Nutritional, Hormonal and Surgical Influences on Food Reward Systems

Dr. Tony Goldstone MA MRCP PhD
Clinician Scientist & Consultant Endocrinologist

Computational, Cognitive and Clinical Neuroimaging Laboratory and Imperial Centre for Endocrinology
Imperial College London, Hammersmith Hospital, London

Association for the Study of Obesity - UK Congress on Obesity 2014
University of Birmingham, 16th Sept 2014
How Did We Get Here?

**Society**

**Food Environment**

**Urban Environment**

- Genetics
- Psychology
- Physiology
Outline

• Neurobiology of food reward
• Obesity influences
• Nutritional state influences
• Gut hormone influences
• Bariatric surgery influences
• Addictive behaviours and overeating
• Future directions
Regulation of Eating Behaviour

External cues:
- Food type
- Sensory system

Internal cues:
- Food intake
- Sensory system
- Nutritional state
- Hormones
- Autonomic nervous system
- Gut
- Fat tissue
- Anterior cingulate & insula cortex
- Ventral striatum
- Amygdala
- DLPFC
- OFC
- Hypothalamus
- Midbrain (VTA)
- Nucleus solitary tract
- Psychological cues
- Gender
- Obesity

Consummatory behaviour
Brain Regions Activated in Response to Palatable Food or Food-Associated Cues

fMRI Study Design

Study Design:

- **Blurred fMRI Study**
- **Picture Duration:** 2.5 sec / picture
- **Inter-stimulus Interval:** 0.5 sec
- **Block Duration:** 6 pictures / block
- **Category Blocks:** 10 blocks / category
- **Runs:** 2 runs

**Questions:**

- "How appealing is this picture to you?
  - Not at all (1)
  - Not really (2)
  - Neutral (3)
  - A little (4)
  - A lot (5)
Reward System Activation to Food Pictures

n=21 fasted, Z>3.2, P<0.05, High-calorie or low-calorie > objects
Food Reward in Obesity

↓ inhibitory control

↑ salience response
anticipatory reward

↓ receipt response
consummatory reward


Mathews J et al. *Arch Gen Psychiatry* 69:1226-37, 2012

Anticipatory Food Reward in Obesity

<table>
<thead>
<tr>
<th></th>
<th>Lean</th>
<th>Overweight</th>
<th>Obese</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>29</td>
<td>28</td>
<td>26</td>
<td>-</td>
</tr>
<tr>
<td><strong>Female n (%)</strong></td>
<td>16 (55)</td>
<td>16 (57)</td>
<td>21 (81)</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>29 [22.8 - 40.0]</td>
<td>30 [23.5 - 37.0]</td>
<td>38 [25.0 - 46.0]</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>European Caucasian (%)</strong></td>
<td>72.4</td>
<td>57.1</td>
<td>50.0</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>22.9 [21.6 - 24.3]</td>
<td>26.7 [25.8 - 27.9]^*</td>
<td>36.5 [32.5 - 42.4]^#</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Body Fat (%)</strong></td>
<td>20.9 [13.7 - 29.4]</td>
<td>31.4 [19.8 - 35.1]^*</td>
<td>46.9 [39.8 - 52.0] ^#</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

No difference in hunger ratings or high-calorie food appeal
No difference in external eating or reward sensitivity questionnaires
Greater emotional eating in overweight/obese
Higher dietary restraint in obese
Lower mood in obese

n=83, fasted overnight
Greater Activation to *High-Energy Foods* in Overweight and Obese Subjects

n=81, ~⅓ lean, ⅓ overweight, ⅓ obese, age 19-55y, 63% female, BMI 19.1-53.1 kg/m²
High-calorie food > Objects, Obese/Overweight > Lean & Obese > Lean
Adjusting for age & gender, P<0.005 uncorrected
## fMRI Studies in Obesity and BED

**Ziauddeen et al. Nat Rev Neurosci 2012**

<table>
<thead>
<tr>
<th>Brain region</th>
<th>Response to presentation of food images</th>
<th>Response to cues signalling imminent presentation of food/juice reward (anticipation)</th>
<th>Response to consumption of reward</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obese</td>
<td>BED</td>
<td>BMI</td>
</tr>
<tr>
<td><strong>Regions associated with the reward circuitry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Striatum</td>
<td>2 ↑53.54, 1 ↓85, 1 ↔85</td>
<td>2 ↔67.88</td>
<td>1 ↑99, 1 ↓90, 1 ↔95.91.92</td>
</tr>
<tr>
<td>Midbrain</td>
<td>4 ↔63-66</td>
<td>2 ↔67.88</td>
<td>5 ↔65.09-92</td>
</tr>
<tr>
<td>PFC (orbital)</td>
<td>1 ↑86, 3 ↔85-85</td>
<td>1 ↑67</td>
<td>1 ↑95, 1 ↔80-92</td>
</tr>
<tr>
<td>PFC (lateral)</td>
<td>3 ↑54-56, 1 ↔83</td>
<td>2 ↔67.88</td>
<td>1 ↑95</td>
</tr>
<tr>
<td>PFC (medial)</td>
<td>2 ↑64.56, 1 ↓85, 1 ↔85</td>
<td>1 ↑67, 1 ↔85</td>
<td>1 ↓92</td>
</tr>
<tr>
<td>Amygdala</td>
<td>4 ↔63-85</td>
<td>2 ↔67.88</td>
<td>5 ↔65.09-92</td>
</tr>
<tr>
<td>Gustatory cortex (AI/FO)</td>
<td>1 ↑53, 3 ↔54-56</td>
<td>1 ↑67, 1 ↓85</td>
<td>1 ↑93, 1 ↔89.90.92, 1 ↔85.91</td>
</tr>
<tr>
<td>Hippocampus/PHG</td>
<td>2 ↑54.56, 1 ↓85, 1 ↔83</td>
<td>2 ↔67.88</td>
<td>1 ↔85</td>
</tr>
<tr>
<td><strong>Brain regions not associated with the reward circuitry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalamus</td>
<td>1 ↓85, 3 ↔63.04.06</td>
<td>2 ↔67.88</td>
<td>5 ↔65.09-92</td>
</tr>
<tr>
<td>Rolandic operculum</td>
<td>4 ↔53-56</td>
<td>2 ↔67.88</td>
<td>5 ↔65.09-92</td>
</tr>
</tbody>
</table>
Predicting Successful Weight Loss or Weight Gain

**Anticipatory Reward to Food Pictures**
Lifestyle Intervention Programme in Obese Adults

**Consummatory Reward to Milkshake**
Non-obese & Obese Young Adults

Higher N Accumbens & Insula response:
Predicts less weight loss in lifestyle intervention for obesity

Less Caudate response:
Predicts greater weight gain over 1 year (if DRD2 A1+)

*Stice E et al. Science 322:449, 2008*

Analysis of Functional MRI

Task FMRI

Tag  Control

Resting-State FMRI & Connectivity

ASL
Increased Salience Resting State Network Integrity in Overweight / Obese Subjects

ICA (20 components) in overweight subjects
n=28, Z>2.3, P<0.05

n=26-29 per group fasted
*P<0.05 vs. lean
Head Motion Increases with BMI

$n=83$ fasted

$r = +0.25, P=0.02$
Normal Motor-Sensory Resting State Network Integrity in Overweight / Obese Subjects

ICA (20 components) in overweight subjects
n=28, Z>2.3, P<0.05

n=83 fasted
Summary – Obesity Influences

Overweight/obesity associated with:

- Greater amygdala, insula, OFC activation during anticipatory reward activation
- Literature very contradictory
- Variable paradigm and statistical methods
- Anticipatory vs. consummatory reward
- Heterogeneous populations e.g. food preference, psychological traits, genetics
- Longitudinal studies may be more informative
- Improved behavioural paradigms needed
- Greater connectivity within salience resting state network
- ?Confound of increased head motion in obesity
Nutritional Influences
High-Energy Foods

Fed

Fasted

Low-Energy Foods

Fed

Fasted

Whole brain analysis > 5 voxels, P<0.05 FDR
n=20 healthy, non-obese

OFC Activation Correlates with Appeal Bias & Hunger Change

- Appeal Bias
  - $r = +0.48, P=0.03$

- Hunger
  - $r = +0.47, P<0.05$

Does Reward System Activation Predict Food Intake?

n=22 (17 male), age 25.9 ± 1.7 y (19-44), BMI 23.9 ± 0.6 kg/m² (19.1-29.9)

Females scanned in follicular phase menstrual cycle

Fasted-Initial visit, then Fed and Fasted visits
Orbitofrontal Cortex Activation to Food Predicts Food Intake when Fed but not when Fasted

n=21 healthy non-obese subjects: scanned after 16h overnight fast or 95 mins after 730 kCal breakfast
Amygdala Activation to High-Calorie Food Predicts Food Intake when Fasted but not when Fed

High-Energy Food

Low-Energy Food

\[ r = +0.44, \ P < 0.05 \]

\[ r = +0.14, \ P = 0.55 \]

\[ r = +0.05, \ P = 0.84 \]

n=21 healthy non-obese subjects: scanned after 16h overnight fast or 95 mins after 730 kCal breakfast
OFC Resting State Network Integrity Predicts OFC Activation to High-Energy Food when Fasted

Food (high- or low-calorie)  
FDR P<0.05, n=21

Salience RSN Z>3.0, n=22

No significant correlation with activation to low-energy foods:  
Fasted: r =+0.31, P=0.18  
Fed: r =+0.05, P=0.84

n=21 healthy non-obese subjects: scanned after 16h overnight fast or 95 mins after 730 kCal breakfast
Summary – Nutritional Influences

- Homeostatic and hedonistic eating behaviour linked
- Fasting biases brain reward systems to high-energy foods
- OFC encodes reward value
- OFC and amygdala responses to food evaluation predict food intake depending on nutritional state & energy density
- OFC connectivity with salience network at rest predicts activation to food depending on nutritional state & energy density
Hormonal Influences
Circulating Hormones Control Eating Behaviour

Food Intake

Hypothalamus

Brainstem

Leptin

Glucose, Insulin

PYY

PP

Oxyntomodulin

GLP-1

CCK

Vagus nerve

Ghrelin

Changes proportional to caloric intake
Does Ghrelin Mimic Effects of Fasting on Food Reward?

22 non-obese healthy adults
age 26 ± 2y, 17 male
BMI 23.9 ± 0.6 kg/m²

Injection: Saline or Ghrelin

<table>
<thead>
<tr>
<th>Breakfast</th>
<th>fMRI</th>
<th>Test meal</th>
<th>Depart</th>
</tr>
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<tbody>
<tr>
<td>mins</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>-15</td>
<td>0</td>
<td>+15</td>
<td>0</td>
</tr>
<tr>
<td>+15</td>
<td>+30</td>
<td>+45</td>
<td>+60</td>
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<tr>
<td>+45</td>
<td>+75</td>
<td>+105</td>
<td>+120</td>
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<td>+75</td>
<td>+105</td>
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<td>+105</td>
<td>+135</td>
<td>+165</td>
<td>+180</td>
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<tr>
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<td>+165</td>
<td>+195</td>
<td>+210</td>
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<tr>
<td>+165</td>
<td>+195</td>
<td>+225</td>
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BLOODS: X X X X X

Fasted overnight from supper (14hr)

730kCal fixed breakfast @ t=0mins or remain fasted

sc Saline or octanoylated Ghrelin injection
(3.6 nmol/kg) 55mins later

fMRI food pictures 40mins later for 20mins (~ 11.30am)

Females scanned in follicular phase menstrual cycle

4 visits (median 16 days apart):
Fasted – Dummy single blind
then in randomised order
Fasted – Saline single blind
Fed – Saline double blind
Fed – Ghrelin double blind

Ghrelin Mimics Fasting to Increase Brain Hedonic Responses to Food

![Graph showing Food Appeal and OFC BOLD activation with statistical significance]

Food Appeal

<table>
<thead>
<tr>
<th>FOOD</th>
<th>HC</th>
<th>LC</th>
</tr>
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<tbody>
<tr>
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<td>**</td>
<td>*</td>
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<td></td>
<td>#</td>
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</tbody>
</table>

BOLD activation (%)

<table>
<thead>
<tr>
<th>FOOD</th>
<th>HC</th>
<th>LC</th>
</tr>
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<tbody>
<tr>
<td></td>
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</table>

Fasted-Saline Fed-Saline Fed-Ghrelin

n=22, mean ± SEM

#P=0.05, *P<0.05, **P<0.01 vs Fed-Saline

**Ghrelin and Fasting Increase Hippocampus Activation to Food**

- Food items presented when fasted or after ghrelin more often recognized at 2\textsuperscript{nd} viewing
  
  *Morris JS et al. J Neurosci 2001; Malik et al. Cell Metab. 2008*

- Ghrelin promotes dendritic spine synapse formation and generation of long term potentiation in hippocampus in rodents
  
  *Diano S et al. Nat Neurosci 2006*

- Ghrelin increases food intake when given in hippocampus and improves memory retention in rats
  
  *Carlini V et al. BBRC 2004*

\[n=21, \text{ mean } \pm \text{ SEM}\]

\[* P<0.05, ** P<0.01 \text{ vs. Fed-Saline}\]

*Goldstone AP et al. AJCN 2014*
No Significant Effect of Ghrelin or Fasting on Auditory, Motor or Visual Cortex Activation in Control Task

n=21, mean ± SEM, * P<0.05, ** P<0.01 vs. Fed-Saline

Summary – Hormonal Influences

• Ghrelin mimics fasting to increase appeal of high-energy foods

• Ghrelin mimics fasting to increase OFC activation during food evaluation task, especially for high-energy foods

• Ghrelin mimics fasting to increase activation of hippocampus to high- and low-energy foods

• Effects of ghrelin occur despite increases in plasma glucose, PYY and GLP-1 (?prokinetic effect on gastric motility)

• Need ghrelin or GOAT antagonists to confirm physiology

• Increase in ghrelin with food restriction increases food hedonics as homeostatic feedback loop to maintain body weight
Surgical Influences

“My daddy is a doctor and he treats diabetes.”
“My daddy is a surgeon and he cures it.”
Bariatric Surgical Procedures

Gastric Banding

Gastric Bypass
Long-term Weight Loss after Bariatric Surgery

Dietary Habits after Bariatric Surgery

Progressive Ratio Task for Appetitive Reward

Miras et al. *Am J Clin Nutr* 2012

**1a** Breakpoint: M&M

**1b** Breakpoint: Vegetable

Data plots showing the last completed ratio (clicks) before and after gastric bypass surgery compared to controls.
### Anticipatory Food Reward in Gastric Bypass vs. Gastric Banding

<table>
<thead>
<tr>
<th></th>
<th>Gastric Banding n=20</th>
<th>Gastric Bypass n=21</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mean ± SEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>median [25% - 75% IQR]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>40.9 ± 2.5</td>
<td>43.5 ± 2.0</td>
</tr>
<tr>
<td>Gender ratio (M:F)</td>
<td>1:19</td>
<td>4:26</td>
</tr>
<tr>
<td>Pre-op BMI (kg/m²)</td>
<td>44.8 [41.9 - 49.2]</td>
<td>48.4 [40.7 - 58.0]</td>
</tr>
<tr>
<td>Current BMI (kg/m²)</td>
<td>35.1 ± 1.4</td>
<td>35.3 ± 1.7</td>
</tr>
<tr>
<td>Body fat impedance (%)</td>
<td>41.9 ± 1.8</td>
<td>41.3 ± 1.9</td>
</tr>
<tr>
<td>% Weight loss</td>
<td>23.1 [14.5 - 29.3]</td>
<td>29.9 [23.4 - 36.5]</td>
</tr>
<tr>
<td>Time since surgery (months)</td>
<td>9.1 [5.2 - 19.2]</td>
<td>8.1 [5.9 - 11.5]</td>
</tr>
<tr>
<td>Pre-operative DM, n (%)</td>
<td>2 (10%)</td>
<td>10 (48%)</td>
</tr>
<tr>
<td>Current DM, n (%)</td>
<td>0 (0%)</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Pre-operative BED, n (%)</td>
<td>4 (25%)</td>
<td>4 (19%)</td>
</tr>
<tr>
<td>Current BED, n (%)</td>
<td>2 (10%)</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>

Unoperated BMI-matched controls (n=25) similar in age, gender ratio, BMI, % body fat and current BED

* P<0.05 vs. Gastric Banding

Scholtz S & Goldstone AP. Gut 63:891-902, 2014
Similarly Reduced Hunger after Gastric Banding and Gastric Bypass

n=20 per group, mean ± SEM, ### P<0.005 vs. BMI-matched

Scholtz S & Goldstone AP. Gut 63:891-902, 2014
Reduced Appeal of High-Calorie Food after Gastric Bypass

A lot

Food Appeal

High-Calorie Food Appeal

n=20 per group, mean ± SEM
*P<0.05, **P<0.05 vs. Gastric Banding, ###P<0.005 vs. BMI-matched

Scholtz S & Goldstone AP. Gut 63:891-902, 2014
Less Activation to *High-Calorie Foods* after Gastric Bypass

High-calorie food > Objects, Banding > Bypass, adjusting age, gender, BMI
n=19-20, cluster threshold Z>2.1 , P<0.05
Less OFC and Amygdala Activation to Food after Gastric Bypass than Gastric Banding

n=19-20 per group
Bilateral activation in fROIs derived from n=24 other overweight/obese subjects
% BOLD signal to any food vs. objects, adjusting for age, gender & BMI
*P<0.05, **P<0.01 vs. Gastric Banding, # P<0.1 vs. BMI-matched

Scholtz S & Goldstone AP. Gut 63:891-902, 2014
n=19-20 per group
Average activation in OFC, amygdala, nucleus accumbens, anterior insula and caudate vs. objects, adjusting for age, gender & BMI

Correlation between Anticipatory and Consummatory Reward after Bariatric Surgery

Scholtz S & Goldstone AP. Gut 2014
Roux-en-Y Gastric Bypass is a Complex Procedure

Miras AD et al. Nat Rev Gastro 2013
Higher Plasma Satiety Gut Hormones and Bile Acids after Gastric Bypass than Gastric Banding

- PYY
- GLP-1
- Acyl Ghrelin
- Total Bile Acids

Scholtz S & Goldstone AP
Gut 2014

n=20-21,
PYY and GLP-1 Suppress Food Intake and Brain Reward System Activation to Food Cues

De Silva et al. Cell Metab 2011
Greater Dumping Symptoms after Gastric Bypass than Gastric Banding

Scholtz S & Goldstone AP. Gut 63:891-902, 2014
Summary - Surgical Influences

Gastric bypass patients have healthier eating behaviour, reduced hedonic and brain reward system responses to high-calorie foods than gastric banding patients – altered gut-brain-hedonic axis

Possible explanations:

• Exaggerated gut hormone responses e.g. PYY, GLP-1
• Bile salt changes, increased FGF-19
• Alterations in dopaminergic and opioid signaling
• Aversion to high fat foods
• Bias in surgery selection (cross-sectional study)
El Tío (The Uncle)  
Lord of the Underworld  
Potosí, Bolivia  
4,090m above sea level
El Tío (The Uncle)
Lord of the Underworld
Potosí, Bolivia
4,090m above sea level
El Tío (The Uncle)
Lord of the Underworld
Potosi, Bolivia
4,090m above sea level
Core Behavioural Components in Addiction that Relate to Obesity

Compulsivity: pre-SMA & PFC

Impulsivity: OFC & PFC

Stress and emotional responses: amygdala & striatum

Reward sensitivity: ventral striatum
Effect of Nutritional State on Addictive Behaviours

- Healthy, non-obese participants
  18 non-obese (23.6 ± 0.7 y, 10 male, BMI 23.0 ± 0.6 kg/m²)

- Fasted vs. Fed (1200 kCal liquid meal)

- Cross-over design
  
  **Study visit 1**
  - Fasted
  - n = 9

  **Study visit 2**
  - Fed
  - n = 9

- Mid-morning after overnight fast
- Women in follicular phase of menstrual cycle
MID Task

Trial

Win trial

Loss trial

Neutral trial

<table>
<thead>
<tr>
<th>Cue</th>
<th>Anticipation</th>
<th>Target</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1000 ms)</td>
<td>(2000-4000 ms)</td>
<td>(150-300 ms)</td>
<td>[current £]</td>
</tr>
</tbody>
</table>

Hit!

Miss!
MID Task: Caudate, Putamen, Amygdala fROIs for Win Anticipation

Win > Neutral anticipation
n=18 fasted or fed visit, cluster Z>2.3, P<0.05
MID Task: Success

n=18 cross-over design

Ali & Goldstone, in preparation
MID Task: Amygdala

- **Anticipation**
- **Outcome**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Fasted</th>
<th>Fed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Win vs Neutral</td>
<td>0.25 (±0.05)</td>
<td>0.10 (±0.05)</td>
</tr>
<tr>
<td>Loss vs Neutral</td>
<td>0.15 (±0.05)</td>
<td>0.05 (±0.05)</td>
</tr>
<tr>
<td>Win vs Loss</td>
<td>0.10 (±0.05)</td>
<td>0.05 (±0.05)</td>
</tr>
<tr>
<td>Loss vs Neutral</td>
<td>0.05 (±0.05)</td>
<td>0.00 (±0.05)</td>
</tr>
<tr>
<td>Win vs Loss</td>
<td>0.00 (±0.05)</td>
<td>0.00 (±0.05)</td>
</tr>
</tbody>
</table>

n=18, * P<0.05, ** P=0.01 paired t-test

Ali & Goldstone, in preparation
MID Task: Putamen

n=18, * P<0.05, ** P=0.01 paired t-test

Ali & Goldstone, in preparation
Emotional Eating

- Stress-induced or emotional eating common in obesity
- Stress precipitant for drug relapse and binge eating

- **Brain responses to negative valence pictures** (e.g. IAPS) attenuated by β-blockers, BZD, anti-depressants

Unpleasant Picture fMRI Task

n=18, cluster threshold Z>2.3, P<0.05
unpleasant > neutral pictures

Ali & Goldstone, in preparation
Food Intake Reduces Brain Response to Unpleasant Images

n=18 non-obese adults
unpleasant > neutral images
fasted overnight or 2hr after 1200kCal meal

Ali & Goldstone, in preparation
Summary - Addictive Behaviour

• Fasting increases striatal and amygdala responses to anticipation of winning money c.f. high-energy foods – multi-modality

• Fasting increases striatal and OFC responses to unpleasant images (negative emotional salience)

• Addictive behaviours are state- as well as trait-dependent

• Related to changes in plasma gut hormone e.g. ghrelin

• Response to obesity treatments

• Predict outcome

• Underlay failure of therapy e.g. diet vs. surgery
Conclusions

• Similar neural networks processing food and other rewards
• Influenced by nutritional state, appetitive gut hormones, obesity, and bariatric surgery
• Neurochemical pathways still to be determined
• Such techniques useful to explore:
  drug targets
  proof-of-concept for drug treatment or devices
  patient stratification
  prediction of natural history or treatment response
  function of implicated genes
  links between core behavioural components in addiction, obesity and BED
• Improved phenotyping of heterogeneity in obesity
Current Studies

• Neurobehavioural studies of food reward, addictive behaviour and cognition in obesity and treatment

• Longitudinal studies comparing bariatric procedures: RYGB, Duodenal-jejunal bypass endoluminal liner, Sleeve gastrectomy

• Dietary manipulations: VLCD, fish oil, resistant starch
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Mustafa Anjari (ACF)
Sarah Ali, Martin Schmidt (CRF)
Waaka Moni-Nwinia (BSc)
Roberta Bowie, Natalie White (MSc)
Emma Hennessey (MSc)
Suzanne Alberts, Shahrzad Deliran (MS)

Imperial Weight Centre & Dept. of Bariatric Surgery
Carel le Roux
Ahmed Ahmed, Torsten Olbers
Robert Steiner MRI Unit
Giuliana Durighel
Emer Hughes
Adam Waldman

Division of Diabetes, Endocrinology and Metabolism
Gary Frost, Steve Bloom
Damian Ashby, Mohammad Ghatei
Michelle Sleeth, Norlida Mat Daud, Nurhafzan Ismail
Kings College London
Royce Vincent
Jamshid Alaghband-Zadeh
Imaging Sciences Dept.
Rita Nunes, Jo Hajnal
Computational, Cognitive & Clinical Neuroimaging Lab
David Sharp
Christian Beckmann
ICCAM
Csaba Orban (MSc), John McGonigle, David Nutt, Anne Lingford-Hughes
Rebecca Elliott, Anna Murphy
Dana Smith, Trevor Robbins

Hammersmith Hospital Trustees’ Research Committee
NIHR Biomedical Research Centre
UK Clinical Research Network
tony.goldstone@imperial.ac.uk

@TonyGoldstone
Emotional Eating

- **Δ putamen** CBF correlates with subjective stress rating, **OFC** CBF correlates with salivary cortisol and HR during mental arithmetic task with performance monitoring
  
  *Wang et al. PNAS 2005*

- Intragastric infusion of fatty acids attenuates brain activation to sad music & faces in: medulla/pons, midbrain, hypothalamus, thalamus, caudate, putamen, cerebellum, hippocampus, ACC, MCC, and PCC
  
  *van Oudenhove et al. JCI 2011*

- **Ghrelin** mediates stress-induced food-reward behaviour in mice (chronic social defeat stress ↑ CPP / intake high fat)
  
  *Chuang et al. JCI 2011*
Impulsivity and Obesity

Increased Impulsivity to Money in Obesity

Weller et al. Appetite 2008

Increased Impulsivity in Overweight associated with Reduced Caudate Activation to Milkshake Receipt

Babbs RK et al. Physiol Behav 2013

Go-NoGo Task

Barratt Questionnaire

subjective Value ($) vs Delay (months)
Resting State fMRI: Independent Component Analysis

Default Mode Network (DMN)

Salience Network (SALN)

n=22, healthy non-obese, 25 ICA components, Z>3.0
Fasting Increases Plasma Acylated Ghrelin

Ghrelin Increases Serum Growth Hormone

n=22, mean ± SEM

Ghrelin Increases Plasma Glucose, GLP-1 and PYY

n=22, mean ± SEM

Fasted-Initial Visit: n=21, FDR P<0.05 High-calorie or low-calorie > objects
No Effect of Fasting or Ghrelin on Resting State Networks

n=22, healthy non-obese
Dual regression analysis
No significant effect of fasting or ghrelin using Whole brain or network restricted analysis:
TFCE P<0.05 corrected, cluster T>2.0 P<0.05, FDR P<0.05 or ROI approach
Reduced Ice-Cream Palatability and Fat Intake after Gastric Bypass

**Ice-Cream Palatability**

- **Tasty**
- **Pleasant**
- **Sweet**

**Diet Composition**

- **Protein**
- **Carbohydrate**
- **Fat**

Scholtz S & Goldstone AP. Gut 63:891-902, 2014

$n=20$, mean ± SEM, *$P<0.05$

$n=15-18$, mean ± SEM, *$P<0.05$
fMRI scanning protocol
No effect of Feeding on Primary Motor Cortex Activation to Button Press

Precentral Gyrus

n=18, unpleasant or neutral images > fixation cross, paired t-test
Fasted overnight or 2hr after 1200kCal meal
UK Congress on Obesity 2014

University of Birmingham, Edgbaston Campus
Tuesday 16th September and Wednesday 17th September 2014