Neuroimaging studies of obesity and drug addiction

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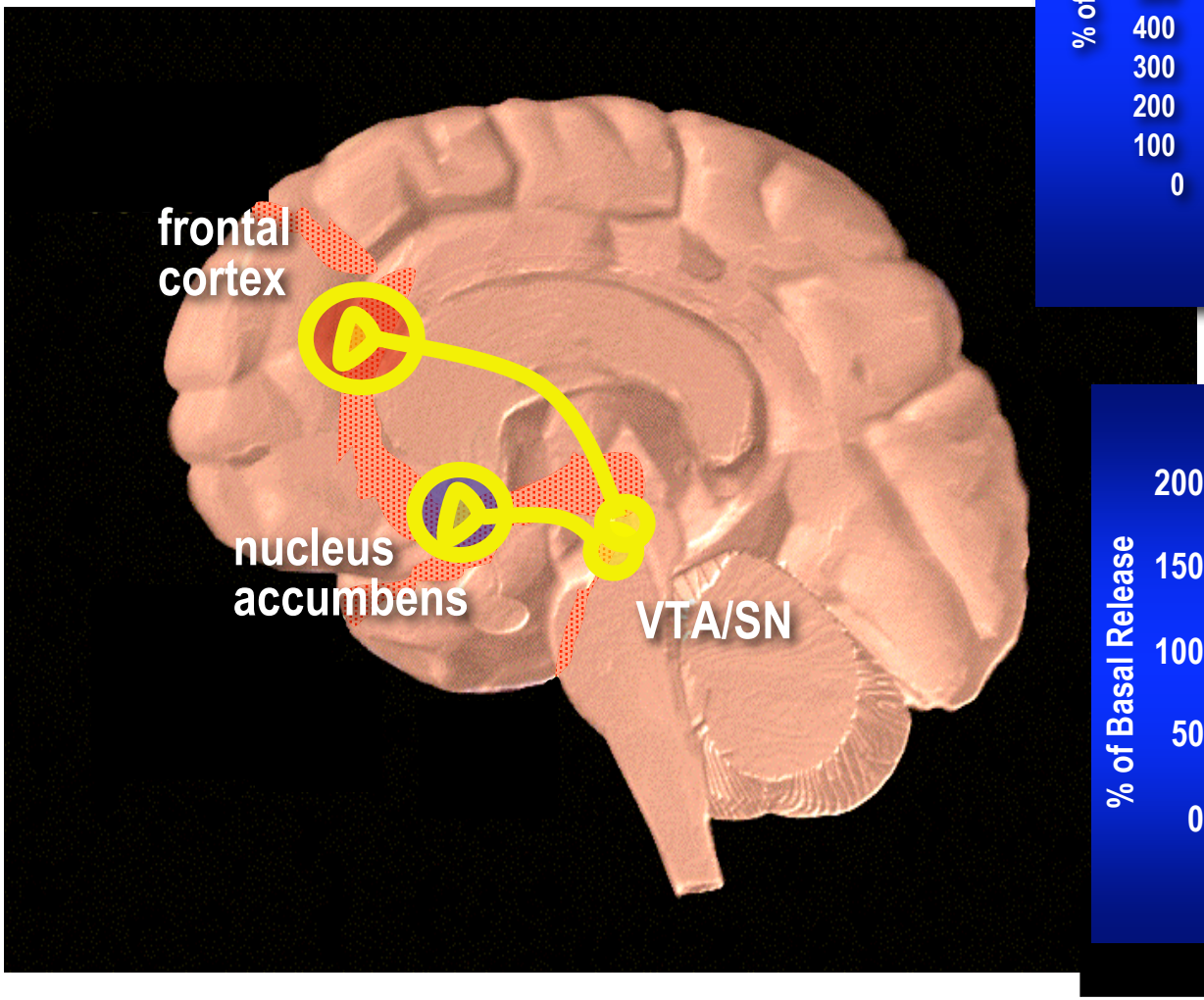
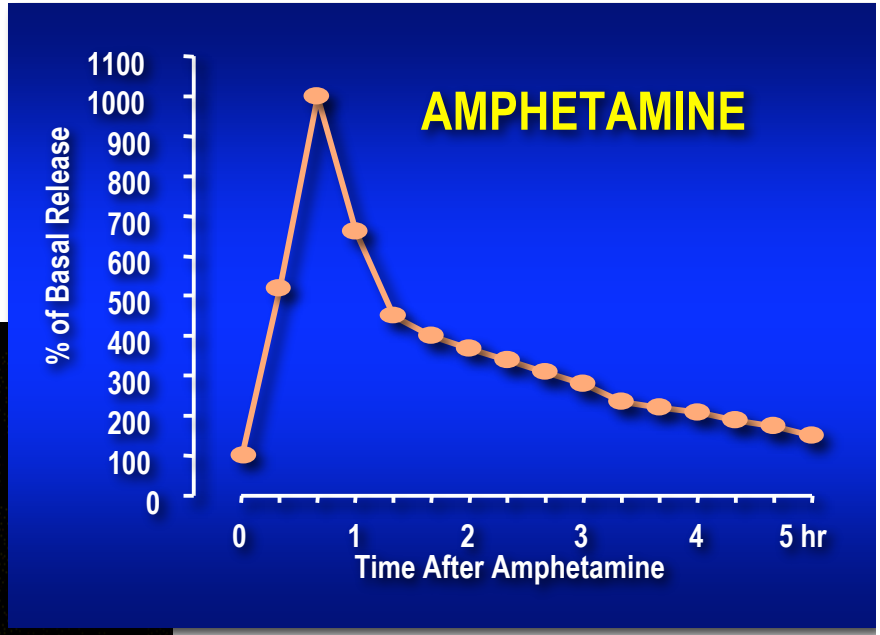
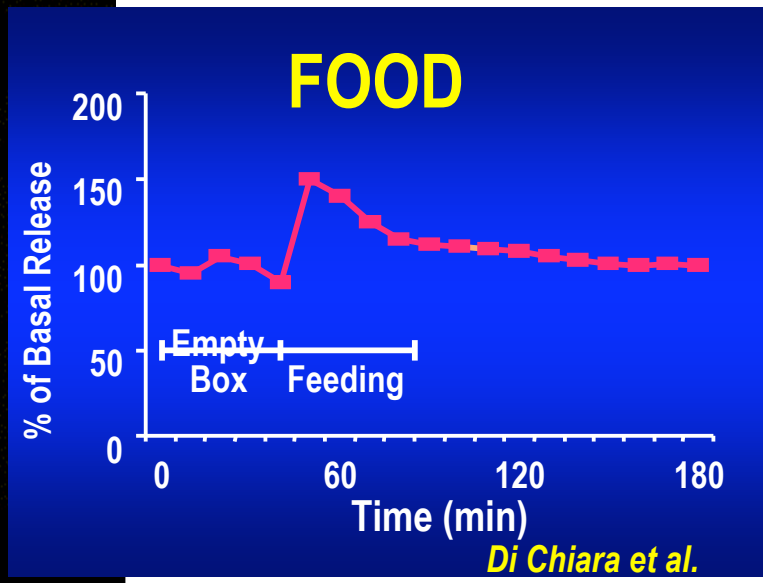
U.S. Department of Energy

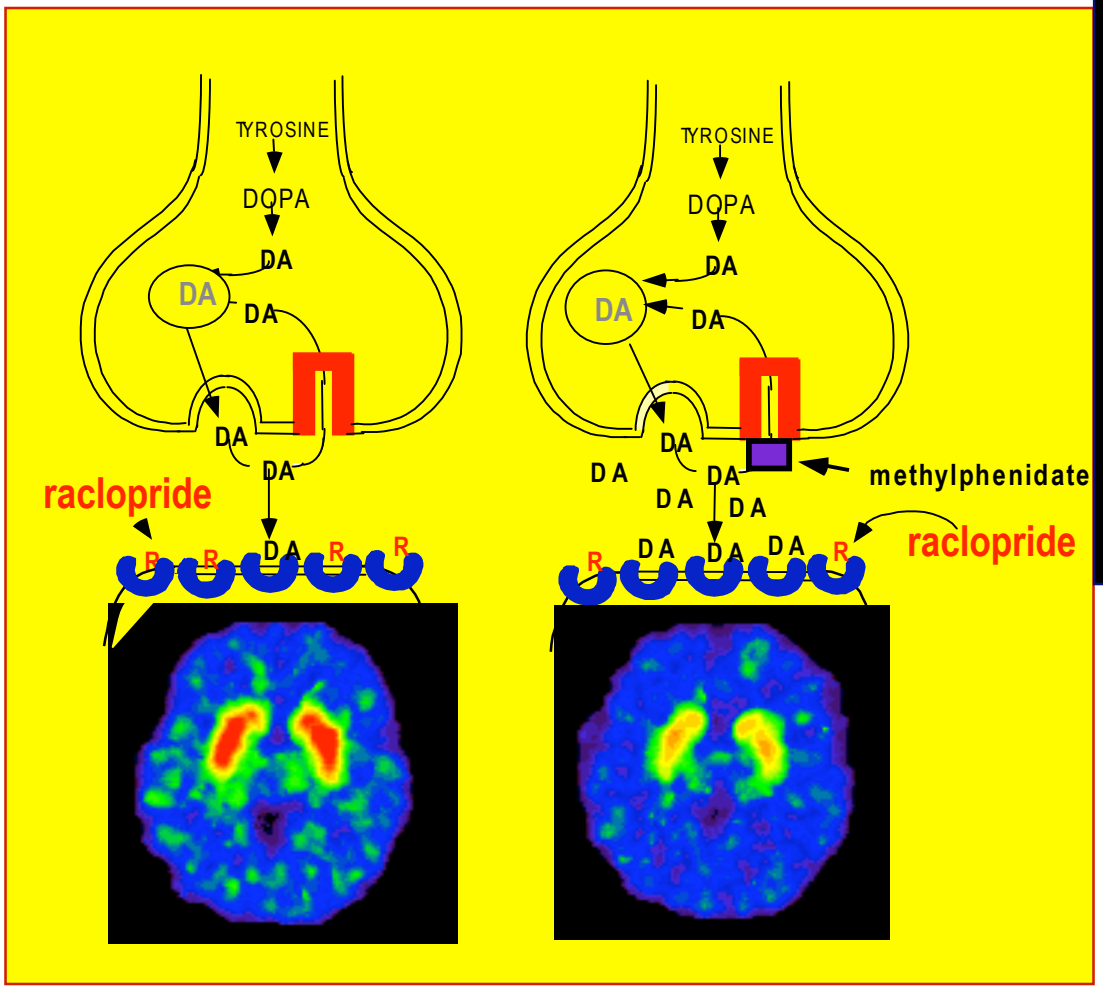
Dopamine Neurotransmission

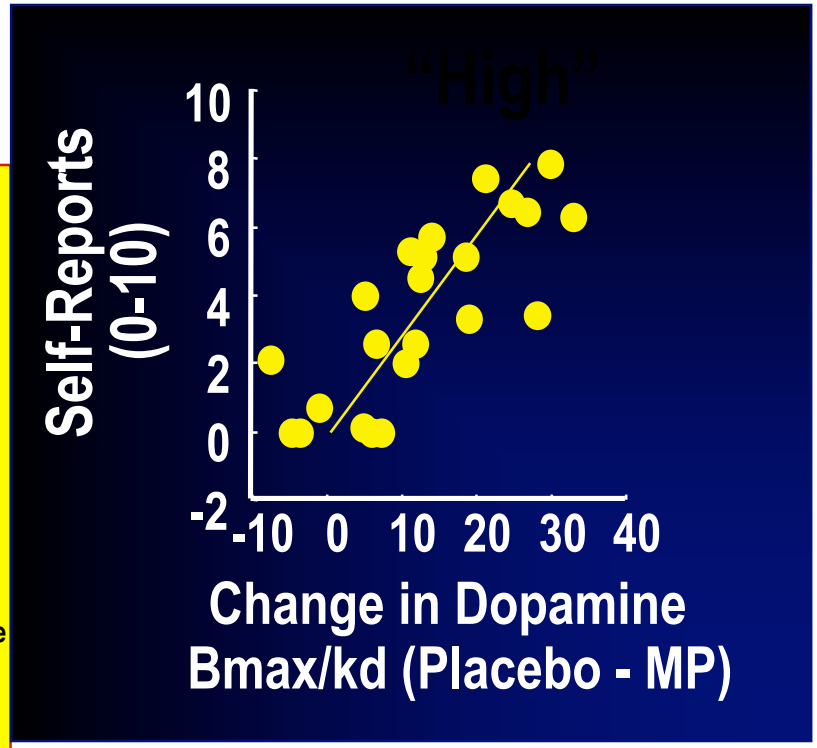






Dopamine and Drug Reinforcement





Dopamine initiates and maintains responses to salient stimuli such as drugs

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Volkow, ND, et al, Am J Psychiatry 1999

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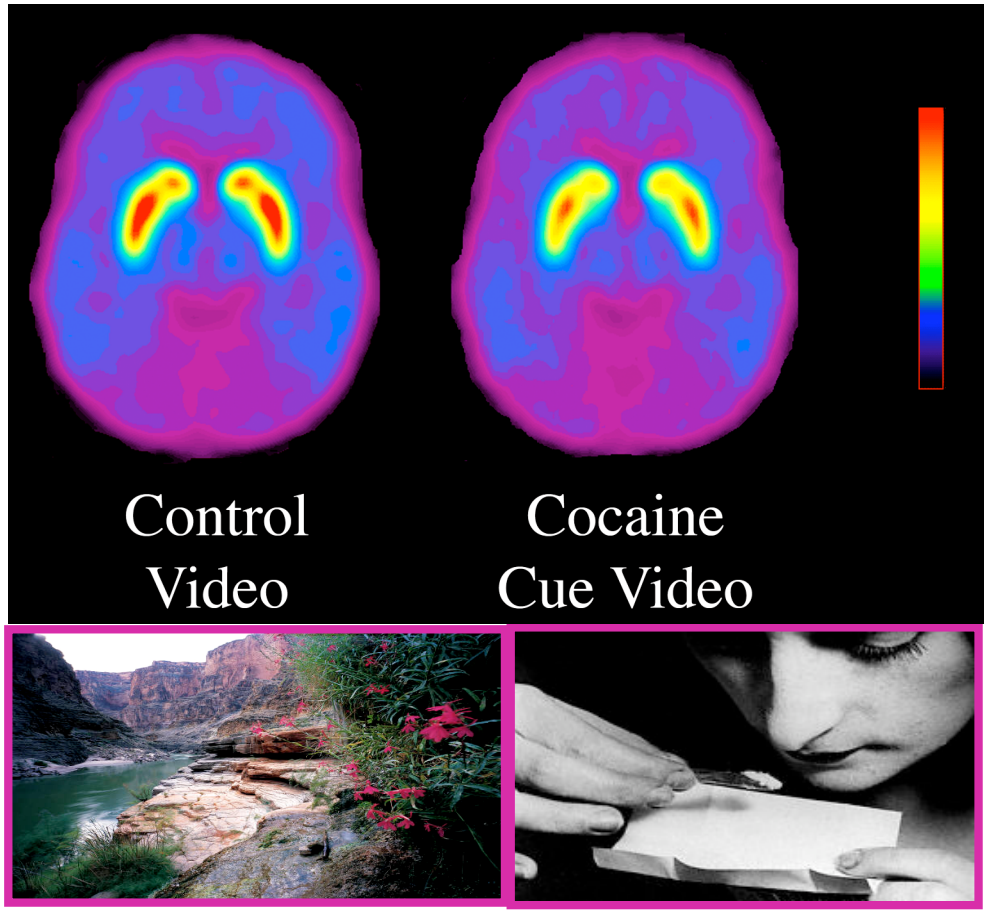
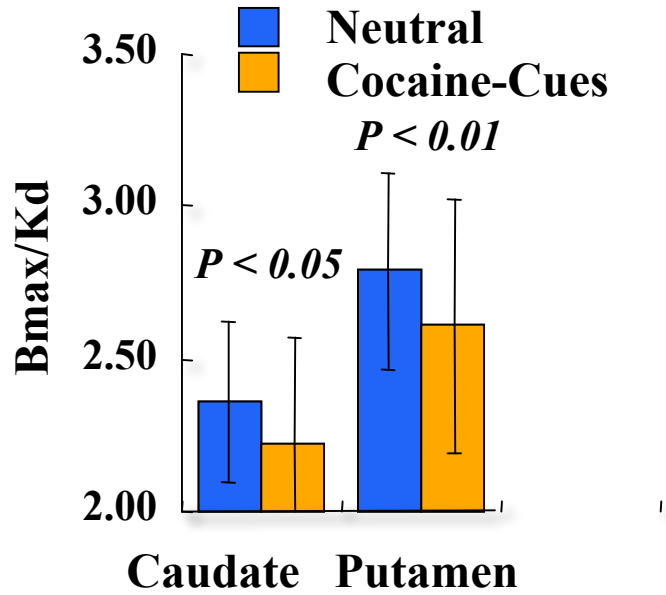
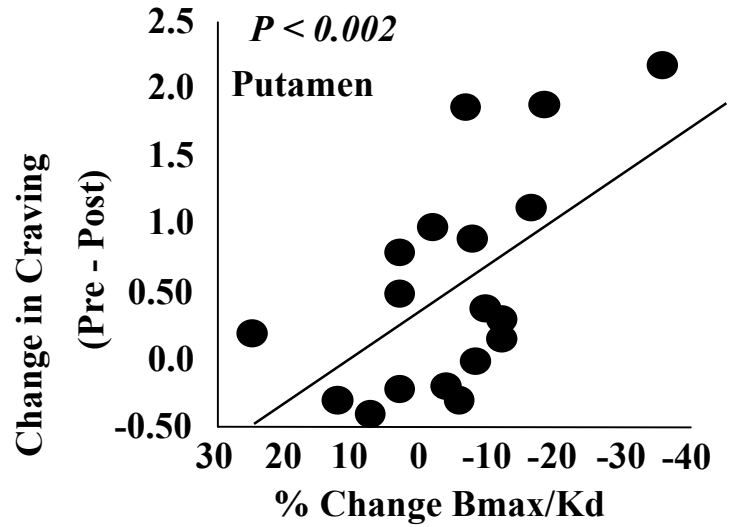
Relationship between Cue-Induced Decreases in [^{11}C]raclopride Binding and Cocaine Craving



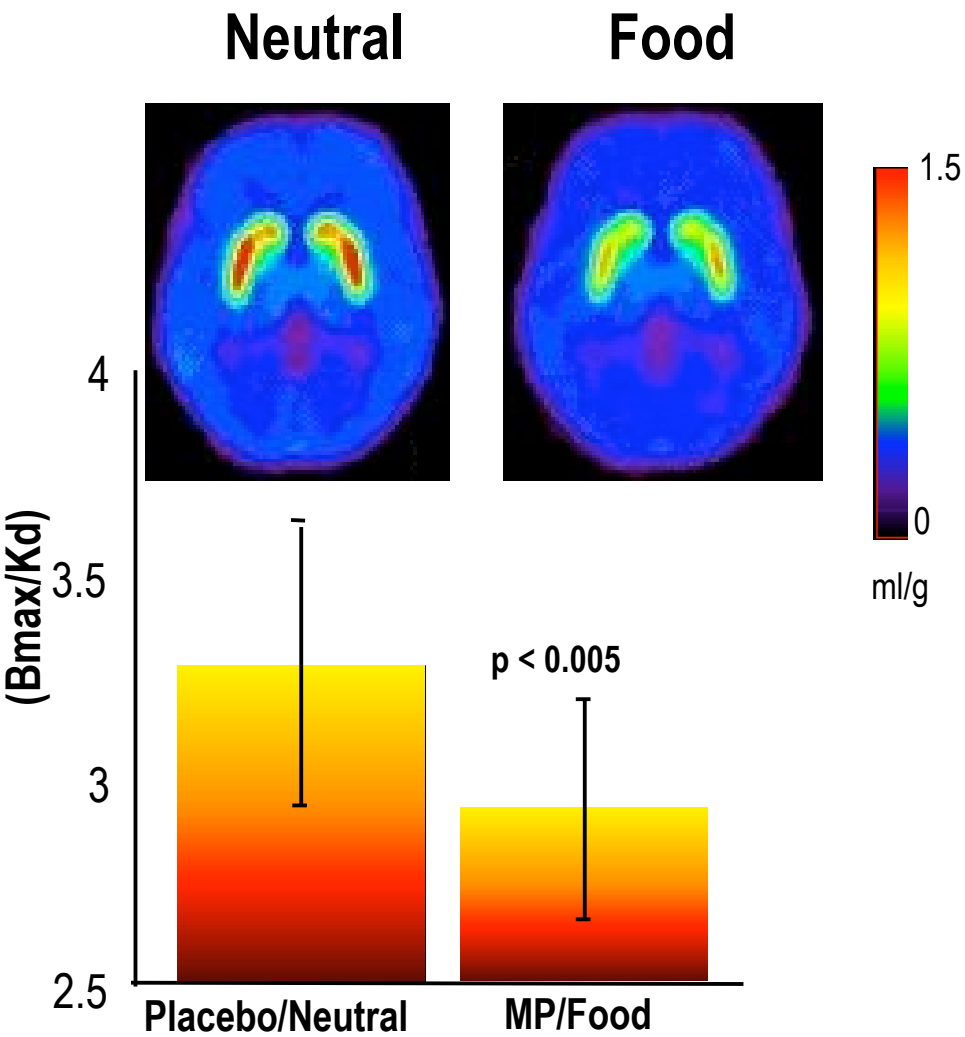


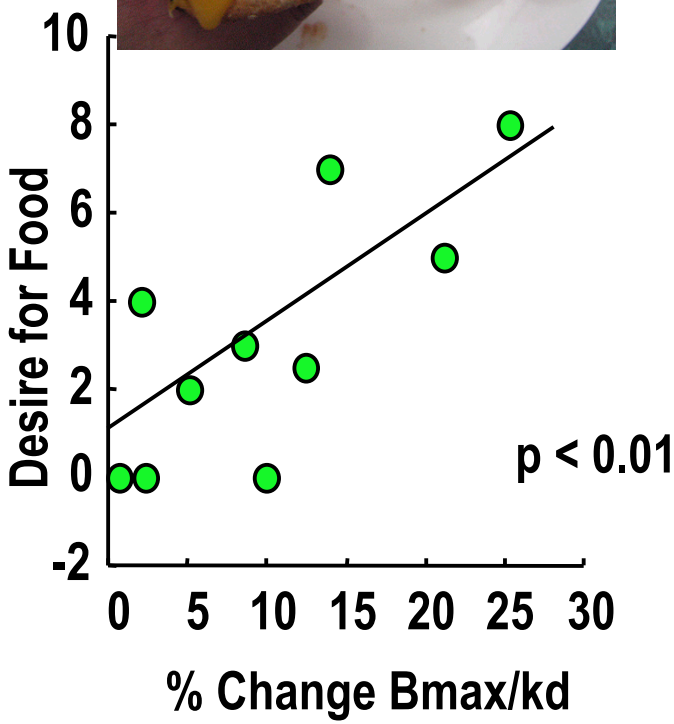


Cue-induced increases in DA were associated with craving

Volkow, et al, J. Neuroscience 2006

Brain Dopamine Response to Food Stimulation





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Volkow, et al, Synapse 2002

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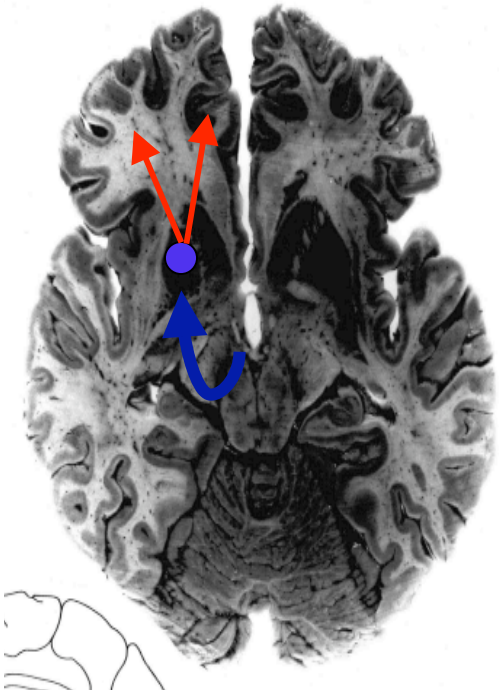
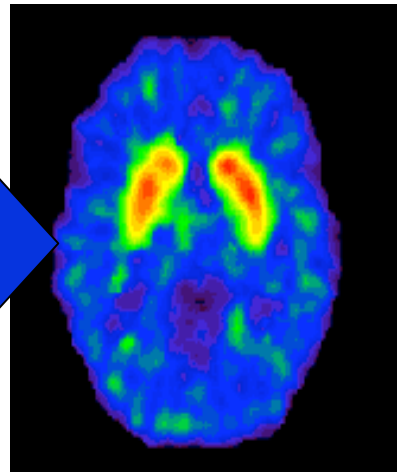
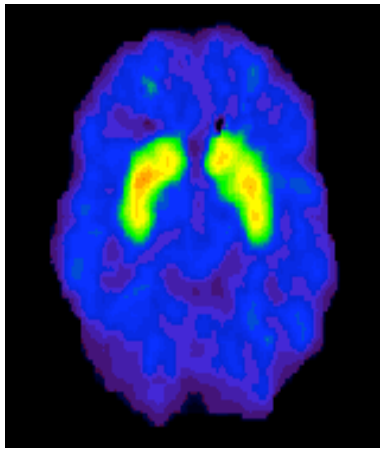
Is DA Involved in Addiction and Obesity?



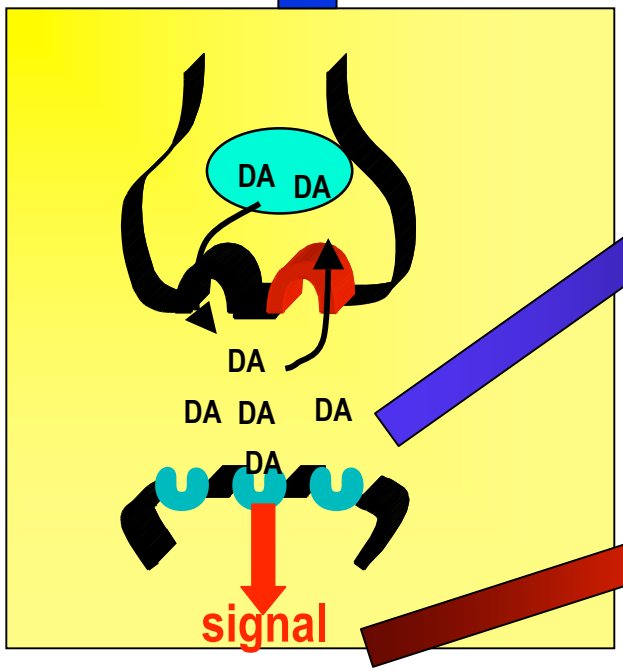
Anatomy



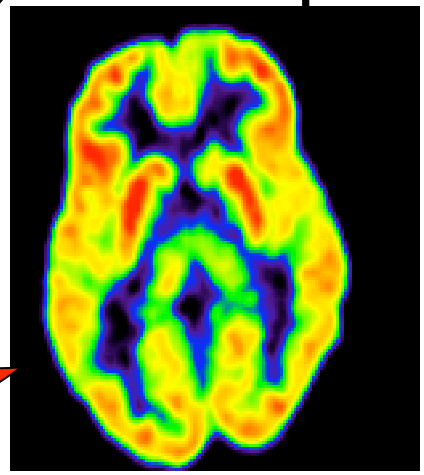
DA Transporters



DA Receptors



Dopamine Cell



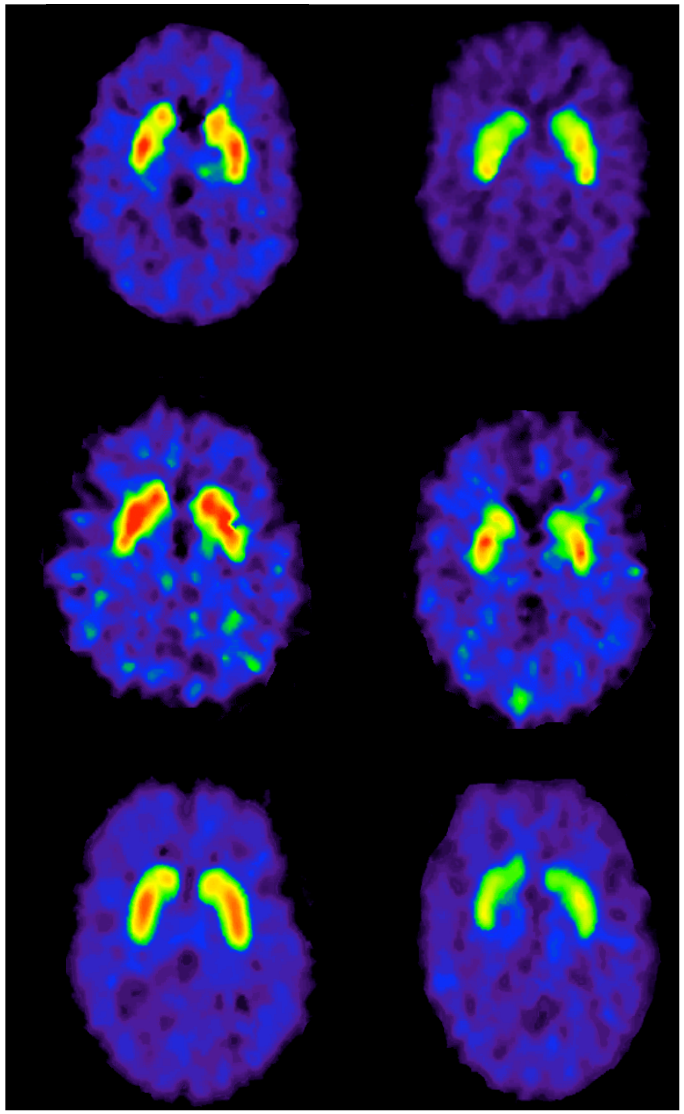
Metabolism

Dopamine D2 Receptors are Lower in Addiction

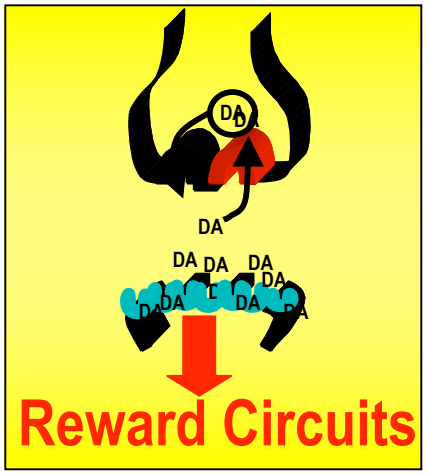
Cocaine

Alcohol

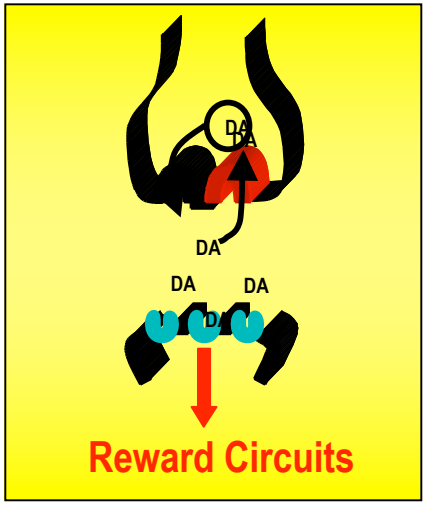
Heroin



control addicted



Non-Drug Abuser



Drug Abuser

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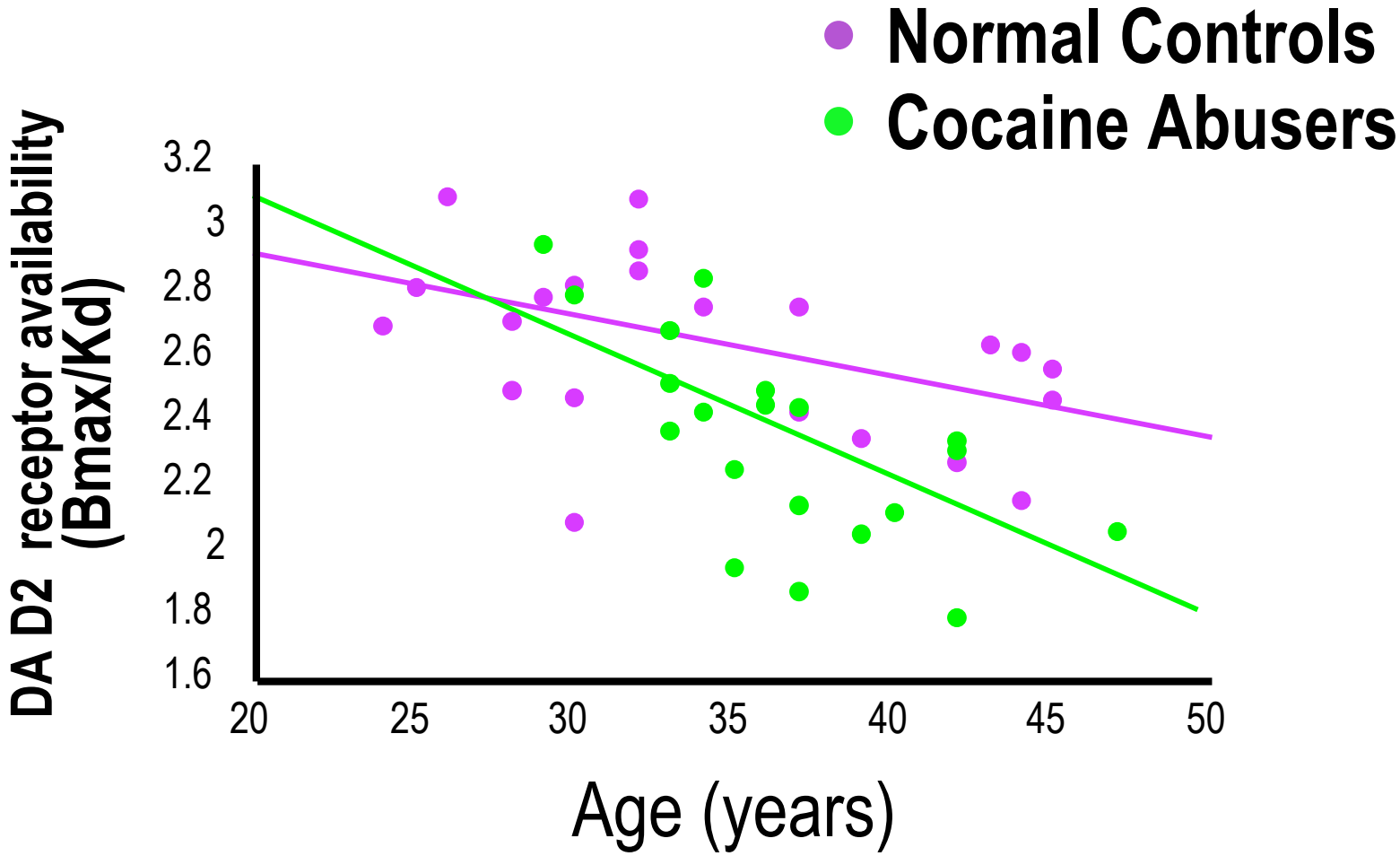
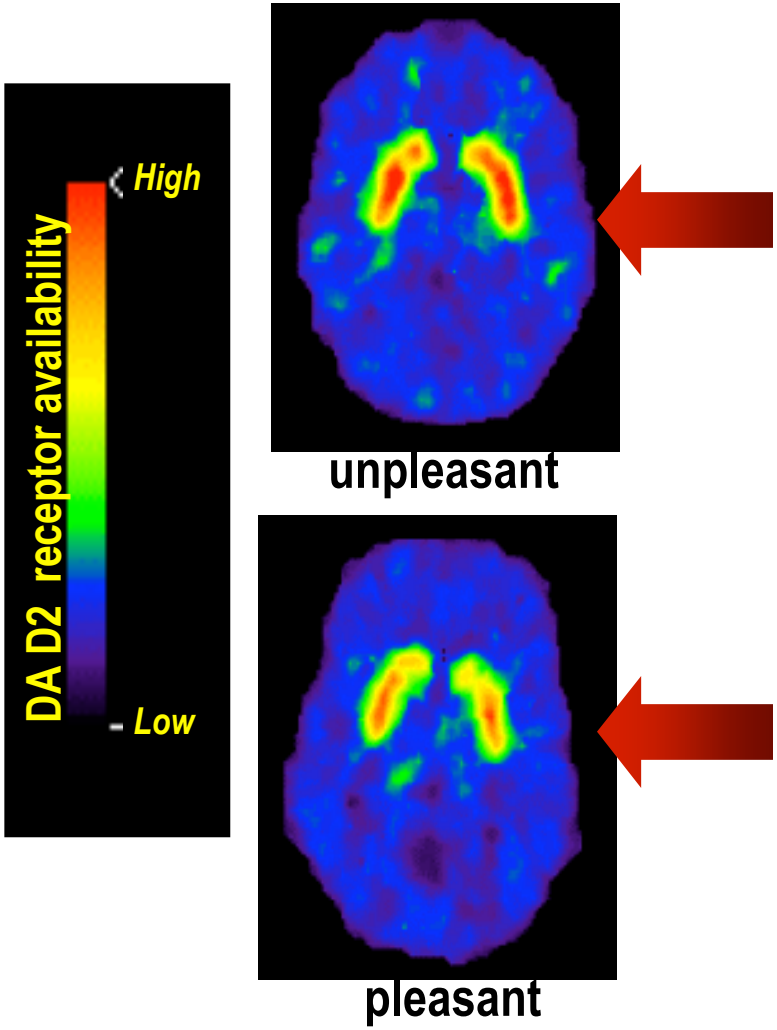
DA D2 Receptors in Controls & Cocaine Abusers



[^{11}C] Raclopride

DA D2 Receptors and Response to Intravenous Methylphenidate



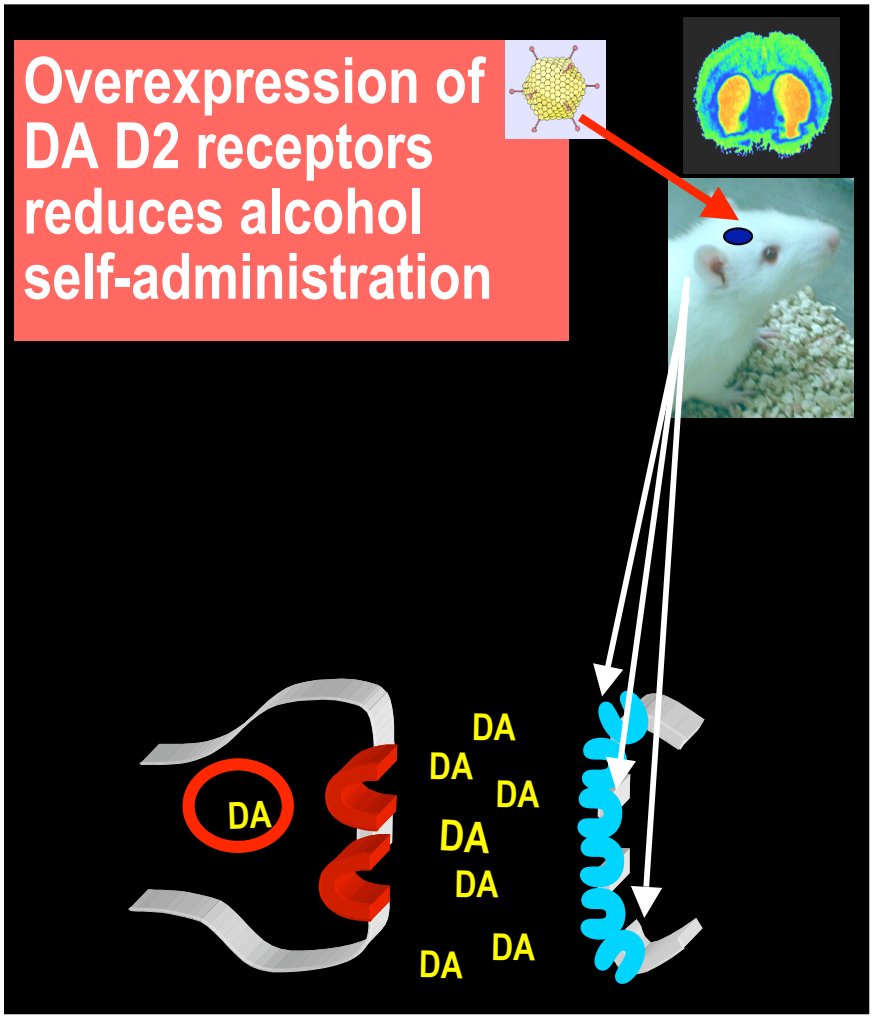
High receptor level = unpleasant response

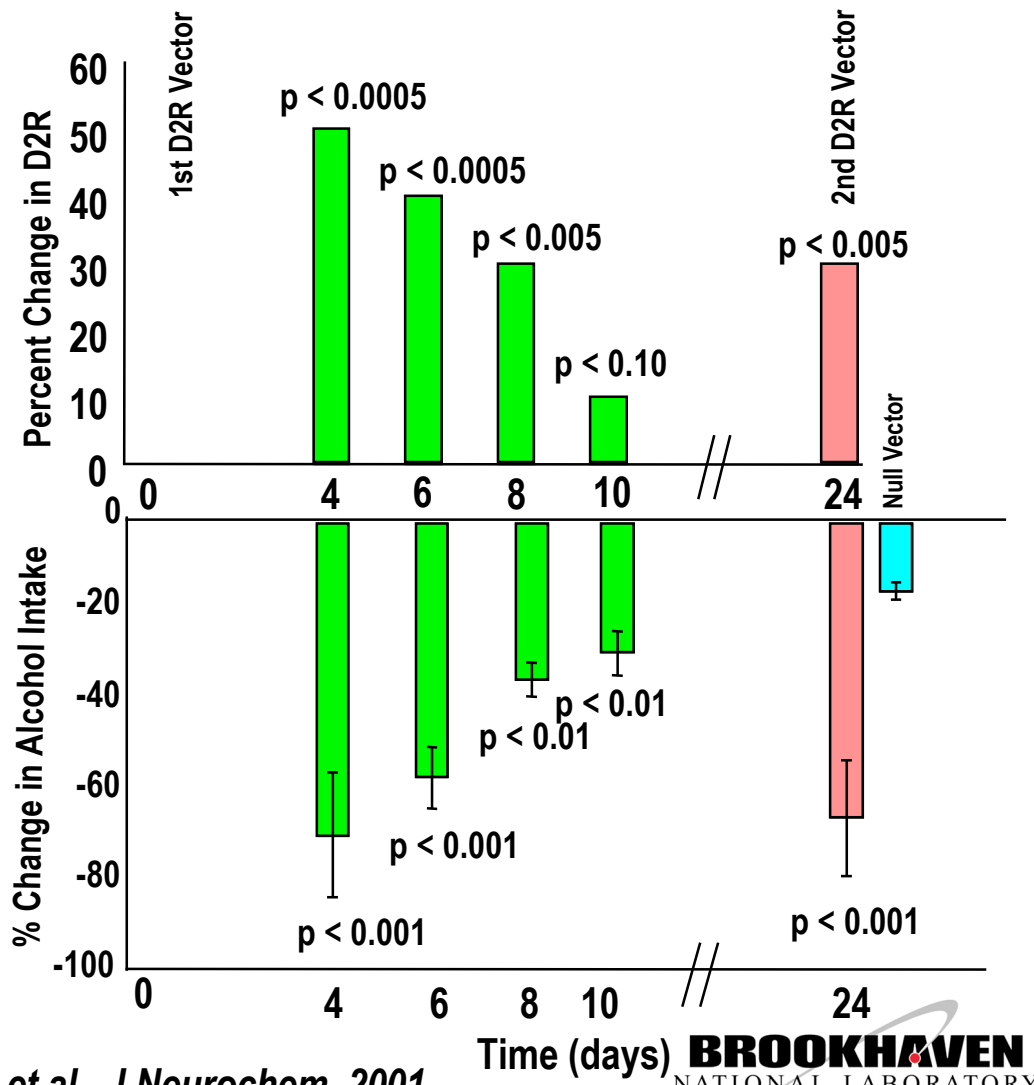
Low receptor level = pleasant response

[^{11}C] Raclopride

Volkow, ND, et al, Am J Psychiatry 1999

Effects of Tx with an Adenovirus Carrying a DA D2 Receptor Gene into NAc in DA D2 Receptors





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Thanos, PK et al., J Neurochem, 2001.

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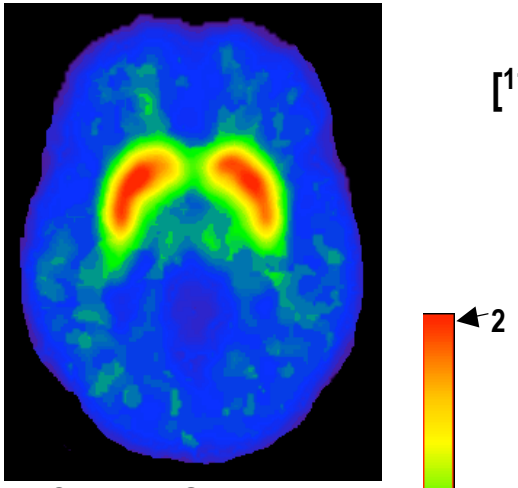
Obesity

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

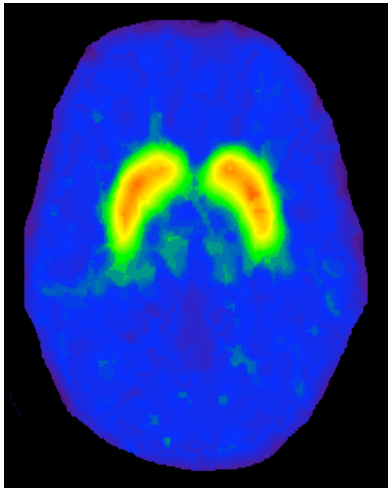
Do obese subjects have abnormal levels of D2-receptor?

10 severely obese subjects (BMI: 51±5 kg/m^2)
10 age-matched controls (BMI: 25±3 kg/m^2)

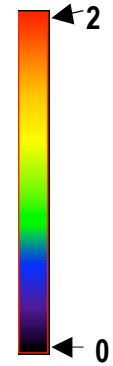
Lower dopamine receptors in obese than in control subjects



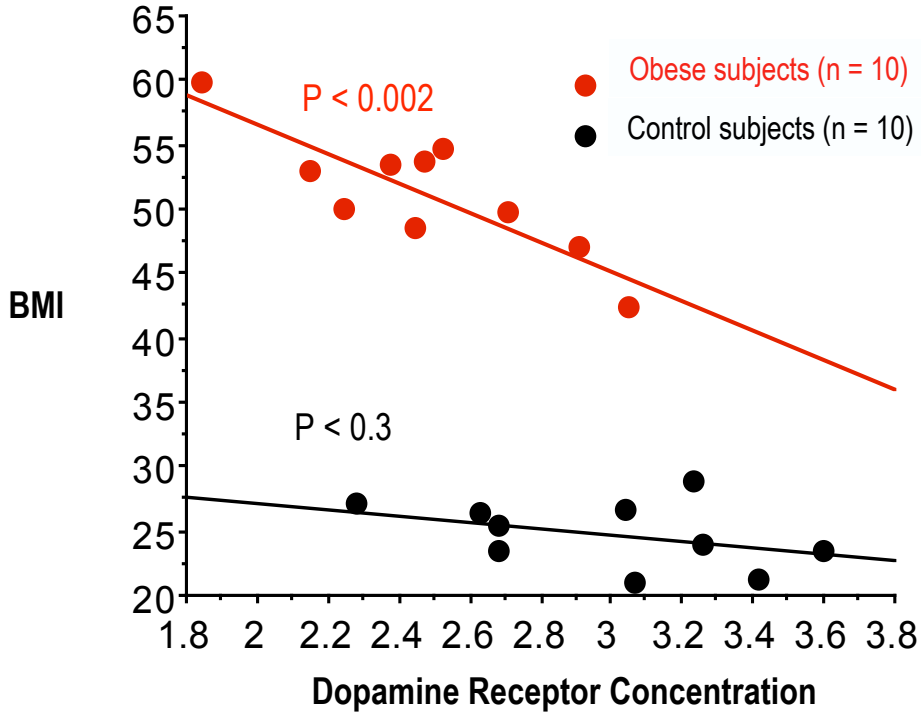
Control Subjects



Obese Subjects

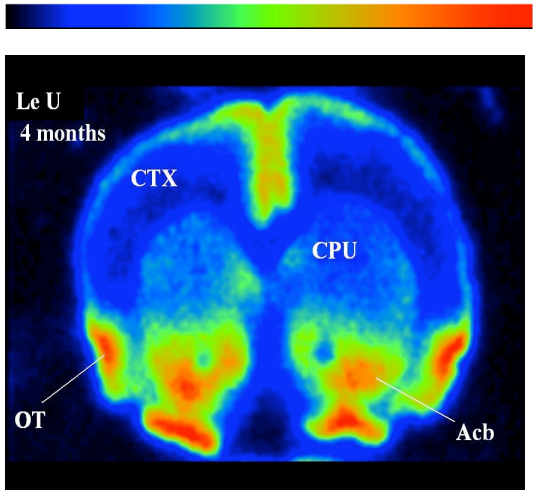


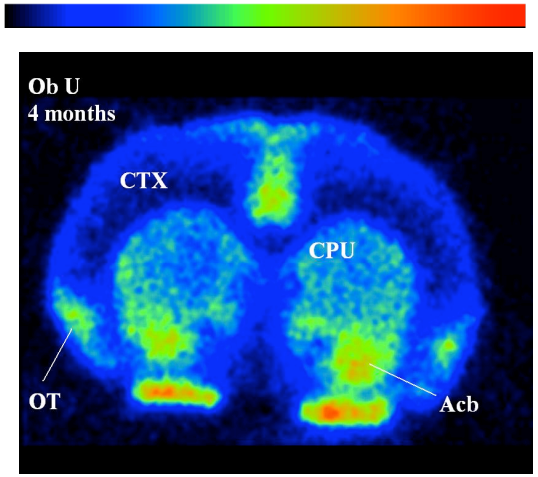
[^{11}C]raclopride

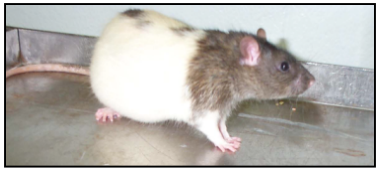


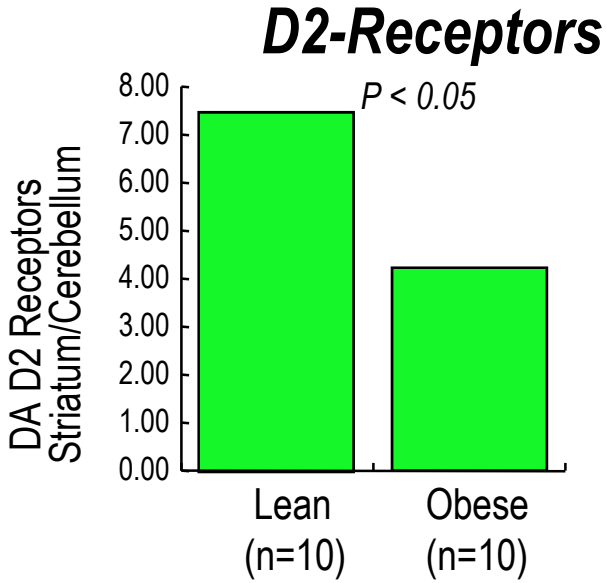
Wang et al, Lancet 2001

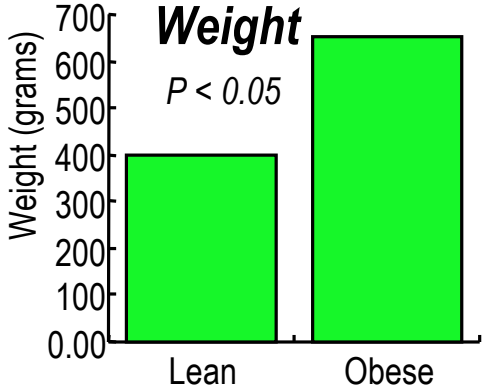
DA D2-R in Zucker Lean and Zucker Obese (fa/fa) Rats

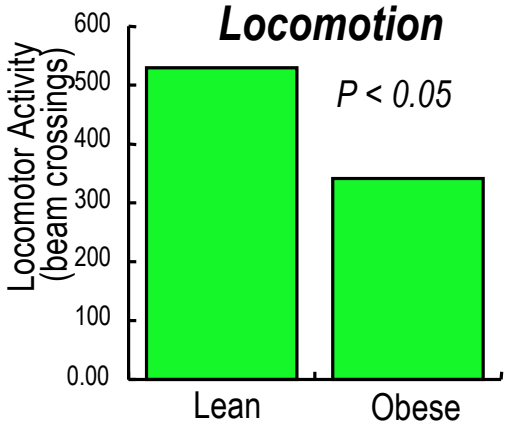












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^{3}H-Spiperone

Thanos et al 2005

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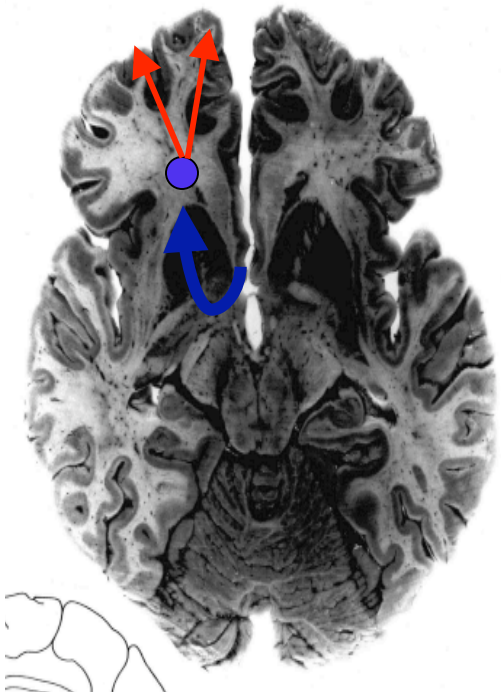
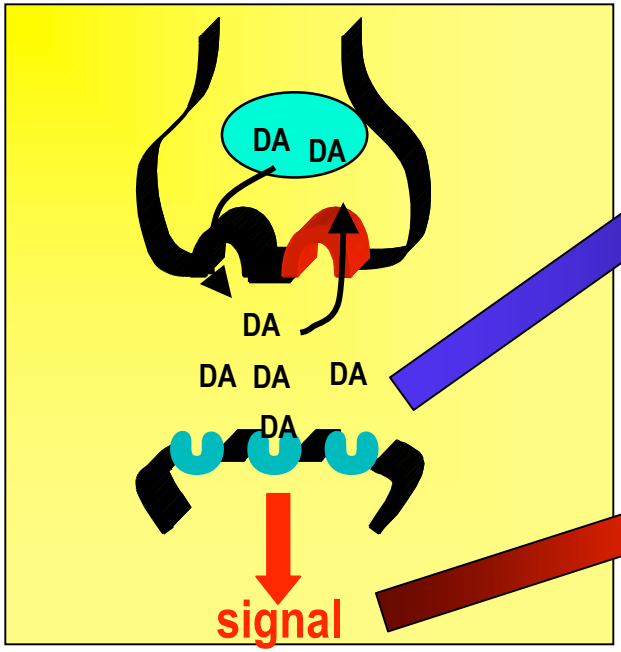
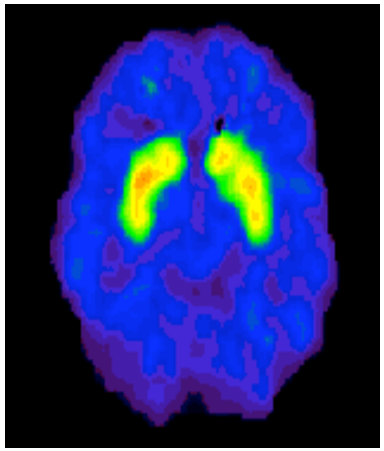
What is the functional significance of low D2-R?



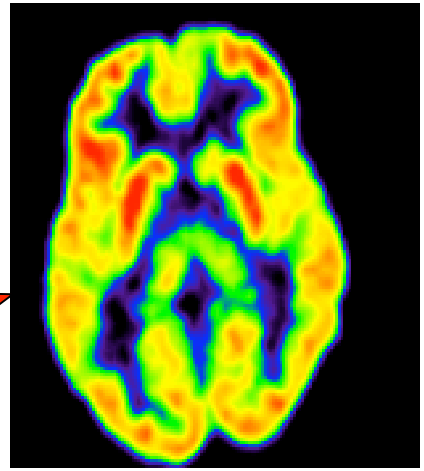
Anatomy



Dopamine Cell

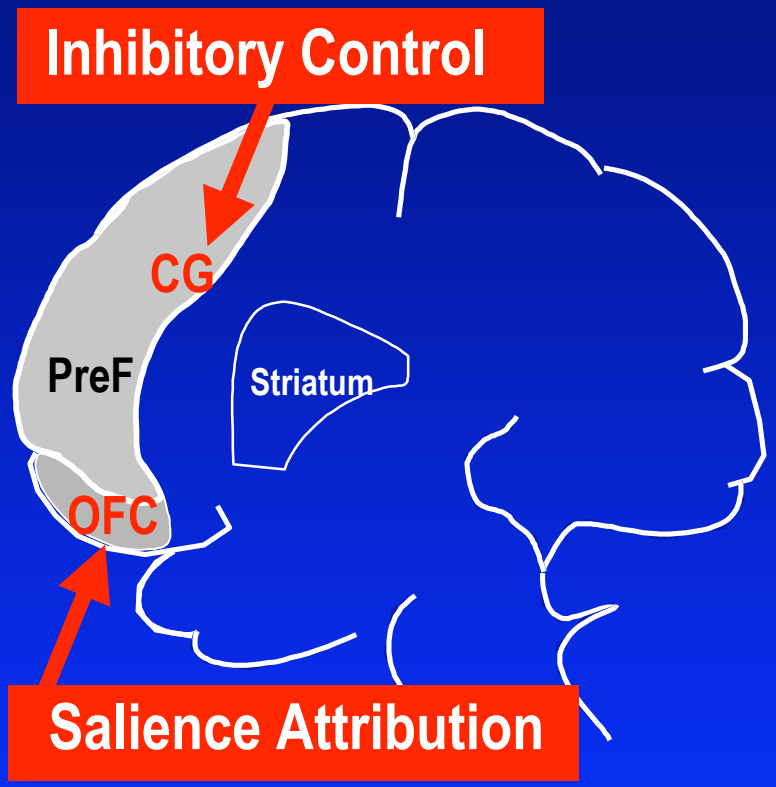


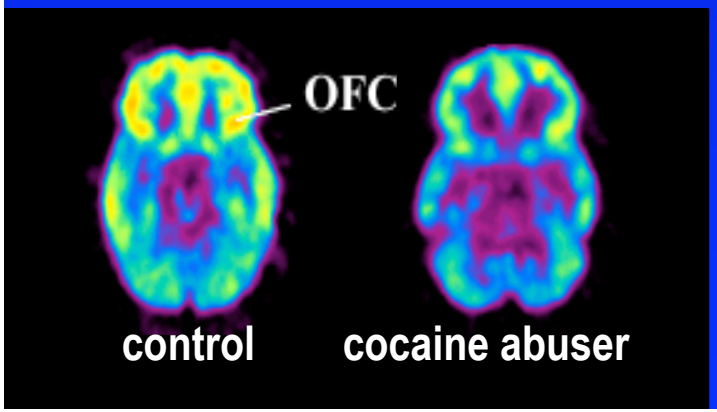
DA Receptors

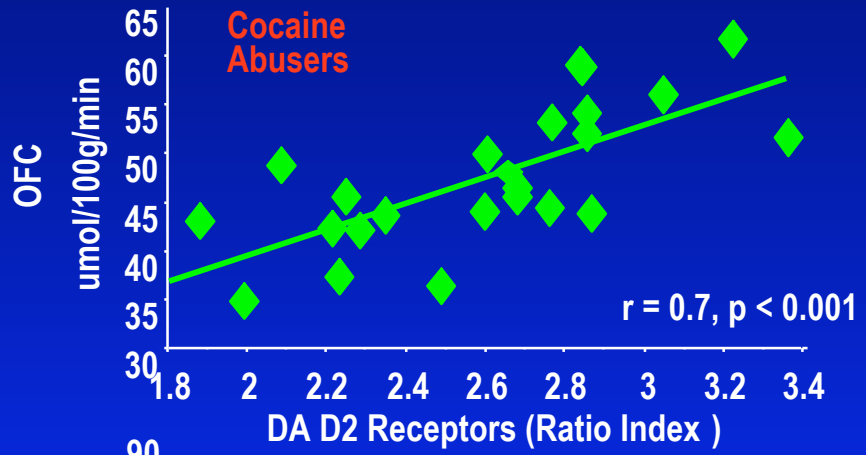


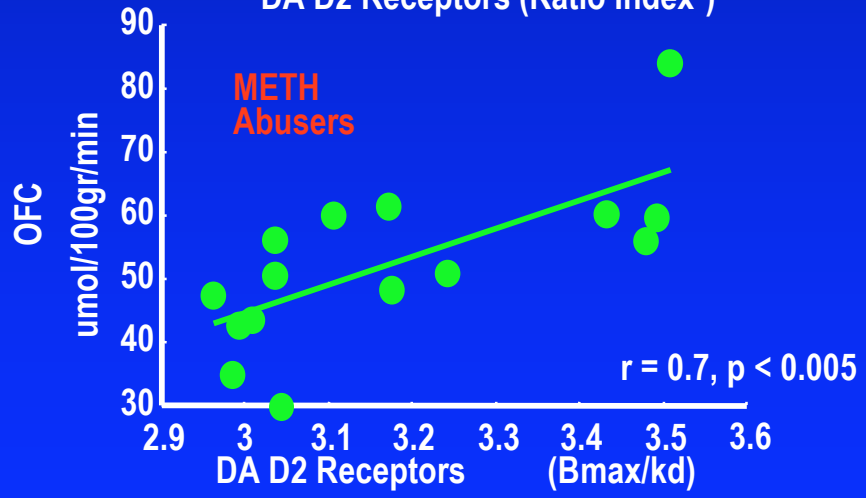
Metabolism

Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism









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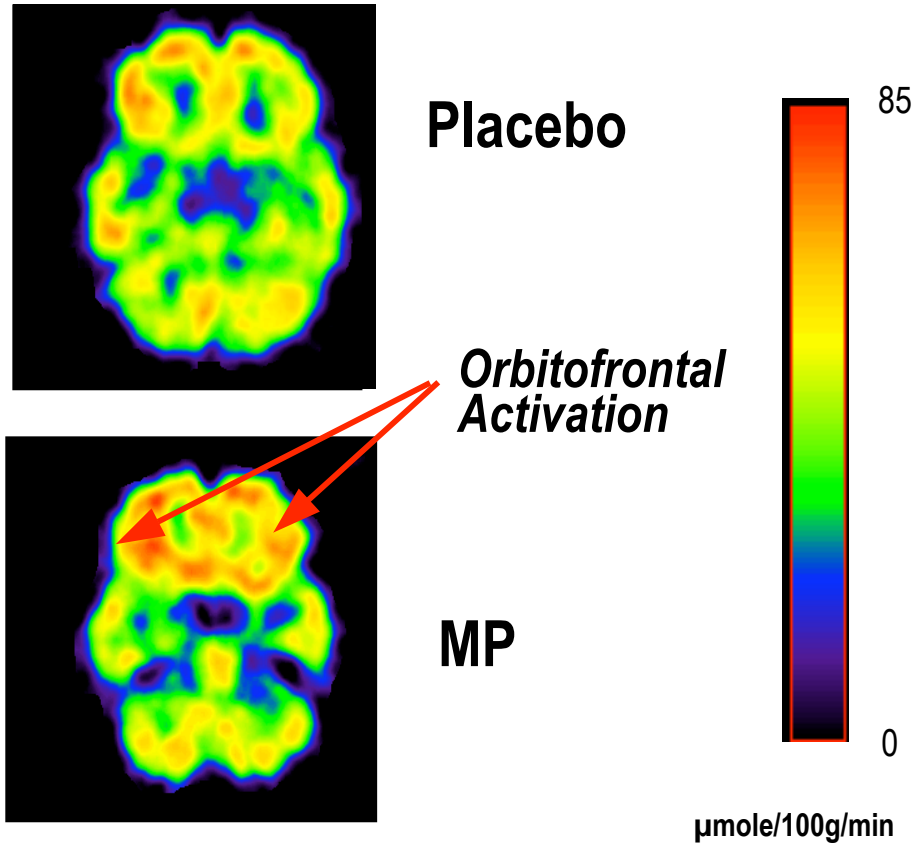
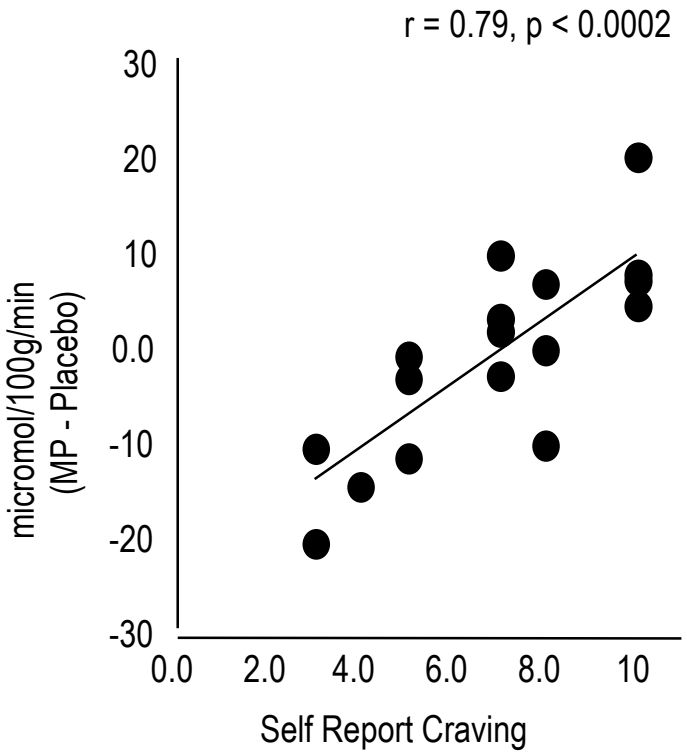
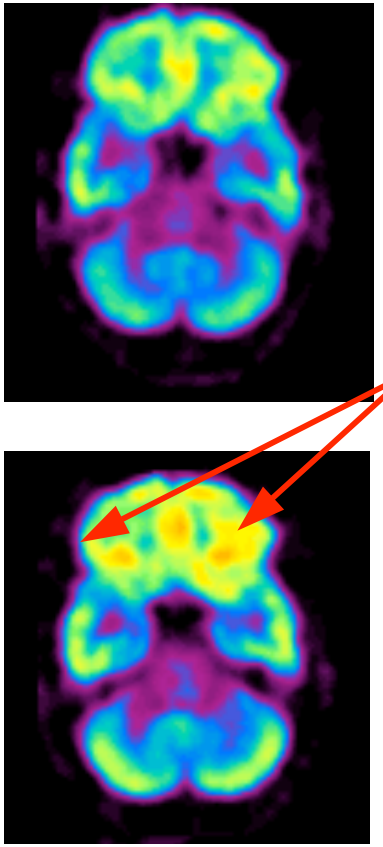
Brain Activation with Methylphenidate Induced Cocaine Craving





Volkow et al Am J Psychiatry 1999

Brain Activation with Food Stimuli

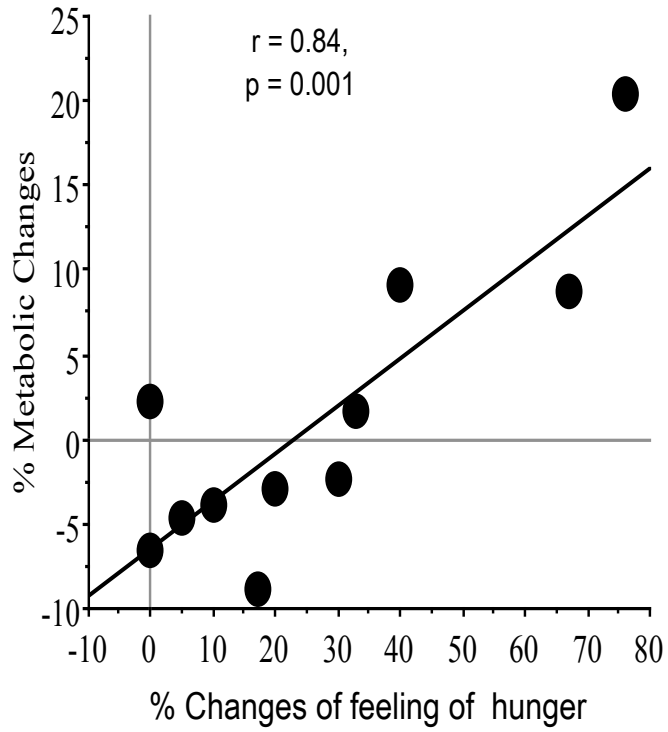


Neutral Stimuli

Orbitofrontal Activation

Food Stimuli

µmole/100g/min

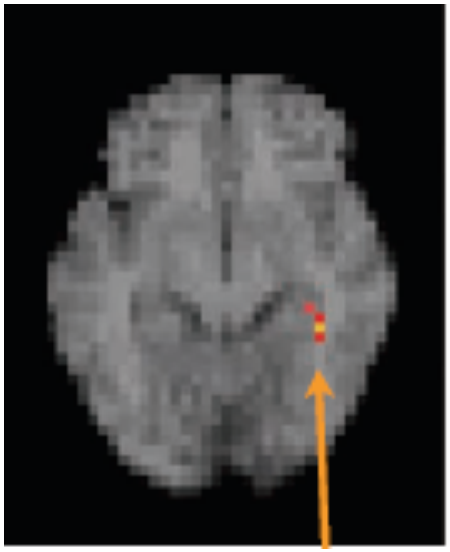


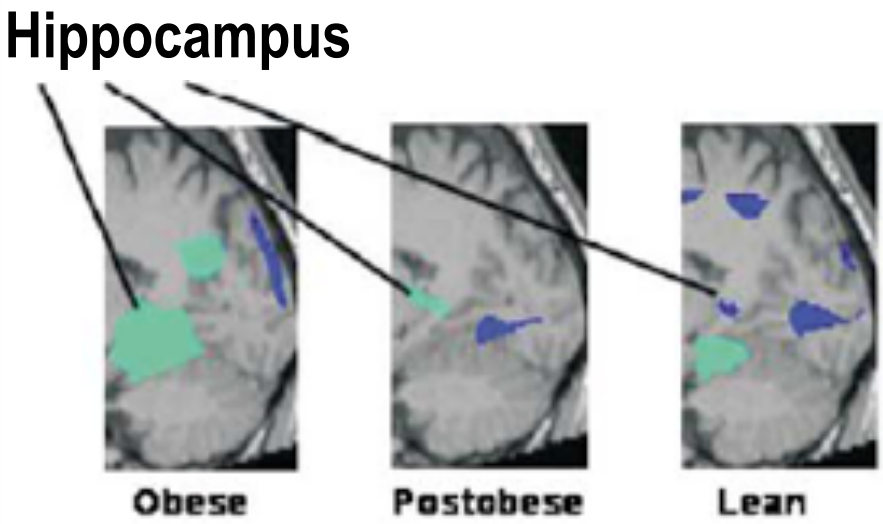
Wang et al, Neuroimage 2004

Activation of hippocampus during craving

Food craving

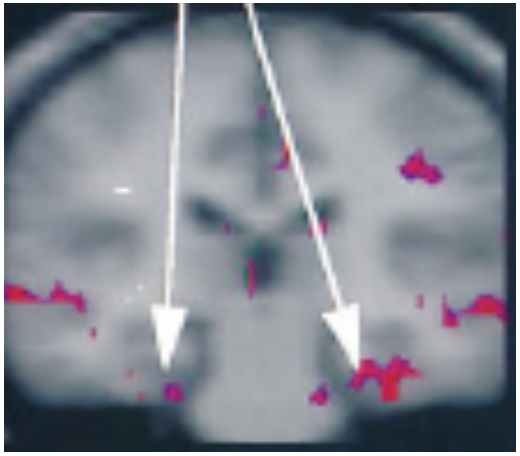
Pelchat et al, 2004





DelParigi et al, 2004

Hippocampus

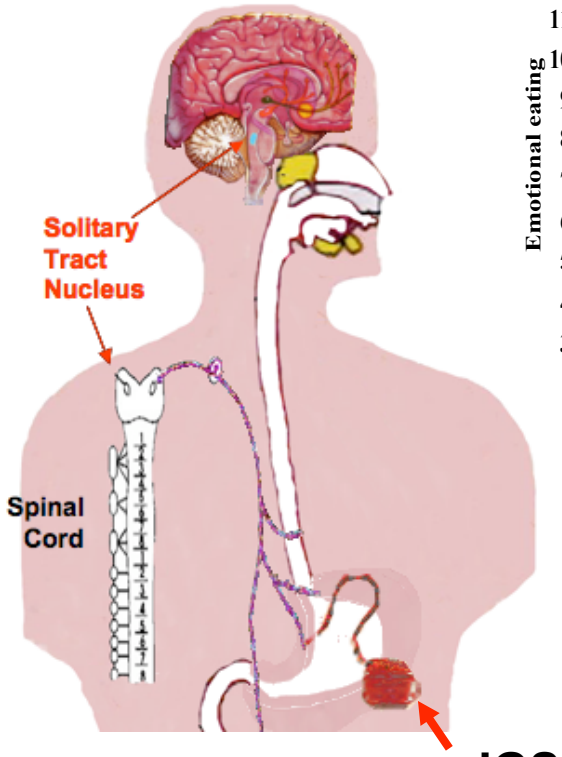


Cocaine craving

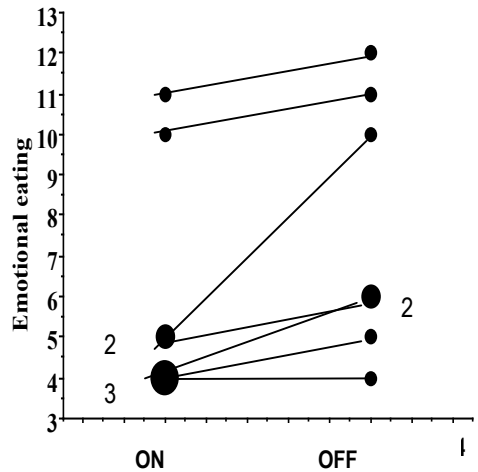
Breiter et al, 1997

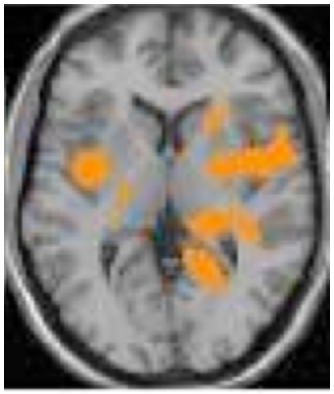
Why do some people continue to eat when the stomach is full?

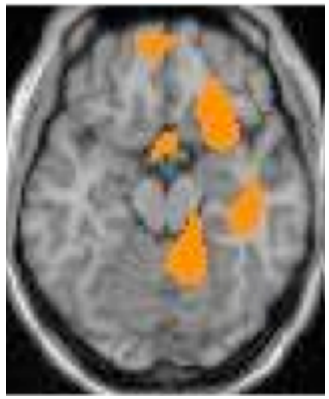
PET-FDG (IGS “on” vs IGS “off” in obese subjects)



Implantable gastric stimulator: **IGS**







- 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.

Wang et al, PNAS USA 2006

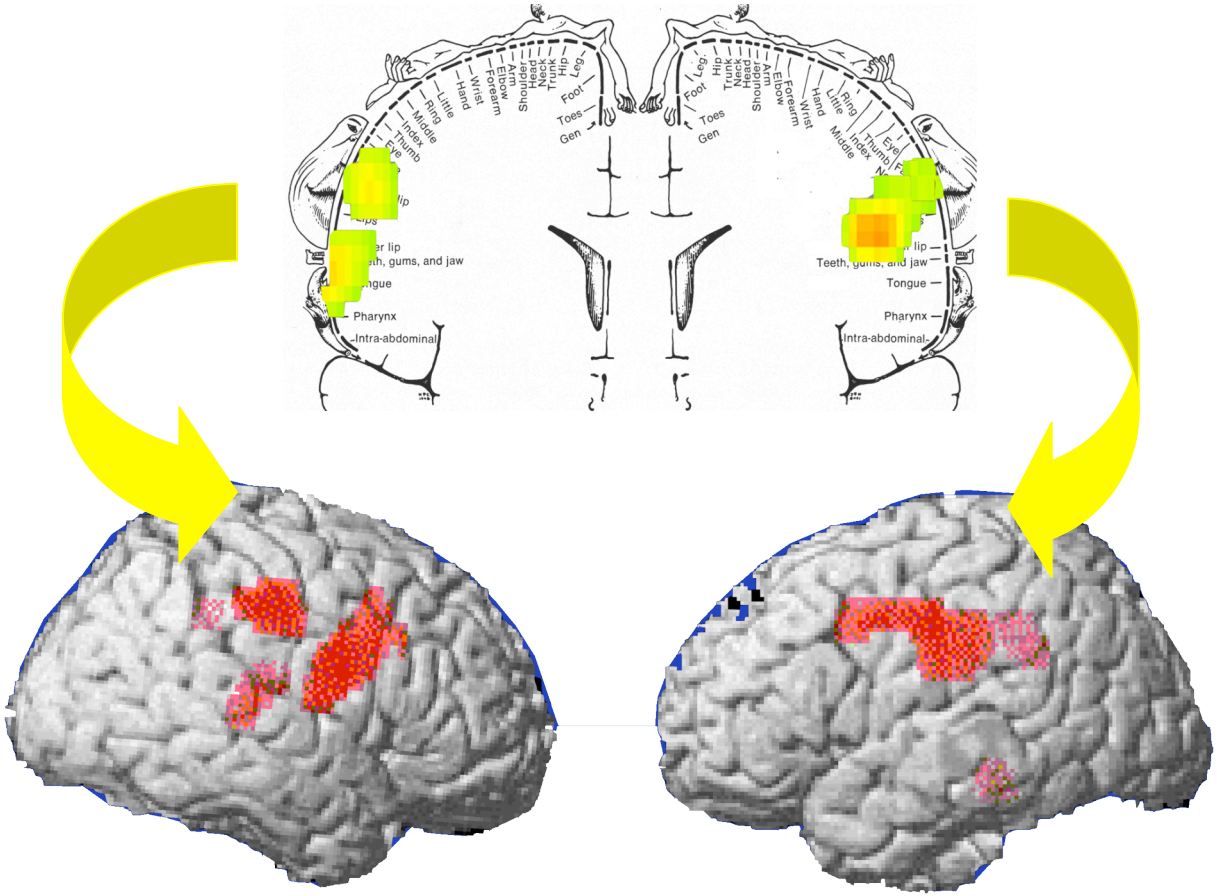
Obesity

vs

Drug Abuse

- What makes obese subjects different from drug abusers?

Regions that are More Active in Obese than Controls

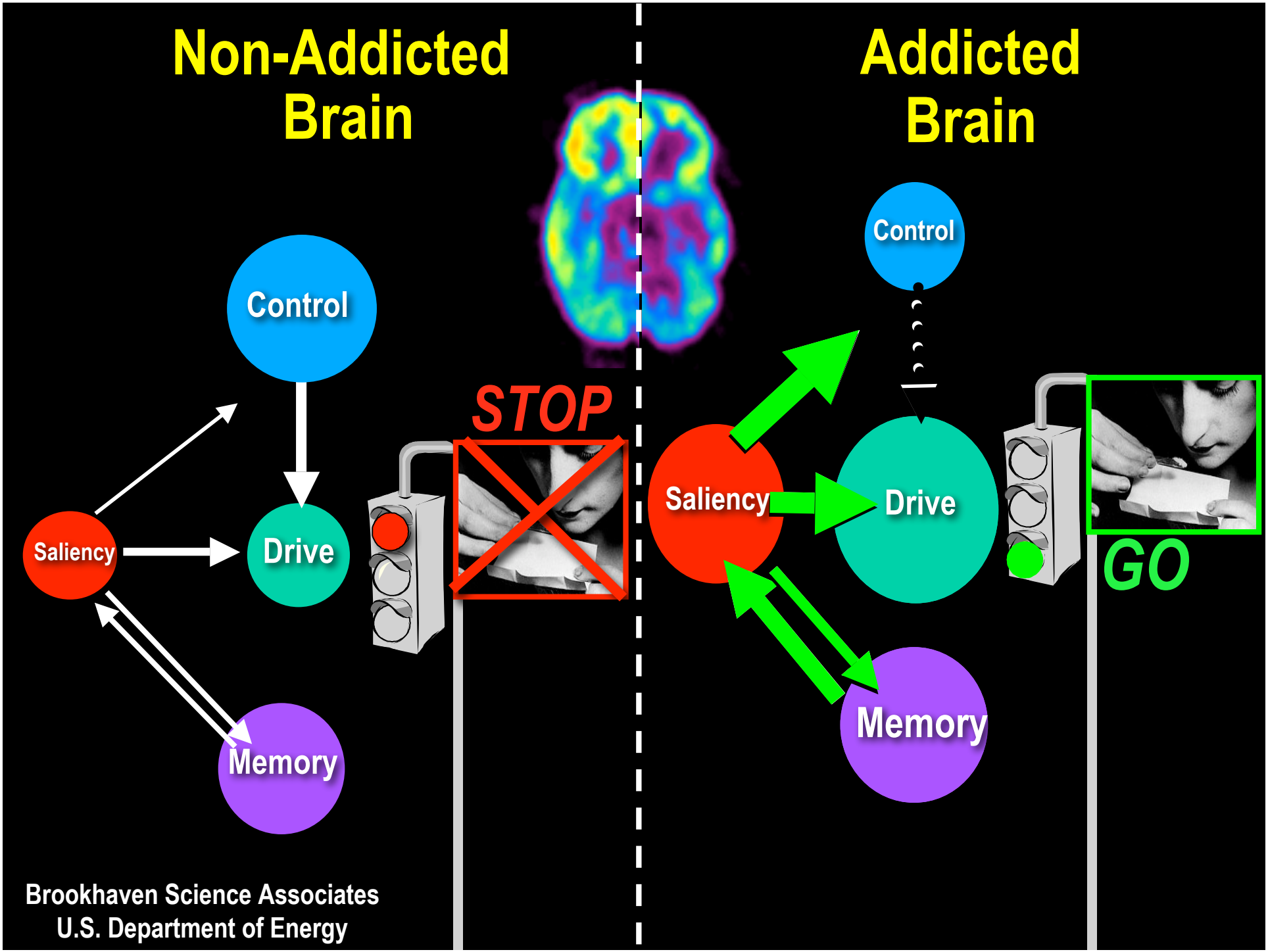


Right Hemisphere

Left Hemisphere

The specificity may be determined by an *enhanced brain sensitivity* to food as a reinforcer

Wang et al, NeuroReport 2002


Non-Addicted Brain
Addicted Brain
Control
Saliency
Drive
Memory
STOP
Control
Saliency
Drive
Memory
GO
Brookhaven Science Associates
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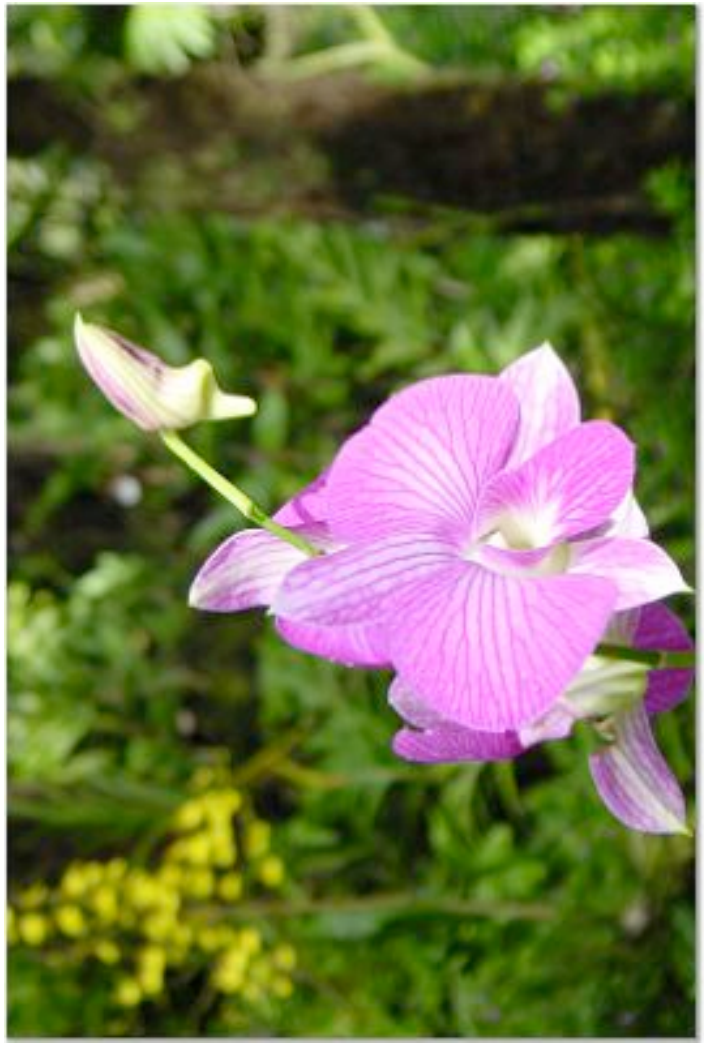
Center for Translational Neuroimaging

D. Alexoff (engineering)
H. Benveniste (medicine)
A. Biegon (pharmacology)
E. Caparelli (physics)
S. Dewey (neuroanatomy)
A. Dilmanian (physics)
C. Du (medical physics)
J. Dunn (microbiologist)
R. Ferrieri (chemistry)
J. Fowler (chemistry)
A. Gifford (pharmacology)
R. Goldstein (psychology)
F. Henn (ALD, psychiatry)
N. Klein (psychology)
J. Logan (modeling)
Y. Ma (image analysis)
L. Miller (biophysicist)
M. Miura (chemist)
L. Pena (neuroscience)
M. Schueller (medical physics)
D. Schlyer (chemistry)
W. Schiffer (neurobiology)
D. Smith (MRI physics)
F. Telang (neurology)
P. Thanos (neuroscience)
D. Tomasi (MRI physics)
P. Vaska (PET physics)
G-J Wang (Chair, medicine)
8 technicians and nurses
13 graduate students and post-docs



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