Sensory Cues for Dietary Fat:
Behavioral Evidence of Gustatory Detection

David W. Pittman, Ph.D.
Department of Psychology,
WOFFORD COLLEGE
Spartanburg, SC

Obesity Trends in the U.S.

Slide courtesy of Tim Gilbertson
What is driving OBESITY?

- Major contributors to obesity formation:
  - Genes (≈5% obesity)
  - Physical Inactivity
  - Over-consumption of high-fat, high-caloric food

Why do we continue to consume high-fat foods?

Dietary Fat = Triglycerides

Lingual lipase hydrolyzes triglycerides into fatty acids

<table>
<thead>
<tr>
<th>Corn Oil</th>
<th>Palmitic</th>
<th>Stearic</th>
<th>Oleic</th>
<th>Linoleic</th>
<th>Linolenic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13</td>
<td>3</td>
<td>31</td>
<td>52</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. Abundance ratio (%) of the hydrolyzed products by rat lingual lipase

<table>
<thead>
<tr>
<th>Reaction Time, s</th>
<th>Triolein</th>
<th>Oleic Acid</th>
<th>Diocetyl Glycerol</th>
<th>Monoleoyl Glycerol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>99.70</td>
<td>0.12</td>
<td>0.03</td>
<td>0.00</td>
</tr>
<tr>
<td>1</td>
<td>96.02</td>
<td>1.48</td>
<td>2.17</td>
<td>2.25</td>
</tr>
<tr>
<td>5</td>
<td>94.87</td>
<td>2.17</td>
<td>2.25</td>
<td>0.36</td>
</tr>
<tr>
<td>10</td>
<td>88.30</td>
<td>5.44</td>
<td>4.66</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Are there receptors for FAs?

Taste Receptor Cell

**Linoleic Acid**

- Linoleic acid and other related free fatty acids inhibited the Shaker Kv1.5 channel
- Linoleic acid enhanced stimulus-induced depolarization of the taste receptor cell


Delayed Rectifying Potassium Channels (DRK)

- Linoleic acid and other related free fatty acids inhibited the Shaker Kv1.5 channel
- Linoleic acid enhanced stimulus-induced depolarization of the taste receptor cell
CD36 – Fatty Acid Transporter Protein

- CD36/FAT protein localized expression in gustatory epithelium
- CD36 knockouts have impaired FA sensitivity

- Psychophysical measurements of FA sensitivity – preferences


This slide contained unpublished data.
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Research objective is to develop an animal behavioral model:

- Does dietary fat stimulate the taste system through fatty acids providing an immediate motivation for consumption?
  - Do fatty acids affect the ingestion of other tastants?
  - Are fatty acids detectable through the taste system?
  - What are the genetic influences on fatty acid sensitivity?

Psychophysics of Animal Taste
Dilog MS-160 ~ Davis Rig

Live Web Cam @ FatTaste.com
1. Do fatty acids affect the ingestion of other tastants?

Licking response to sucrose and glucose in water-replete, male, Sprague-Dawley rats

Linoleic acid increased licking to appetitive stimuli – *increase in perceived intensity*
1. Do fatty acids affect the ingestion of other tastants?

Water-restricted, male, Sprague-Dawley rats

Lick Ratio: Licks stimulus / Licks water
1.0 stimulus = water  0.0 stimulus avoided
1. Do fatty acids affect the ingestion of other tastants?

Linoleic acid decreased licking to aversive stimuli – *increase in perceived intensity*
1. Do fatty acids affect the ingestion of other tastants?

**Evidence:**

- Both linoleic and oleic acid (88µM) increased licking to appetitive stimuli and decreased licking to aversive stimuli
- **Increase in perceived intensity of tastants**
- **Linoleic acid produced greater effects than oleic acid**

Pittman DW, Labban CE, Anderson AA, O’Connor HE. Linoleic and oleic acids alter the licking responses to sweet, salt, sour, and bitter tastants in rats. Chem Senses. 2006 Nov;31(9):835-43.

2. Are fatty acids detectable through the taste system?

- **Conditioned Taste Aversion (CTA)**
  - Pair fatty acid consumption with either LiCl injection (CTA) or saline (control)
- Measure detection of the fatty acid by future avoidance during brief access trials
Involvement of the Taste System

- CT = anterior 2/3 tongue
- GL = posterior 1/3 tongue
- Converge in the brainstem and then go on to taste perception areas of the brain

2. Are fatty acids detectable through the taste system?

(A) Linoleic Acid (uM) vs. Lick Ratio (8s)

(B) Oleic Acid (uM) vs. Lick Ratio (8s)

8s trials
2. Are fatty acids detectable through the taste system?

A. 8s trials

B. 30s trials

C. Oleic Acid (μM)

D. Linoleic Acid (μM)
2. Are fatty acids detectable through the taste system?

A

B

C

D

3 consecutive days of CTA pairings

Pre-CTX

Post-CTX
2. Are fatty acids detectable through the taste system?

Evidence:
- Micromolar linoleic and oleic acid can be avoided in brief access trials following CTA
- Increasing trial duration or CTA pairings increases the sensitivity to fatty acids
- Eliminating the chorda tympani gustatory nerve impairs the ability to detect fatty acids
- The gustatory system (CT) plays a role in the detection of fatty acids
- Linoleic is more salient than oleic acid

Pittman D, Crawley ME, Corbin CH, Smith KR. Chorda tympani nerve transection impairs the gustatory detection of free fatty acids in male & female rats. Brain Res. 2007 Jun 2;1151:74-83.

3. Genetic influences on fatty acid sensitivity?


**p<0.001 compared w/ O-M
Slide courtesy of Tim Gilbertson
This slide contained unpublished data.

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3. Genetic influences on fatty acid sensitivity?

**Evidence:**
- O-M (obesity-prone) show stronger conditioned avoidance than S5B (obesity-resistant) rats
- Females show stronger conditioned avoidance than male rats
- **Similar detection capabilities between O-M & S5B and male & female rats**
- **Subtle differences in FA-sensitivity**
Physiological Evidence for the Gustatory Detection of FAs

Putative FA Receptors
- Valine
- Furfural
- Folate

linoleic
control
-60 mV
10 mV
100 ms
stimulus
C18:2 (10 µM)
200 pA
50 ms
-80 mV
+40 mV
control
C18:2 (10 µM)
200 pA
50 ms
-80 mV
+40 mV

Food Intake (g/day)

p<0.001 compared w/ O-M

Behavioral Evidence for the Gustatory Detection of FAs

FA Modulation
FA Detection
CT Nerve Involved in FA Detection

Fatty Acid Sensitivity
Collaborations with Tim Gilbertson:

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- IF&F

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