Neuroimaging studies of obesity and drug addiction

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Dopamine Neurotransmission

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U.S. Department of Energy
Dopamine and Drug Reinforcement

Dopamine initiates and maintains responses to salient stimuli such as drugs

Relationship between Cue-Induced Decreases in $[^{11}\text{C}]$raclopride Binding and Cocaine Craving

Cue-induced increases in DA were associated with craving

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Brain Dopamine Response to Food Stimulation

Volkow, et al, Synapse 2002
Is DA Involved in Addiction and Obesity?
Dopamine D2 Receptors are Lower in Addiction

Cocaine
Alcohol
Heroin

Drug Abuser
Non-Drug Abuser

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DA D2 Receptors in Controls & Cocaine Abusers

![Graph showing DA D2 receptor availability (Bmax/Kd) vs age (years) for Normal Controls and Cocaine Abusers. The graph includes data points for both groups, with a trend line for each.]

[11C] Raclopride
DA D2 Receptors and Response to Intravenous Methylphenidate

High receptor level = unpleasant response
Low receptor level = pleasant response

[¹¹C] Raclopride

Overexpression of DA D2 receptors reduces alcohol self-administration

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Compulsive overeating shares many of the same characteristics as drug addiction.

*Do obese subjects have abnormal levels of D2-receptor?*

10 severely obese subjects (BMI: 51±5 kg/m²)
10 age-matched controls (BMI: 25±3 kg/m²)
Lower dopamine receptors in obese than in control subjects

Control Subjects

Obese Subjects

[11C]raclopride

Bmax/Kd
BMI
Control subjects
Obese subjects (n = 10)
Control subjects (n = 10)

Wang et al, Lancet 2001
DA D2-R in Zucker Lean and Zucker Obese (fa/fa) Rats

**D2-Receptors**

**Weight**

<table>
<thead>
<tr>
<th></th>
<th>Lean (n=10)</th>
<th>Obese (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (grams)</td>
<td>400</td>
<td>700</td>
</tr>
</tbody>
</table>

**Locomotion**

<table>
<thead>
<tr>
<th></th>
<th>Lean (n=10)</th>
<th>Obese (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locomotor Activity (beam crossings)</td>
<td>500</td>
<td>600</td>
</tr>
</tbody>
</table>

P < 0.05

**3H-Spiperone**

Thanos et al 2005
What is the functional significance of low D2-R?
Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism

Inhibitory Control

Salience Attribution

Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism

Cocaine Abusers

METH Abusers

DA D2 Receptors (Ratio Index)

DA D2 Receptors (Bmax/kd)

OFC umol/100g/min

r = 0.7, p < 0.001

r = 0.7, p < 0.005
Brain Activation with Methylphenidate Induced Cocaine Craving

Placebo

Orbitofrontal Activation

MP

Self Report Craving

micromol/100g/min

μmole/100g/min

r = 0.79, p < 0.0002

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Volkow et al Am J Psychiatry 1999
Brain Activation with Food Stimuli

Neutral Stimuli

Orbitofrontal Activation

Food Stimuli

μmole/100g/min

% Metabolic Changes

% Changes of feeling of hunger

$r = 0.84, \ p = 0.001$

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Wang et al, Neuroimage 2004
Activation of hippocampus during craving

Food craving
Pelchat et al, 2004

Cocaine craving
Breiter et al, 1997
Why do some people continue to eat when the stomach is full?

PET-FDG (IGS “on” vs IGS “off” in obese subjects)

- Higher metabolism in brain reward pathways when a "stomach stimulator" is turned “on” to simulate fullness vs. “off”.
- The same areas are also activated during drug craving in addicted subjects, supporting similarities between compulsive overeating and drug addiction.

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Wang et al, PNAS USA 2006
What makes obese subjects different from drug abusers?
Regions that are More Active in Obese than Controls

The specificity may be determined by an enhanced brain sensitivity to food as a reinforcer.
Center for Translational Neuroimaging

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