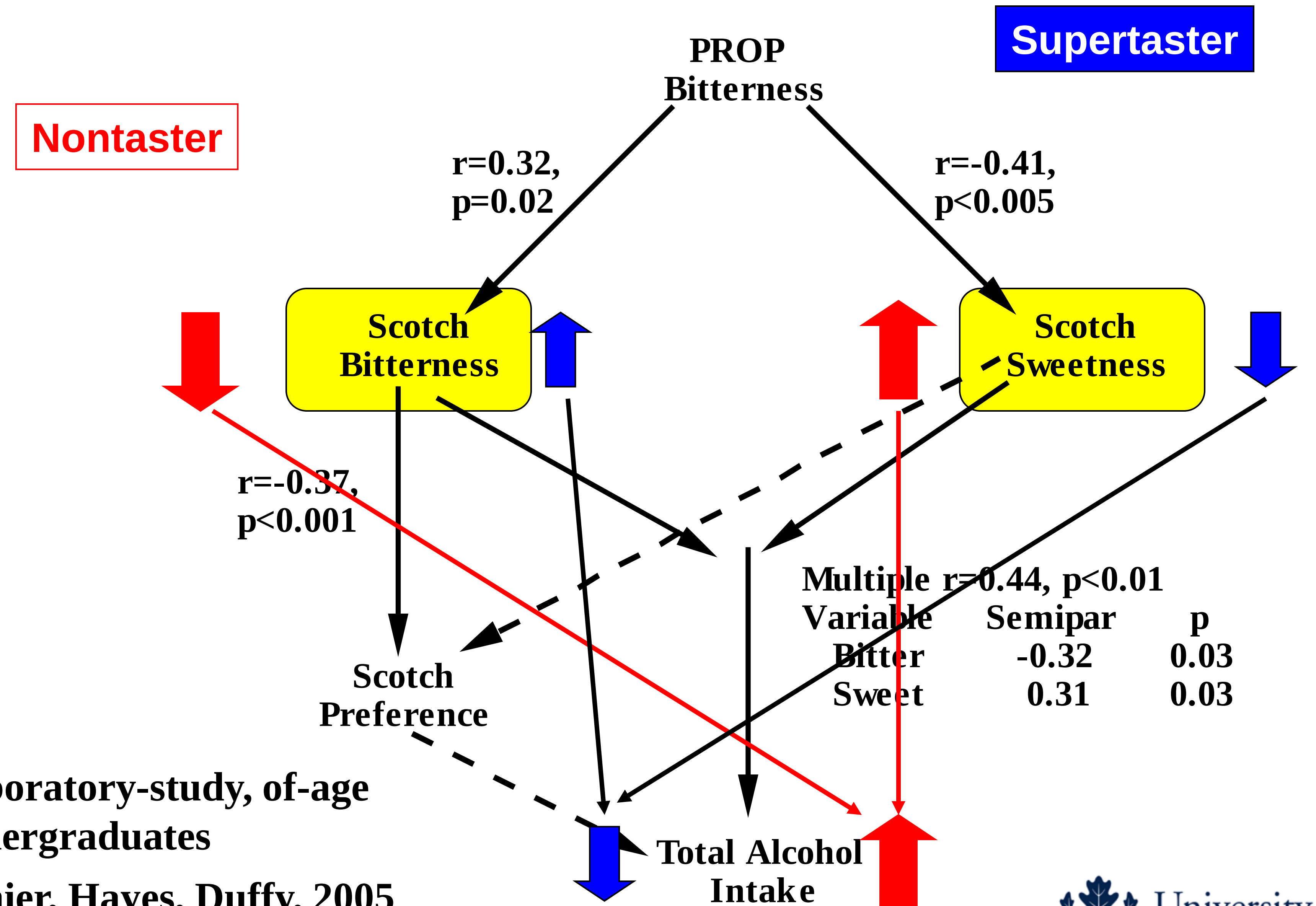
Duffy et al, 2004

- **Wang et al, Functional variants in TAS2R38 and TAS2R16 influence alcohol consumption in high-risk families of African-American Origin. Alc Clin Exp Res, 2007**



Hayes et al, Chemical Senses in Press, different SNP
Lack of LD – both could exert unique effects on alcohol intake

PROP bitterness, alcohol sensation, preference & intake



Laboratory-study, of-age undergraduates

Lanier, Hayes, Duffy, 2005

University of Connecticut

Human Heredity

Hum Hered 2010;70:177–193
DOI: 10.1159/000317056

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Using a Pharmacokinetic Model to Relate an Individual's Susceptibility to Alcohol Dependence to Genotypes

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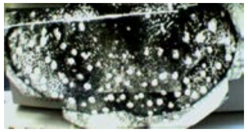
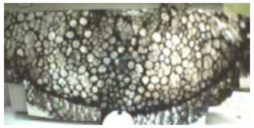
"However, it appears that the protective effect of TAS2R38 * 1 somewhat overrides the risk conferred by ADH1B * 1 , similar to our hypothesis; individuals are not likely to develop AD [Alcohol Dependence] if they rarely drink, despite any metabolic predisposition they may have."

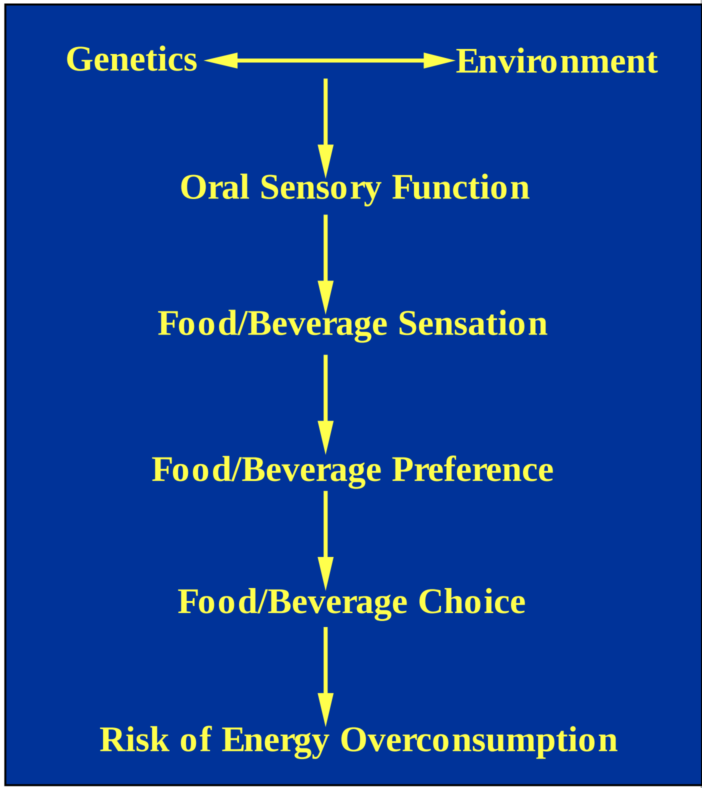
Summary and preference to link taste and health

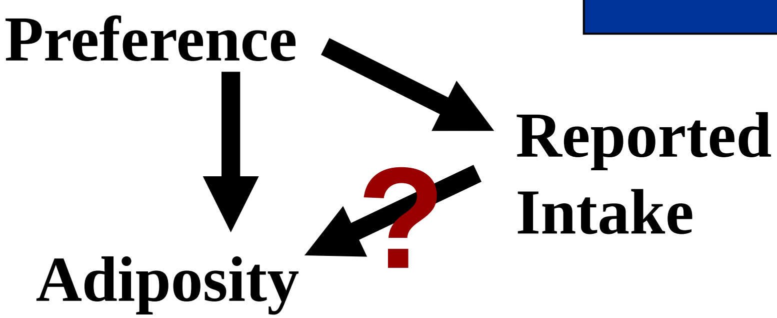
Oral Sensory Function
Multiple markers to capture variation
Emerging genotypes




Matching foods/ beverages with oral sensory variation



Include preference evaluation to assess diet-health relationships



PREVENTING CHRONIC DISEASE
PUBLIC HEALTH RESEARCH, PRACTICE, AND POLICY
VOLUME 4: NO. 2 APRIL 2007

SPECIAL TOPIC

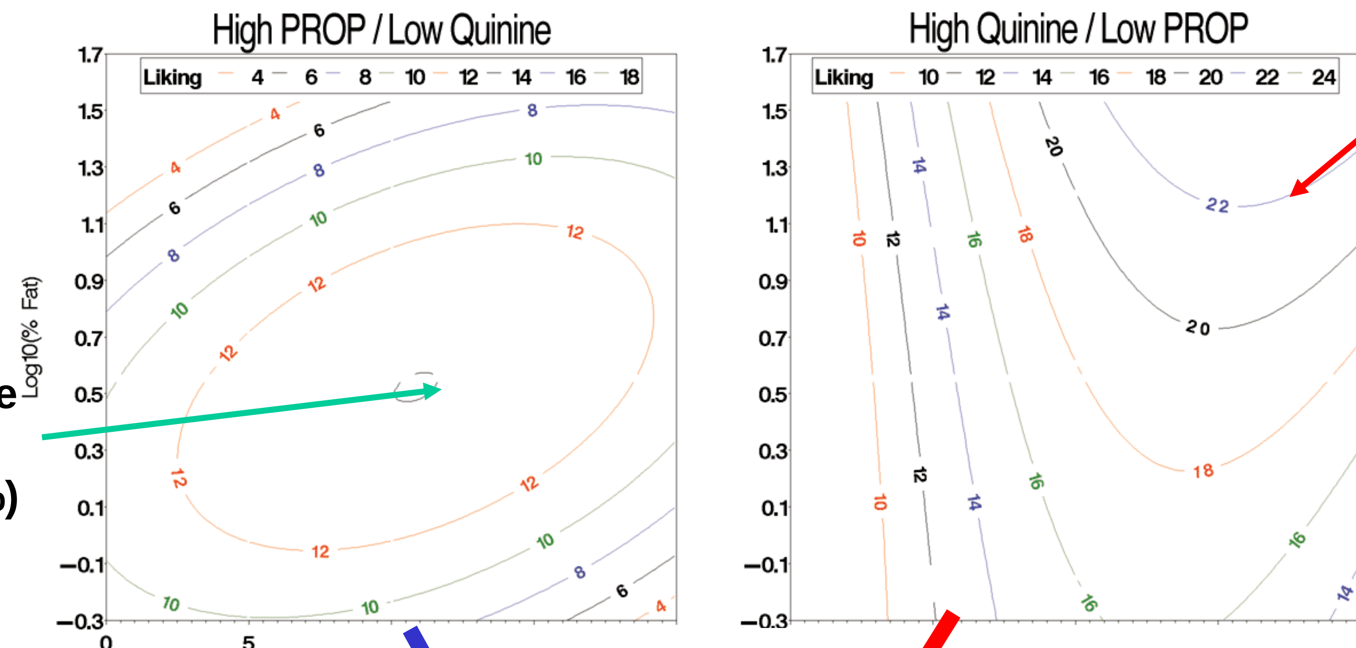
Addressing the Obesity Epidemic: A Genomics Perspective

Examples of Genes Involved in Obesity and Their Associated Phenotypes

Gene	Associated Phenotype (Characteristic)
Leptin	Satiation, metabolism
Melanocortin	Feeding behavior, binge eating
Ghrelin	Appetite stimulation
Neuromedin β	Feeding behavior, satiety
PROP	Taste preference
PPAR	Fat metabolism
Mitochondrial uncoupling proteins	Energy expenditure
Melanocortin and MC4R	Energy expenditure

For detailed information about single-gene mutations and their association with obesity, see the *Obesity Gene Map Database* (9) and CDC's *Obesity and Genetics: A Public Health Perspective* (10).

Normal Weight Adults: Fat/Sweet Mixtures Revisited Response Surface Models (Hayes & Duffy 2008)

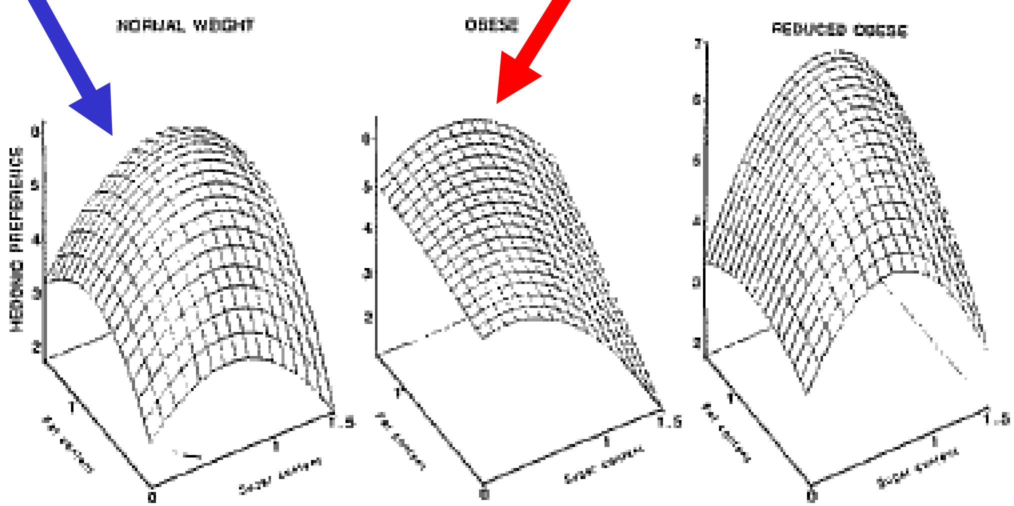


15% sucrose Light cream (soda 9-10%)

Like > a lot

10% sucrose whole milk (soda 9-10%)

Like ok



Drewnowski et al, 1985

University of Connecticut

Variation in the Bitter-taste Receptor Gene *TAS2R38*, and Adiposity in a Genetically Isolated Population in Southern Italy

Beverly J. Tepper[1], Yvonne Koelliker[1], Liqiang Zhao[1], Natalia V. Ullrich[1], Carmela Lanzara[2], Pio d'Adamo[2], Antonella Ferrara[2], Sheila Ulivi[2], Laura Esposito[2] and Paolo Gasparini[2]

Female PROP nontasters heavier than supertasters

Table 3 Age-adjusted, BMI and WC as a function of PROP phenotype or *TAS2R38* haplotype

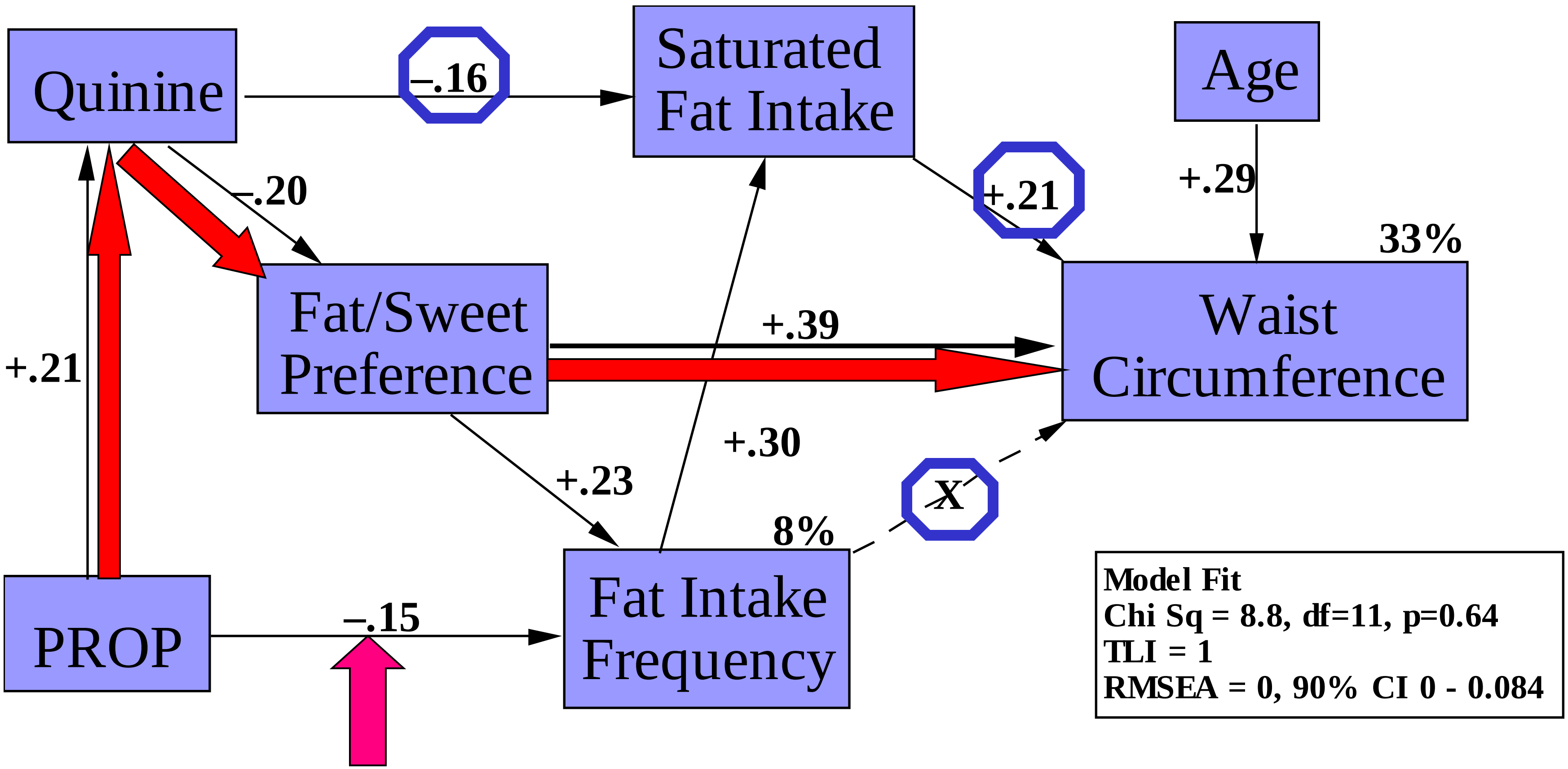
	PROP phenotype				*TAS2R38* haplotype			
	Nontaster	Medium taster	Super-taster	*P*	AVI/AVI	PAV/AVI[a]	PAV/PAV	*P*
BMI (kg/m²)								
Males	26.7 ± 0.4	26.4 ± 0.4	25.0 ± 132	0.50	25.9 ± 0.5	26.1 ± 0.4	27.7 ± 0.6	0.08
Females	29.5 ± 0.6 [a]	26.8 ± 0.6 [b]	26.3 ± 0.7 [b]	0.001	28.4 ± 0.6	27.3 ± 0.5	26.9 ± 0.8	0.26
WC (cm)								
Males	93.2 ± 1.4	93.0 ± 1.6	91.1 ± 4.0	0.80	91.2 ± 1.6	92.5 ± 1.5	96.4 ± 2.1	0.10
Females	90.7 ± 1.6 [a]	85.6 ± 1.5 [b]	82.7 ± 1.6 [b]	0.001	89.3 ± 1.6	85.0 ± 1.3	85.6 ± 2.2	0.23

Values are means (±s.e.m.). Values with different superscripts are significantly different at $P < 0.01$ by Duncan's Multiple Range Test.
[a]AVI/* individuals ($n = 31$) were included with the PAV/AVI group.

Effects modified by dietary restraint and not captured by haplotype

Structural Equation Modeling

Linking Taste Markers with central adiposity thru survey fat/sweet liking



Hayes et al, Pangborn 2007

Liking/Disliking for high-fat and sweet foods explains greater variance in adiposity

L/D as a value-added measure

Predicting WC in hierarchical regression

Step	Predictor	total R^2	delta R^2	p change	final sr	final p
Model 1						
1	Age	8.6%	-	.004	.290	.001
2	Saturated Fat	18.5%	9.8%	.001	.188	.030
3	Liking/disliking	33.0%	14.5%	<.001	.381	<.001
Model 2						
1	Age	8.6%	-	.004	.285	.001
2	Liking/disliking	29.5%	20.8%	<.001	.374	<.001
3	Saturated Fat	32.7%	3.3%	.037	.181	.037

L/D as an alternative predictor

Response to a Buffet Meal – Nontaster women consume more

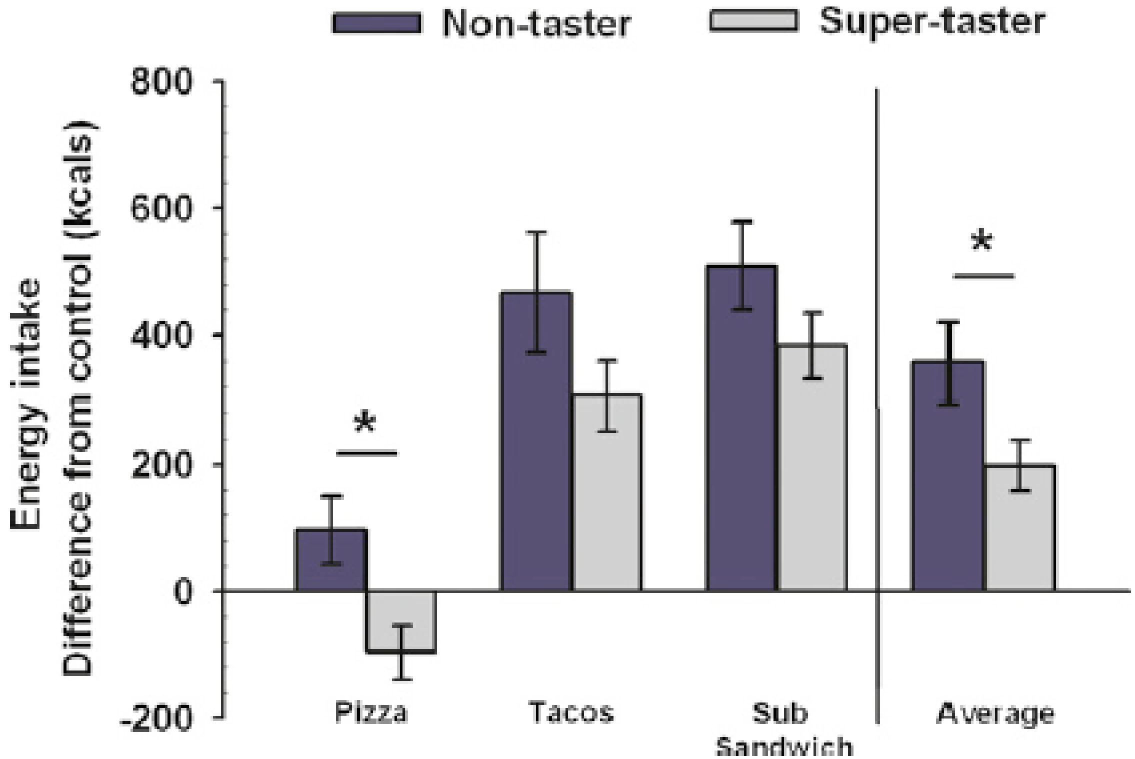


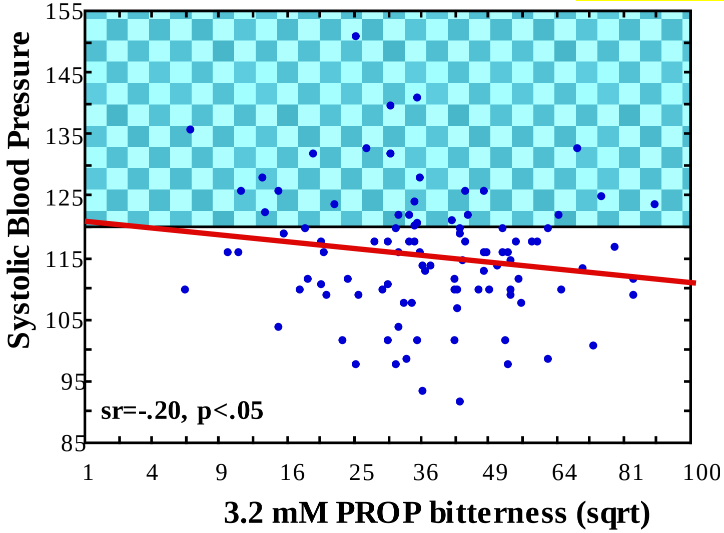
Fig. 1. Mean differences (±SEM) in energy intake (kcal) between the control meal and the buffet meals in non-taster ($n = 14$) and super-taster ($n = 18$) women. Energy intakes differed between groups for the pizza buffet lunch and the average of the three buffet lunches. $^*p < 0.0$.

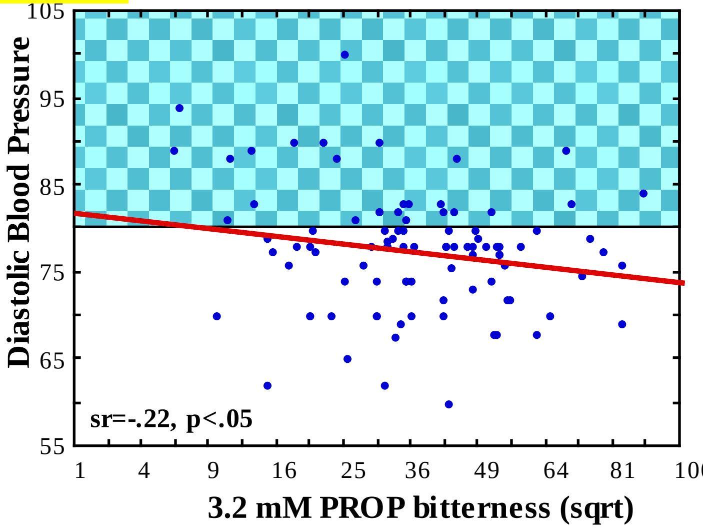
Tepper et al, 2010 – Appetite, in press

Dietary Risk	AHA Guidelines 2007	Orosensory Variation
Saturated fat, trans fat and cholesterol	High intake can elevated LDL-cholesterol	Low tasters like and consume more fat
Added Sugars	Elevated intakes, especially as liquids, increases risk of energy over-consumption and obesity	Low tasters like and consume more sweets
Salt	Elevated intakes, especially in salt-sensitive individuals, can elevate blood pressure	Supertasters like and consume more
Alcohol	While moderate intakes can lower CVD risk, high intakes increase blood pressure	PROP nontasters like and consume more
Obesity	Increases risk of elevated blood pressure and dyslipidemia	Low tasters show greater obesity risk
Fruits, Vegetables and whole grains	Low intakes may increase risk of overweight and elevated blood pressure and cholesterol	supertasters consume fewest vegetables

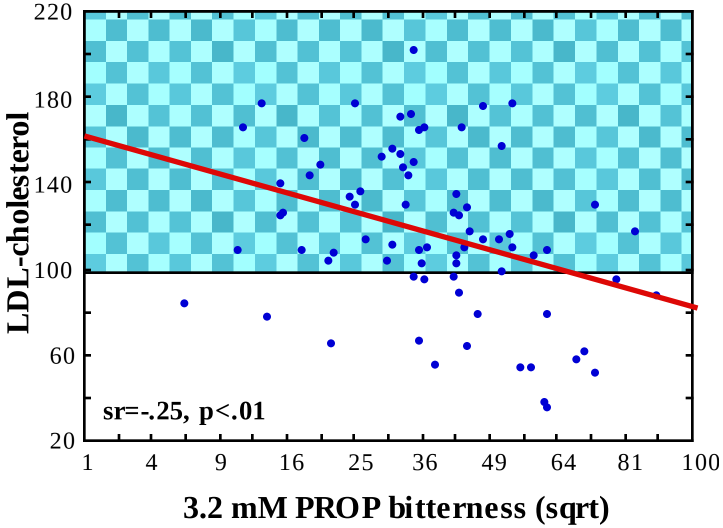
PROP Bitterness Associates with CVD Risks

Blood Pressure





LDL Cholesterol



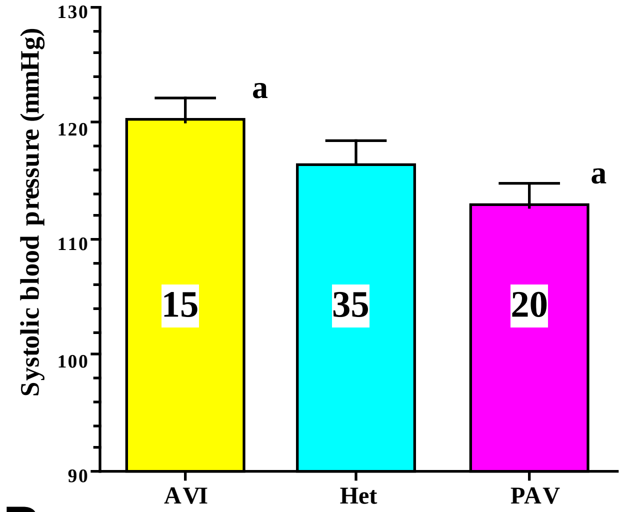
Multiple Linear Regression

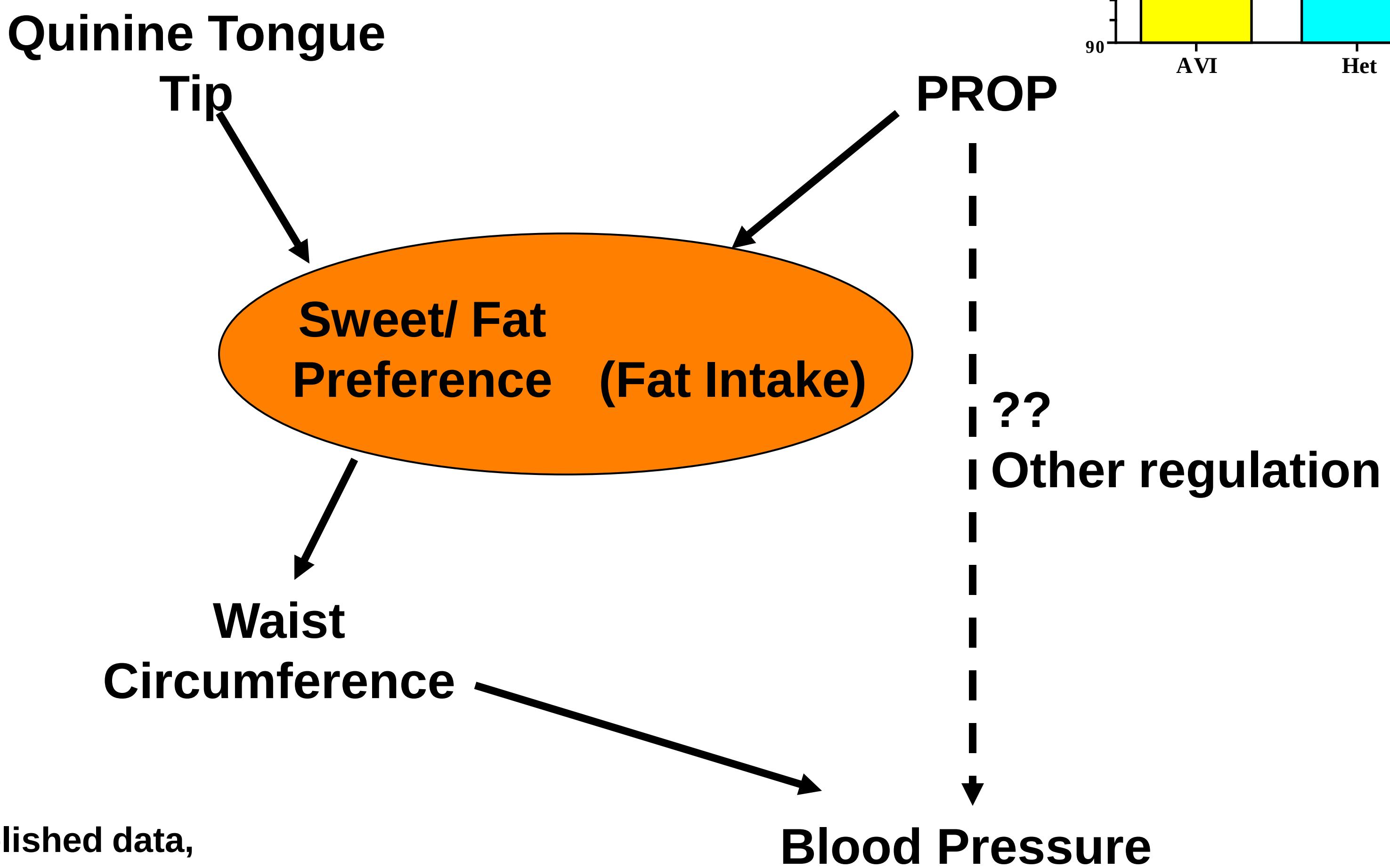
Non-significant
Total Cholesterol
HDL-cholesterol
TG

Unpublished data,
conference presented

Summary Blood Pressure

Taste Receptor Gene (ANCOVA)

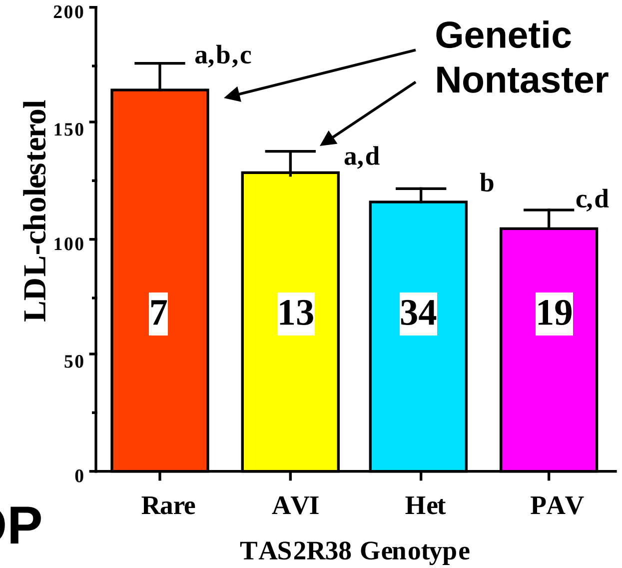


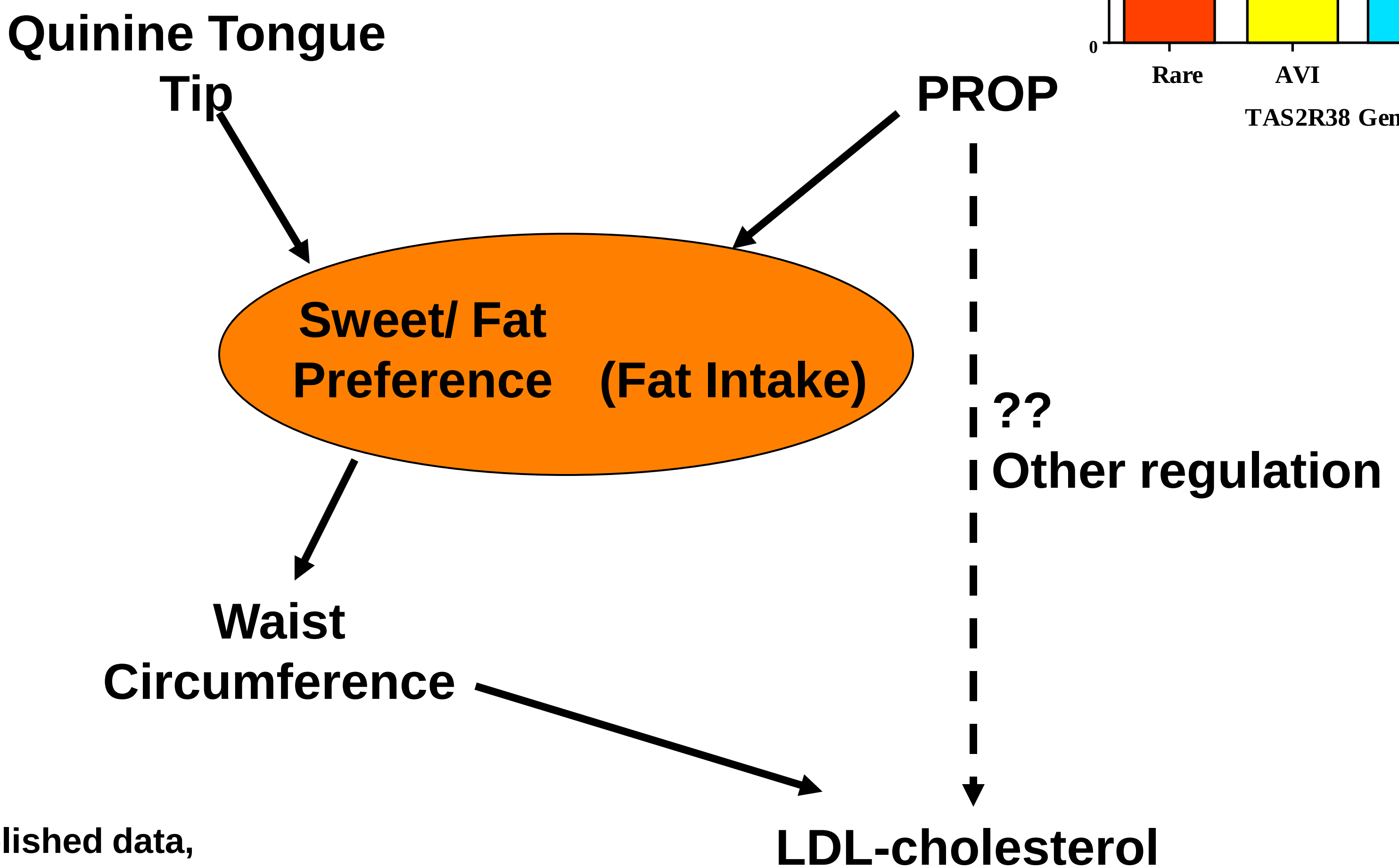


Unpublished data,
conference presented

Summary LDL-cholesterol

Taste Receptor Gene (ANCOVA)



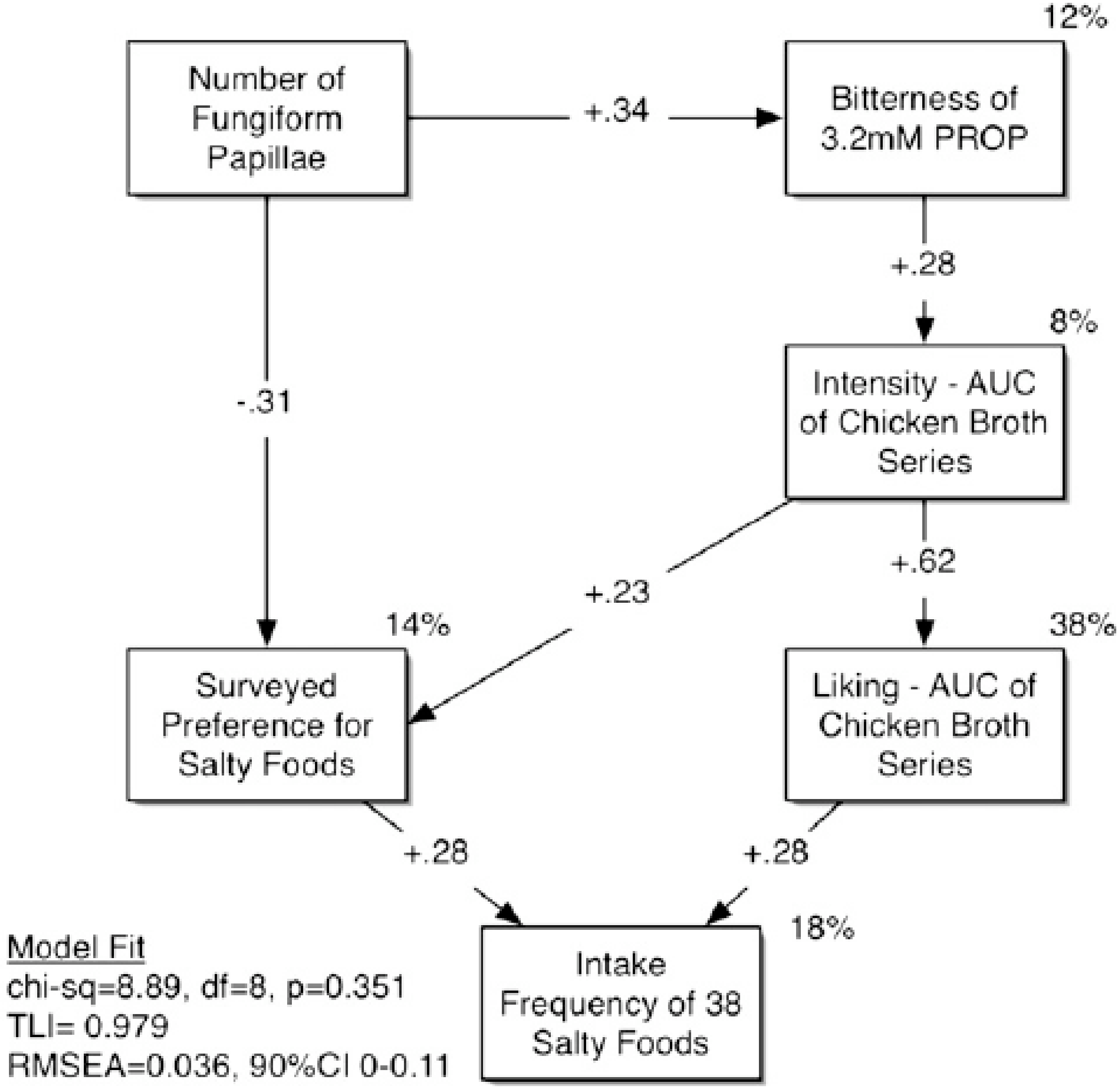


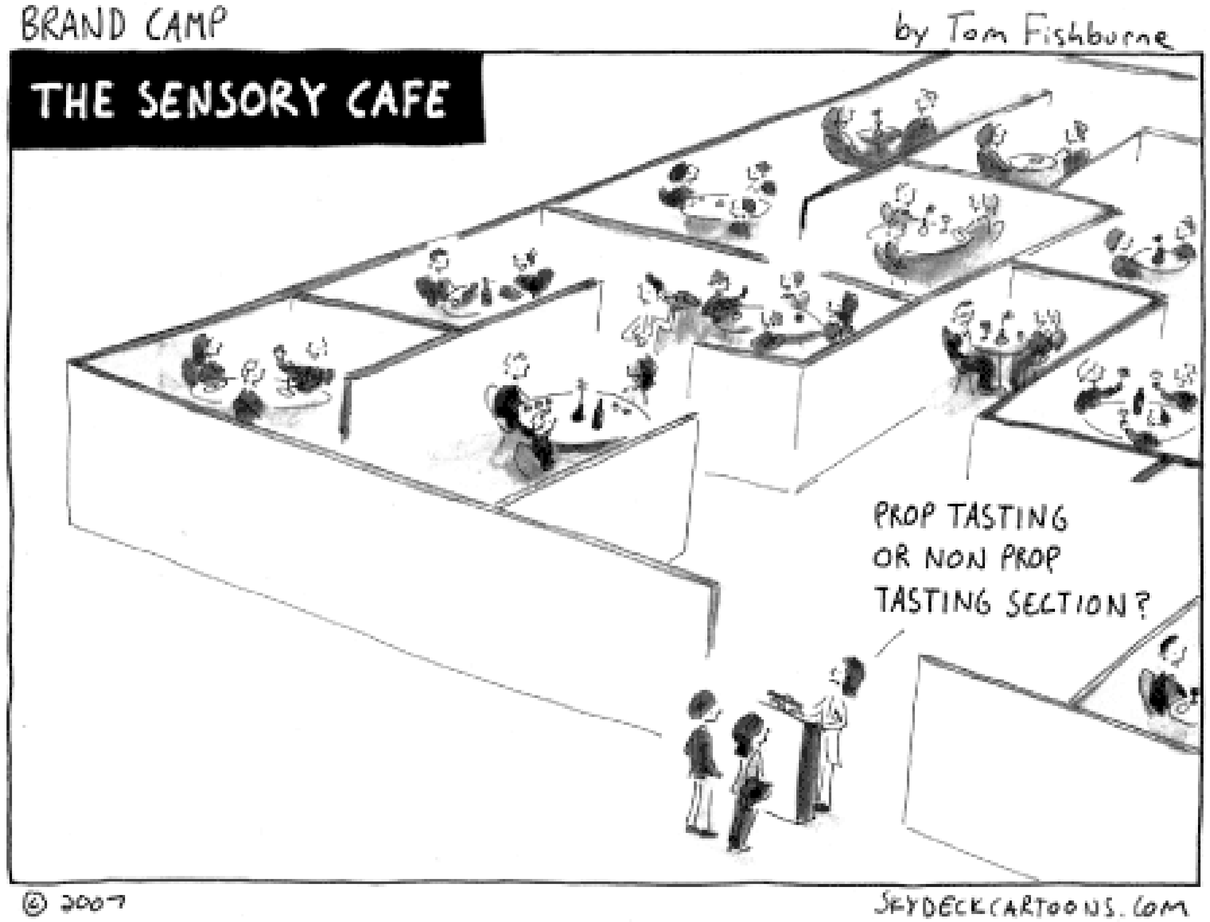
Unpublished data, conference presented

Salt Sensation, Liking and Intake: Indirect Taste Genetic Effects

- Sex effects modulate taste genetic effects
- NaCl as a taste and an irritant
- PROP supertasters – more aware of intensity differences in salt concentration
- Effects on food liking are food specific
  - In snack foods, supertasters like the salt more (salt is an important sensation)
  - In cheese, supertasters dislike low sodium cheese as it is more bitter
  - Nontasters add salt more at the table – flavor enhancer?
- PROP bitterness and FP density have indirect impact on sodium intake via liking/preference (Hayes, Sullivan, Duffy, 2010).

Indirect effects of taste genetics




BRAND CAMP
by Tom Fishburne
THE SENSORY CAFE
PROP TASTING OR NON PROP TASTING SECTION?
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SKYDECKCARTOONS.COM

NIH Toolbox

- brief measures for the assessment of cognitive, emotional, motor, and sensory function for use in clinical trials, epidemiological and longitudinal studies.

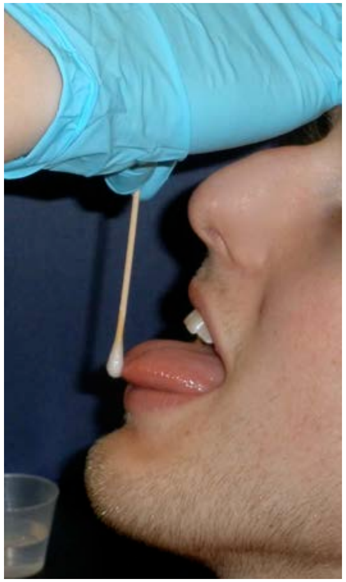
- taste perception is assessed as one of six areas of sensory function.

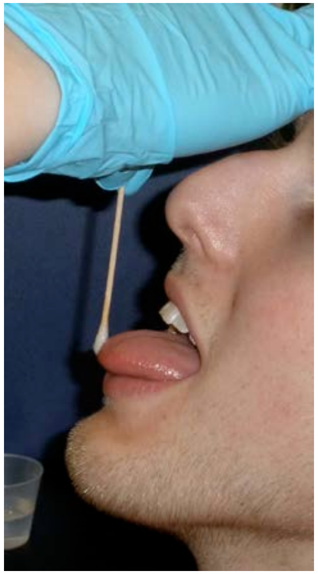
- Three taste measures, one for pediatric populations (J. Menella et al) and two for adult populations, were selected by a team of eleven scientists with expertise in taste perception.

Chemosensory Function – Population Based Study

- Anterior tongue and whole mouth

Water
1 mM QCHl
1 M NaCl





- 3.2 mM PROP bitterness
- Data treatment – PROP, PROP ratio, quinine tip/whole mouth, salt tip/whole mouth, quinine/PROP concordance and discordance
- Brief odor identification taste

Summary of Need

- Phenotypes or genotypes that are markers for dietary intake and/or differential risk of chronic conditions (susceptibility biomarker)
  - chemosensory-related genotypes
  - chemosensory phenotypes
  - preference phenotypes
- Consistent measures of phenotyping for multi-center clinical studies
- Measures that have utility, validity, and feasibility for epidemiological studies.
- Intervention studies that consider variation in taste and oral sensation

Research Support / Grants

- USDA NRI and Hatch
- American Diabetes Association Foundation
- NIH DC00283 and NIH Chemosensory Research Project
- NIH Toolbox
- NIDCD/Westat

Past Students and Current Students

- Julie Peterson MS, RD
- Megan Phillips PhD, RD
- Audrey Chapo MS, RD
- Heather Hutchins PhD, RD
- Sarah Lanier MS, RD
- Mary Dinehart, MS, RD
- Bridget Sullivan MS, RD
- Shristi Rawal, BS
- Katryna Minski, RD
- Kerah Kennedy, MS, RD

Collaborators

- UCONN Allied Health —Judy Brown, Denise Anamani, Pouran Faghri, Maria-Luz Fernandez
- Linda Bartoshuk, PhD, Margaret Wallace—Univ of Florida
- Ken & Judith Kidd—Yale University
- John Hayes, PhD—Penn State University