Individual Differences in Sensory Perception and Human Health

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….no two people are exactly alike in their sensory reactions….Blakeslee, 1935

Assertion: People differ in their sensory experience of food and drink and these differences may account in part for food likes and dislikes and food choice and intake

Unpacking this assertion:
• Sensory differences
• Likes and dislikes
• Intake
Sensory differences are common

2-ethyl fenchol – *mushroom*
Beta-ionone – *violets*
Capsaicin – *burning, spicy*
Citric acid – *sour*
Galaxolide – *musk*
Guaiacol – *liquid smoke*
Menthol – *cooling*
NaCl – *salty*
PEA – *phenyl ethyl alcohol - rose*
PTC – *phenylthiocarbamide – bitter*
Sucralose – *high potency sweetener*
TMA – *trimethylamine - fish*

Scale of big data and genome wide association studies

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**Ongoing**

Million Veterans Program
All of Us
Scale of big data and genome wide association studies

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UK Biobank - what data are available?
Genotypes, 13,791,467 markers
Food intake, up to four 24-hour diet recalls
No taste or smell data except ICD-10 codes
About how many pieces of FRESH fruit would you eat per DAY?
(Count one apple, one banana, 10 grapes etc as one piece; put '0' if you do not eat any)

Please provide an average considering your intake over the last year
Fruit intake data from the UK Biobank

Data-Field 1309
Description: Fresh fruit intake
Category: Diet - Lifestyle and environment - Touchscreen - UK Biobank Assessment Centre

- Participants: 501,647
- Item count: 565,655
- Stability: Complete
- Value Type: Integer, pieces/day
- Item Type: Data
- Sexed: Both sexes
- Debut: Jan 2012
- Version: Sep 2019
- Defined instances: 4
- Array: No

565,655 items of data are available, covering 501,647 participants. Some values have special meanings defined by Data-Coding 100373. Defined instances run from 0 to 3, labelled using Instancing 2. Units of measurement are pieces/day.

- Maximum: 50
- Decile 9: 4
- Decile 8: 3
- Decile 7: 2
- Decile 6: 2
- Median: 2
- Decile 4: 2
- Decile 3: 1
- Decile 2: 1
- Decile 1: 1
- Minimum: 0

- There are 41 distinct values.
- Mean = 2.29456
- Std.dev = 1.60712
- 3915 items above graph maximum of 7
- 17989 items have value -10 (Less than one)
- 400 items have value -3 (Prefer not to answer)
- 2049 items have value -1 (Do not know)

Counts of participants/items last updated 07 Sep 2019.
GWAS: Breaking it down
Statistical significance is striking but effect size is small

beta = -0.049, p = 3.95e-47

**OR6B1 genotype effect on Fresh fruit intake**
Post GWAS studies: Related phenotypes and PheWAS#
mRNA and protein expression
Function

#PheWAS == one variant, many or all phenotypes (traits)
Which of the following ice cream flavors do you like best?

- Vanilla
- Chocolate
- Strawberry
- None of the above
OR6B1 variants are associated with strawberry ice cream preference

Figure 4. Genome-wide association study Manhattan plot for ice cream flavor preferences. Possible responses were “vanilla” (n = 123,599) or “strawberry” (n=45,423). This model treated the responses as binary variables, and adjusted for age, sex, genotyping platform, and the top-5 principal components of genetic ancestry.
Post GWAS studies:
Related phenotypes and PheWAS
mRNA and protein expression
Function
Olfactory epithelium tissue for mRNA transcript profiling by endoscope
OR6B1 mRNA is highly expressed in human olfactory receptor neurons

All olfactory receptors, rank ordered by average counts in humans

[Graph showing normalized mRNA transcript counts for OR6B1]
OR6B1 is not expressed in other tissues tested except testes

https://www.gtexportal.org/home/gene/OR6B1
Post GWAS studies:
Related phenotypes and PheWAS
mRNA and protein expression
Function
Olfactory receptor functional assay

1. Olfactory receptors are GPCRs; activated, they produce cAMP
2. We transfect cells with (a) the receptor (genotypes) and (b) a reporter
3. When an odor is delivered, the cells glow yellow
4. Light production increases as odor amount increases for a dose-response curve
Luciferase Assay

Normalized Response

- OR7D4 RT
- OR7D4 WM

[end diagram]
Cell-based assays to find flavor ligands for olfactory receptors OR2A25 (near OR6B1) but no ligands yet for OR6B1

Linalool – found in essential oils and many plants

Different genotypes
- SVA
- NAP
- NVP
- NVA
- SVP

10.1073/pnas.1804106115
Wrapping up

• Sensory differences are common
• Fruit intake GWAS points to olfactory receptors (OR)
• Functional OR studies are underway

Future
• Volatile cheminformatics common to many fruits
Looking ahead

Scale and big data
• Data scientists trained in chemosensory biology and nutrition
• Phenotyping, chemosensory measures and food intake data

Public policy, medicine and food implications
• Using genetic information for the forces of good
• Tailoring foods including plants
Most significant associations are on top of \textit{OR6B1}, an olfactory receptor.
Genetic variants on human chr 7 and fresh fruit intake
The consensus OR for subfamily hOR6 has ethyl 3-methyl-3-phenylglicidate (also known as 'strawberry glycidate’) and 3-methyl-1-butanethiol as top ligands.

https://www.biorxiv.org/content/biorxiv/early/2019/04/10/605337.full.pdf
81+ volatile compounds from strawberries