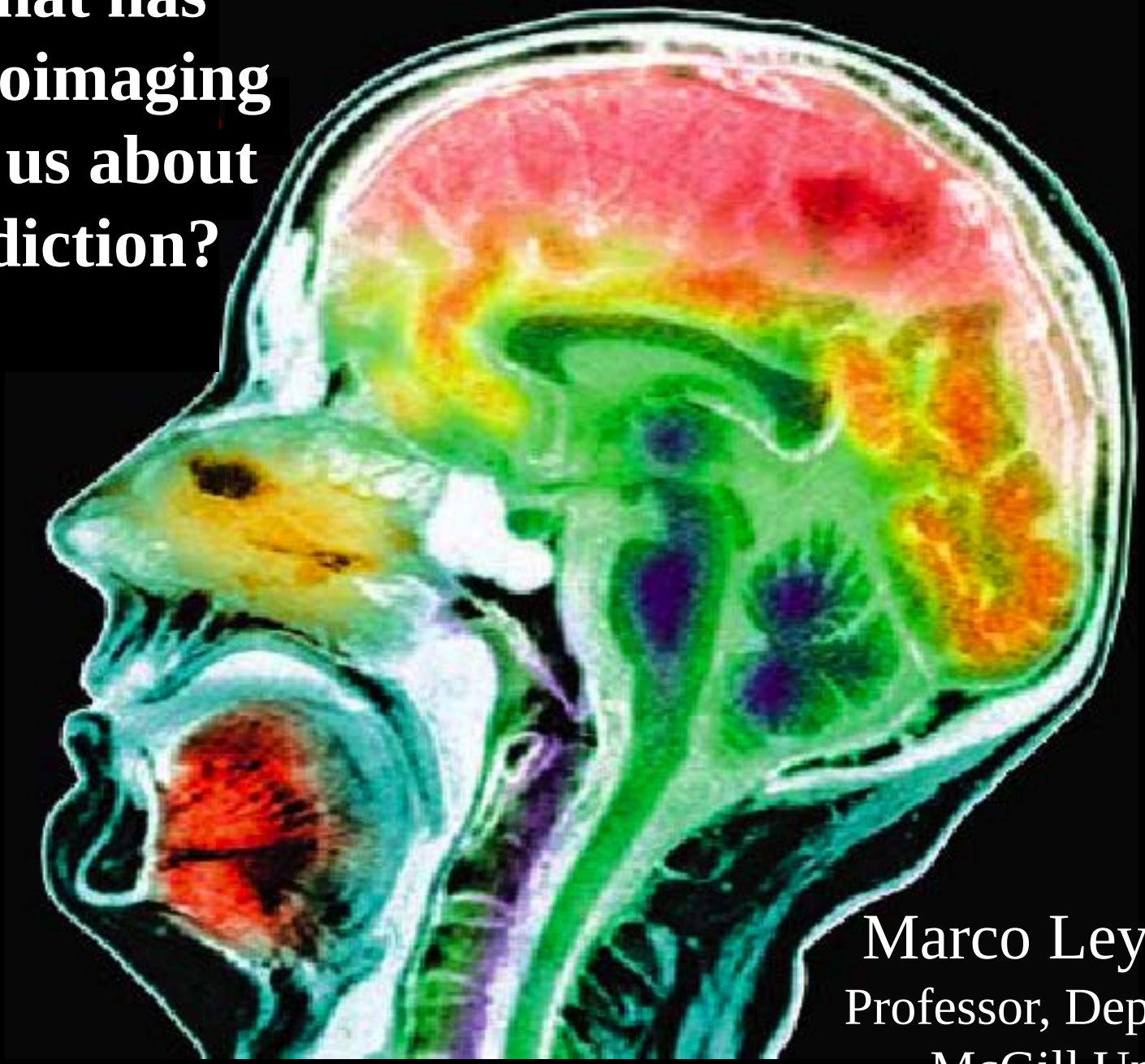
What has neuroimaging told us about addiction?

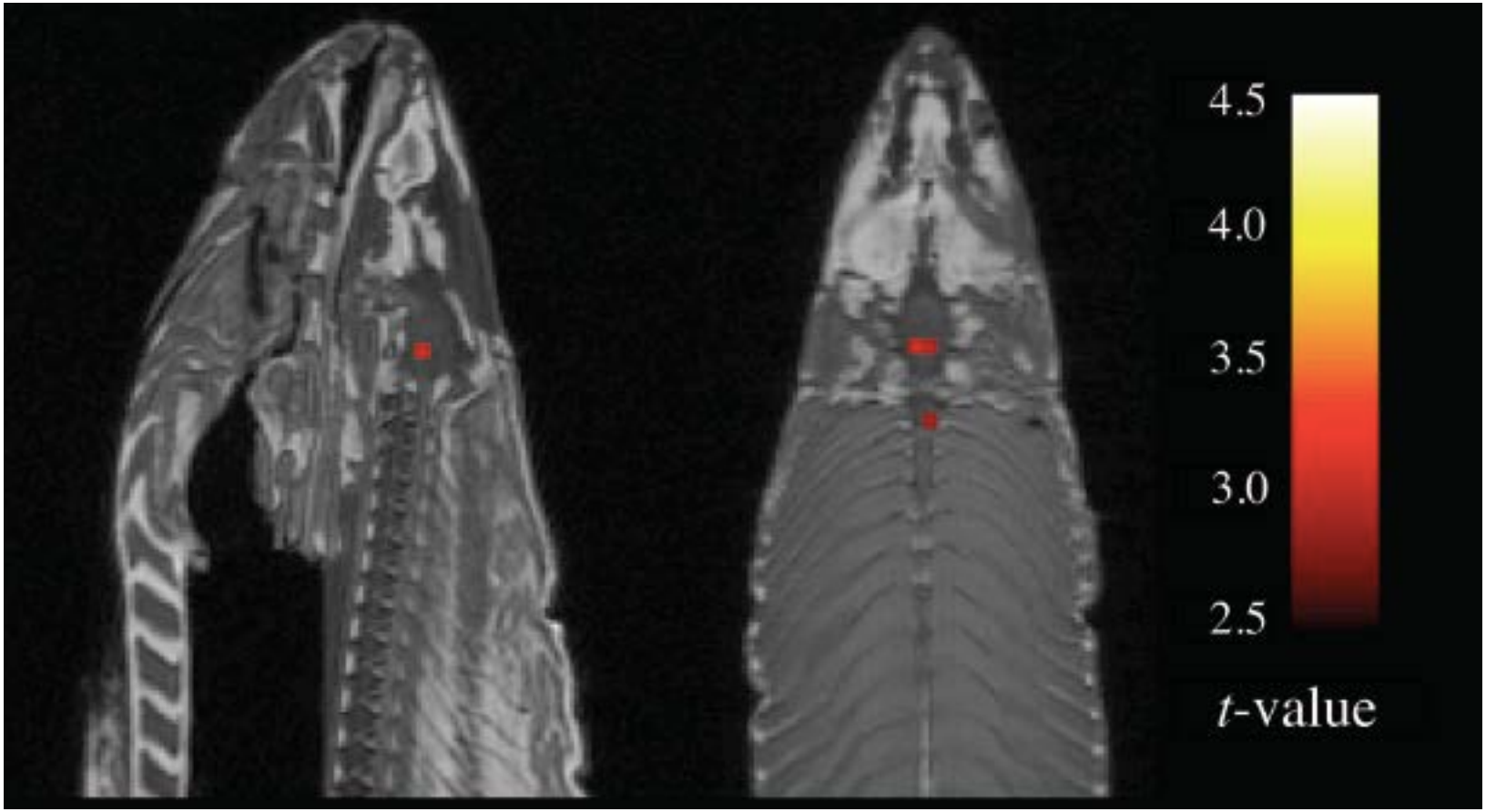


Marco Leyton, PhD
Professor, Dept Psychiatry
McGill University

Neuroimaging Methods

Method	Anatomical Resolution	Temporal Resolution	Transmitter Specificity	Cost
Anatomy				
CAT	Medium	Zero	Zero	Medium
MRI	Excellent	Zero	Zero	Medium
MRI-DTI	Excellent	Zero	Zero	Medium
Activity				
PET	Medium	Poor	Good	High
SPECT	Medium	Poor	Good	Medium
fMRI	Excellent	Good	Zero/Medium	Medium
Spectroscopy	Excellent	Zero	Good	Medium
EEG	Poor	Excellent	Zero	Low

Caution Before Enthusiasm



Social perspective taking task
Higher ichthyological cognition?

Bennett et al *JSUR* 2010

What Would We Like Neuroimaging To Tell Us to be Useful?

Reske *Addiction* 2013

What Would We Like Neuroimaging To Tell Us to be Useful?

1. Integration of findings.

Reske *Addiction* 2013

What Would We Like Neuroimaging To Tell Us to be Useful?

1. Integration of findings.

2. Identification of risk factors.

Reske *Addiction* 2013

What Would We Like Neuroimaging To Tell Us to be Useful?

1. Integration of findings.

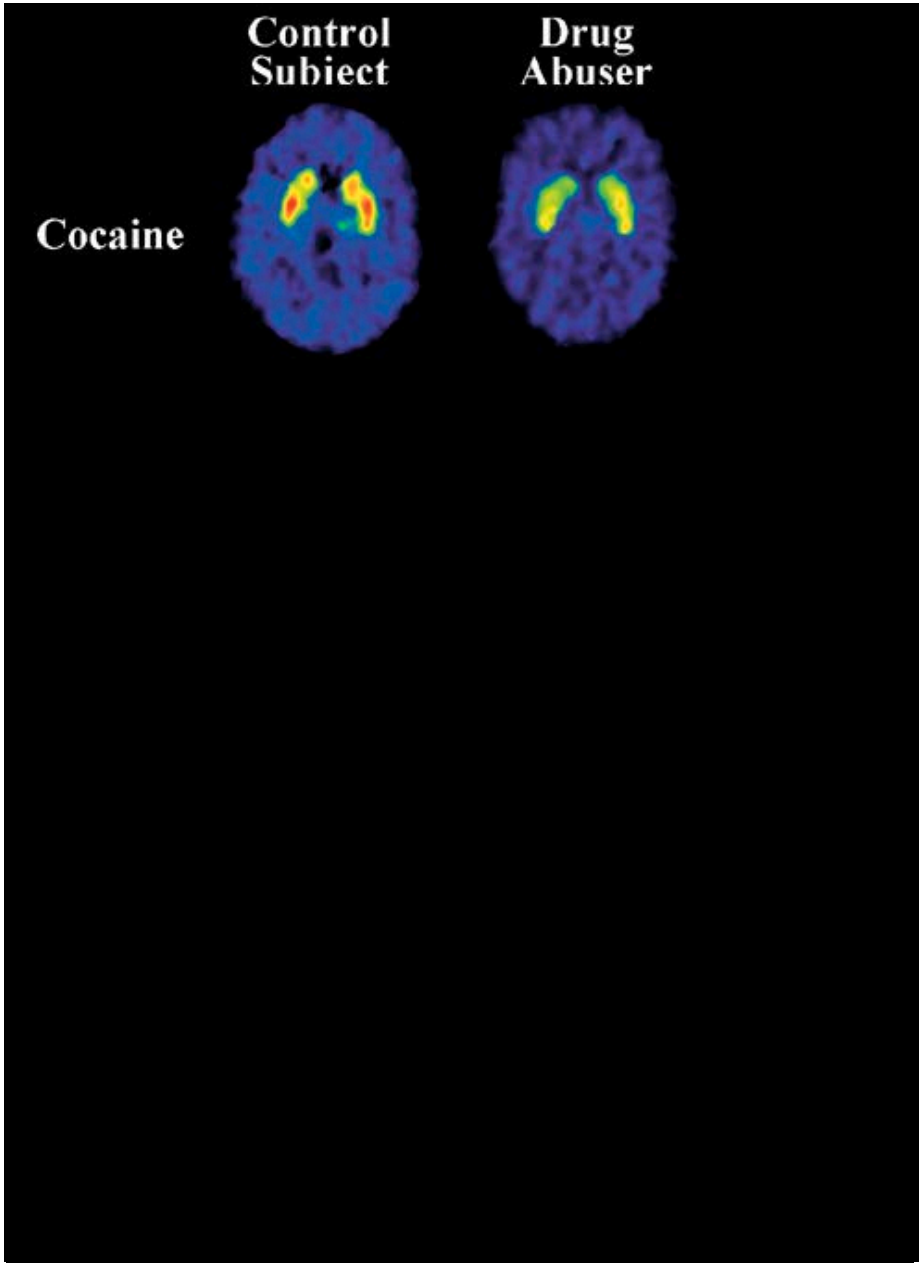
2. Identification of risk factors.

3. Information that can inform treatment.

Reske *Addiction* 2013

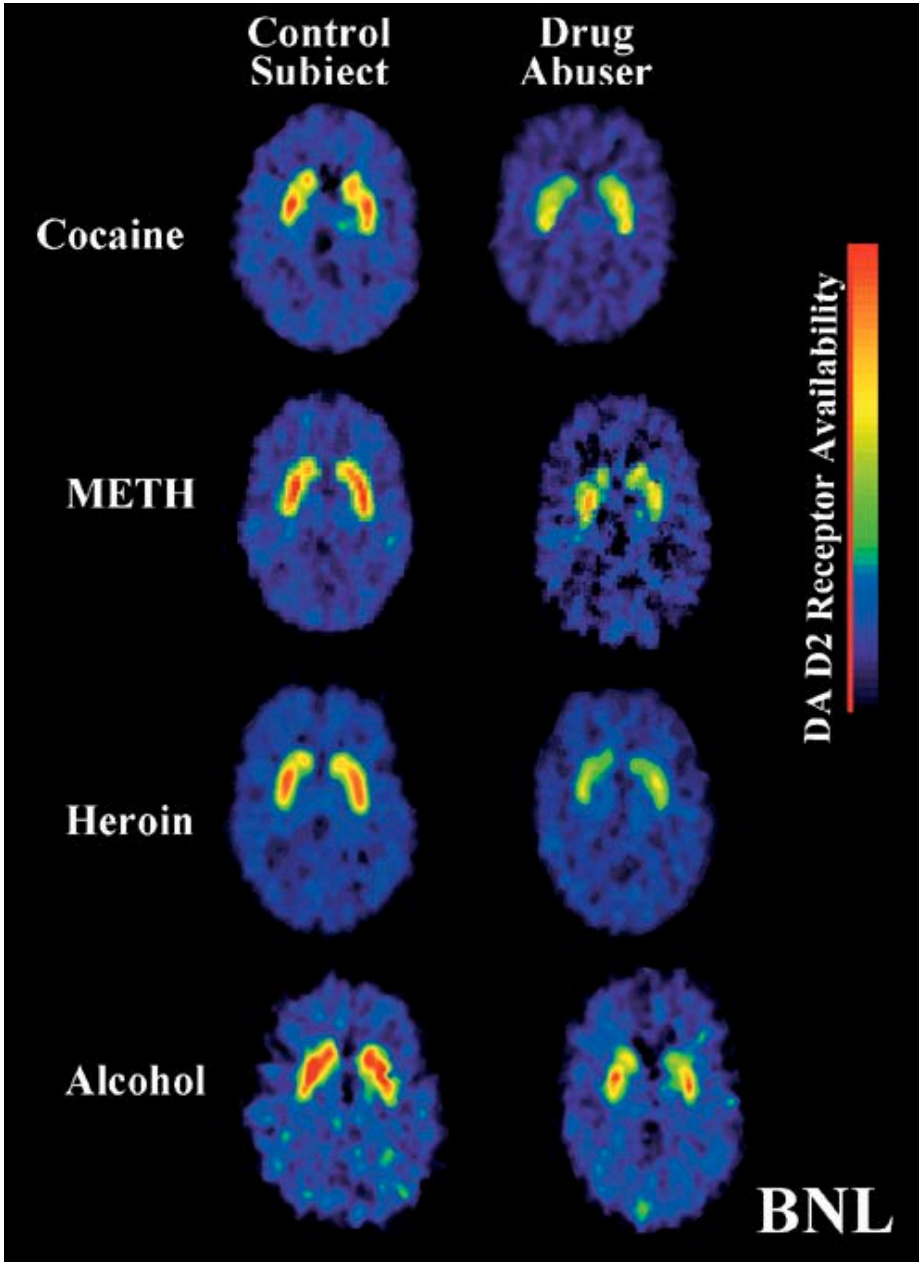
Consistent Findings in Neuroimaging Literature

Low ‘Baseline’ Striatal DA D2



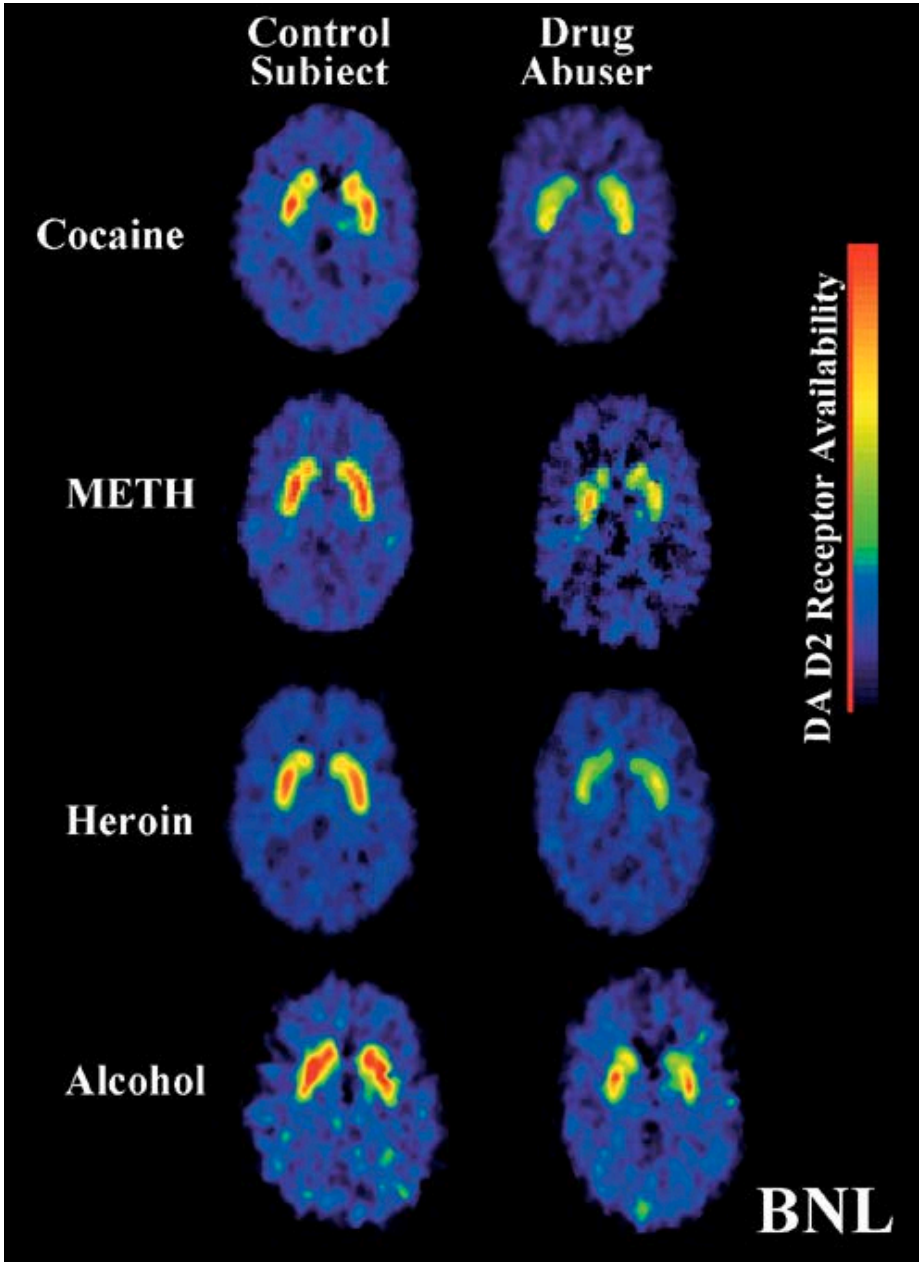
Volkow et al 1997 *Nature*

Low ‘Baseline’ Striatal DA D2



Volkow et al 2004 *Mol Psychiatry*

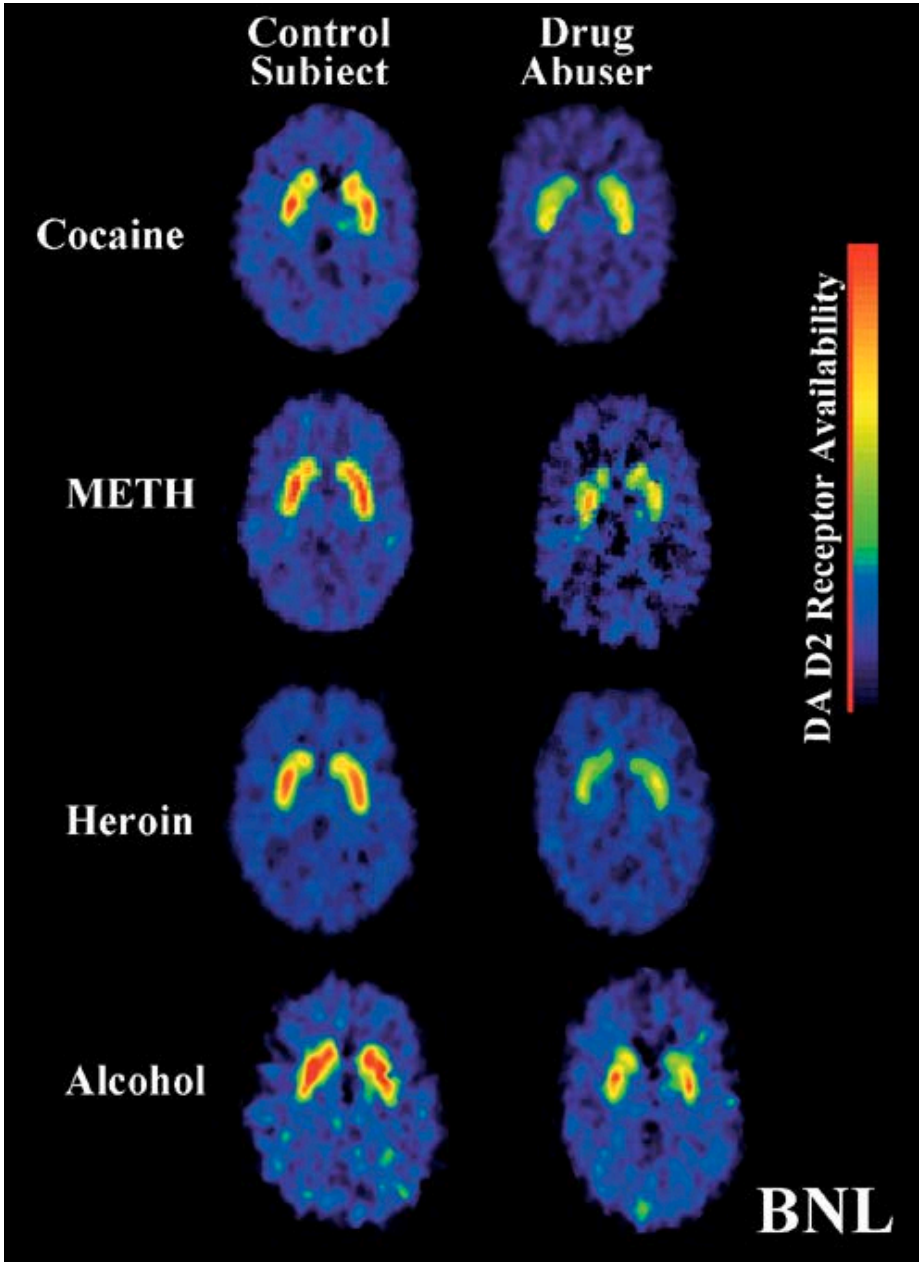
Low ‘Baseline’ Striatal DA D2



Drug	Low DA D2	No Diff
Cocaine	6 studies	1 study
Alcohol	8 studies	2 studies
Opiates	3 studies	1 study
Meth-amphetamine	4 studies	0 studies
Cigarettes	5 studies	0 studies
Total:	26	4

Volkow et al 2004 *Mol Psychiatry*

Low ‘Baseline’ Striatal DA D2



Drug	Low DA D2	No Diff
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Alcohol	8 studies	2 studies
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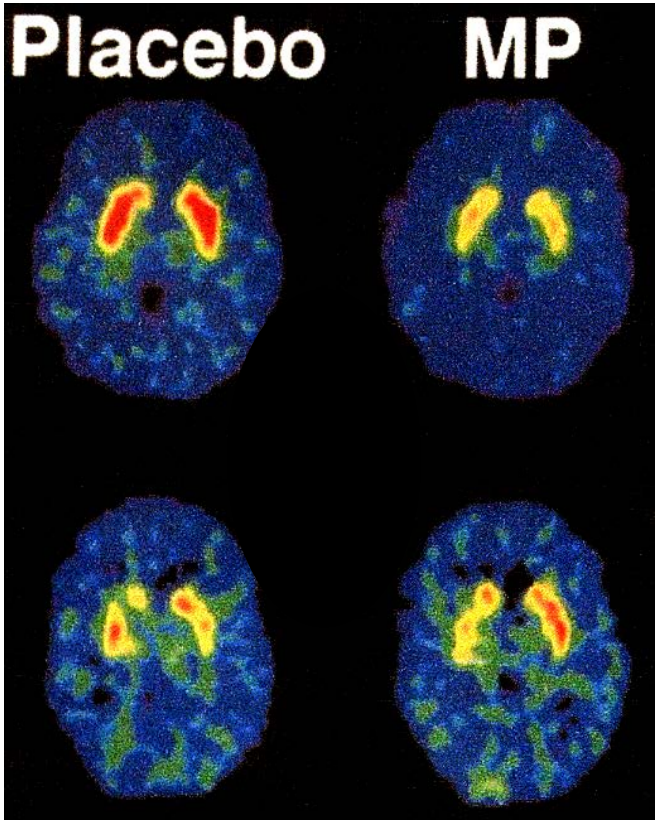
Meth-amphetamine	4 studies	0 studies
Cigarettes	5 studies	0 studies
Cannabis	0 studies	4 studies
Total:	26	4+4

Volkow et al 2004 *Mol Psychiatry*

Low Stimulant Drug-Induced Striatal DA Release

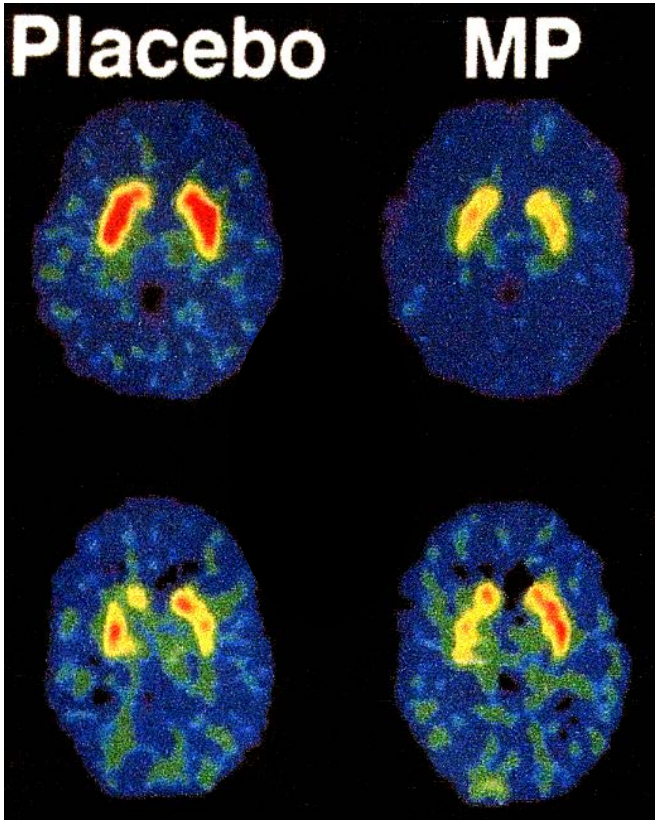


Healthy controls

Cocaine dependent

Volkow et al 1997
Nature

Low Stimulant Drug-Induced Striatal DA Release



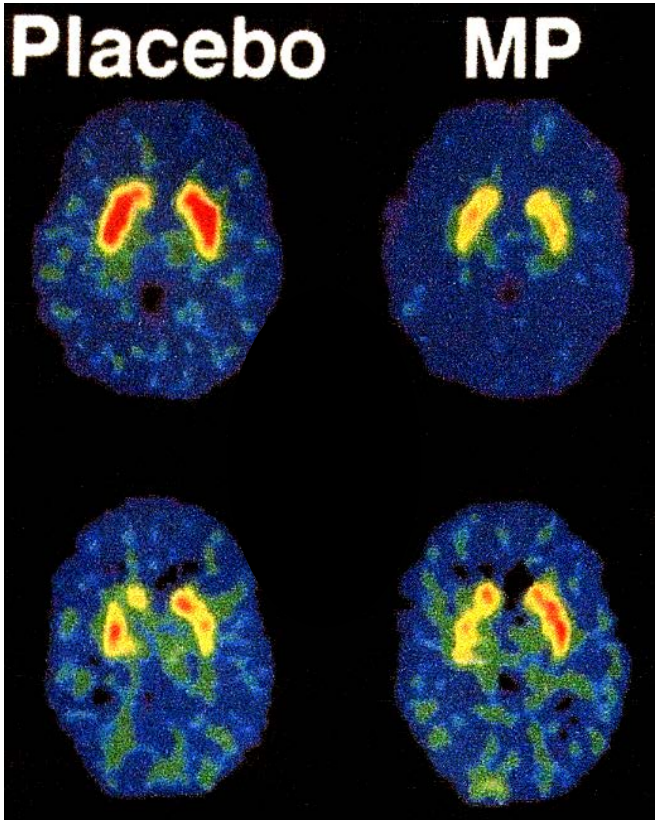
Healthy controls

Cocaine dependent

Drug	Low DA Release	No diff
Cocaine	4 studies	0 studies
Alcohol	2 studies	0 studies
Opiates	1 study	0 studies
Meth-amphetamine	1 study	0 studies
Total:	8	0

Volkow et al 1997
Nature

Low Stimulant Drug-Induced Striatal DA Release



Healthy controls

Cocaine dependent

Drug	Low DA Release	No diff
Cocaine	4 studies	0 studies
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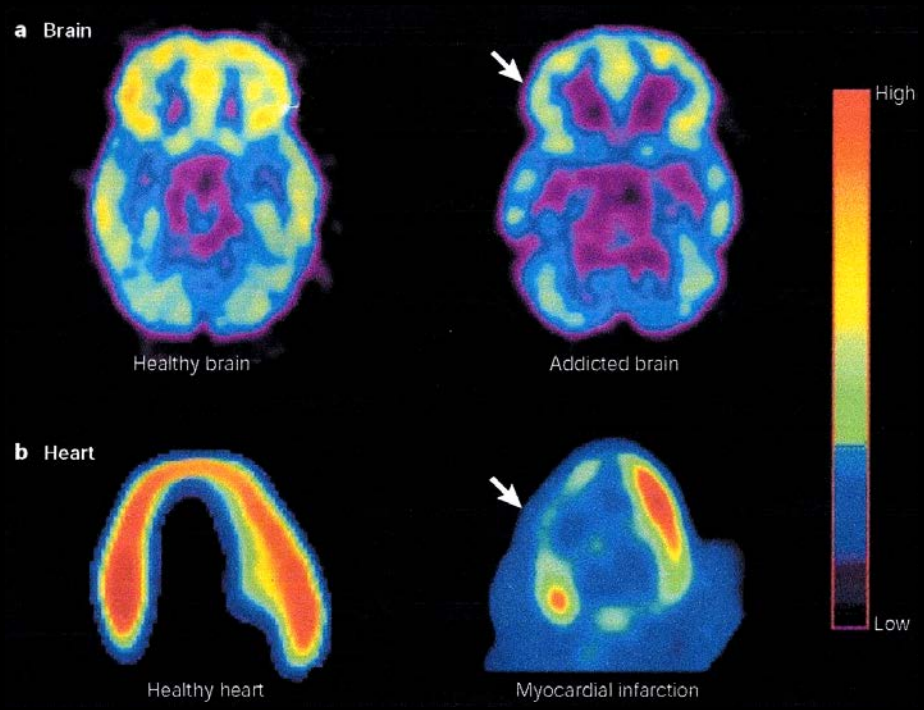
Opiates	1 study	0 studies
Meth-amphetamine	1 study	0 studies
Cannabis	*1 study	1 study
Total:	9	1

***Subjects with co-morbid schizophrenia**

Volkow et al 1997
Nature

Low Cortical Function

Lower resting OFC FDG Uptake



Volkow & Li *Nat Rev: Neurosci* 2004

Low Cortical Function

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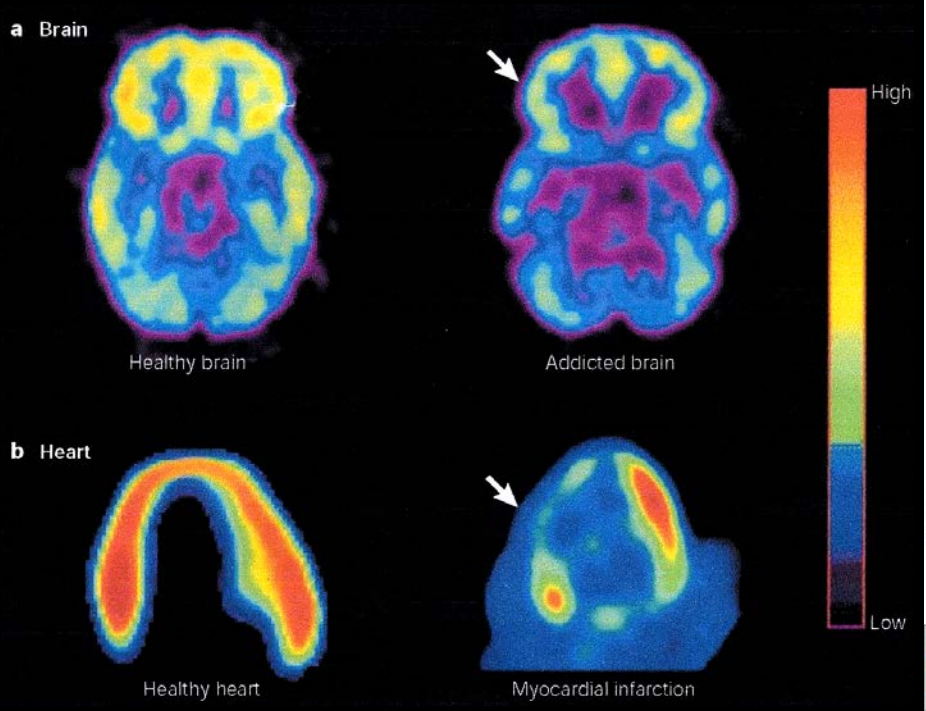
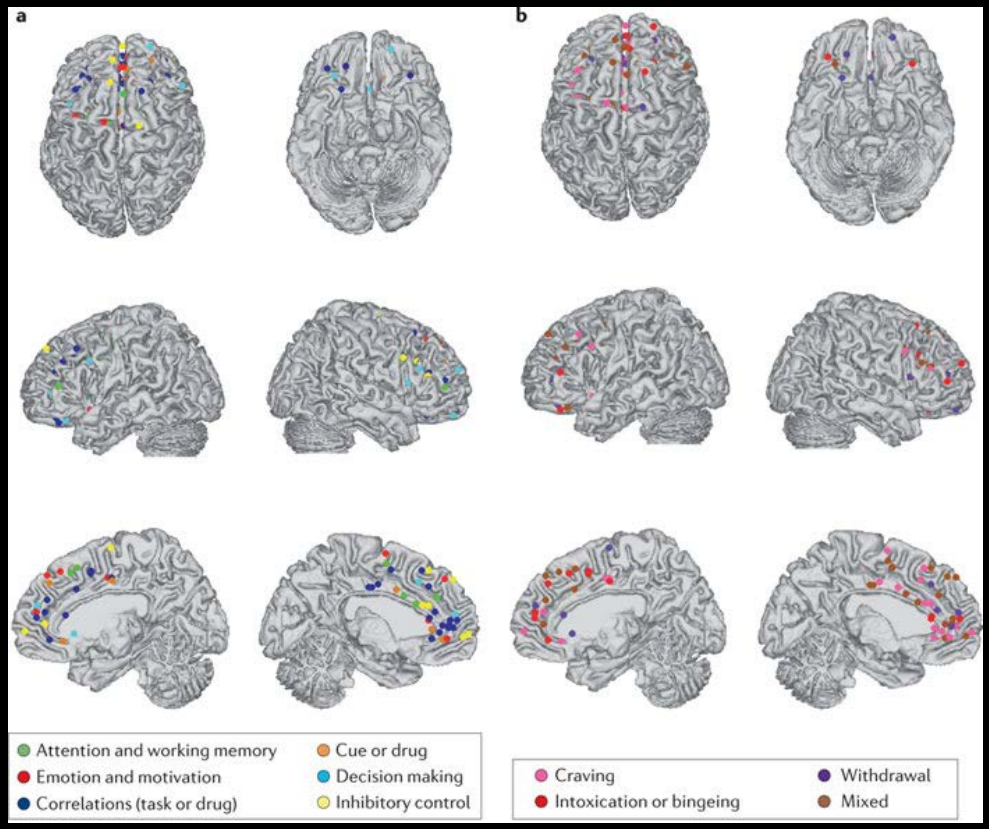
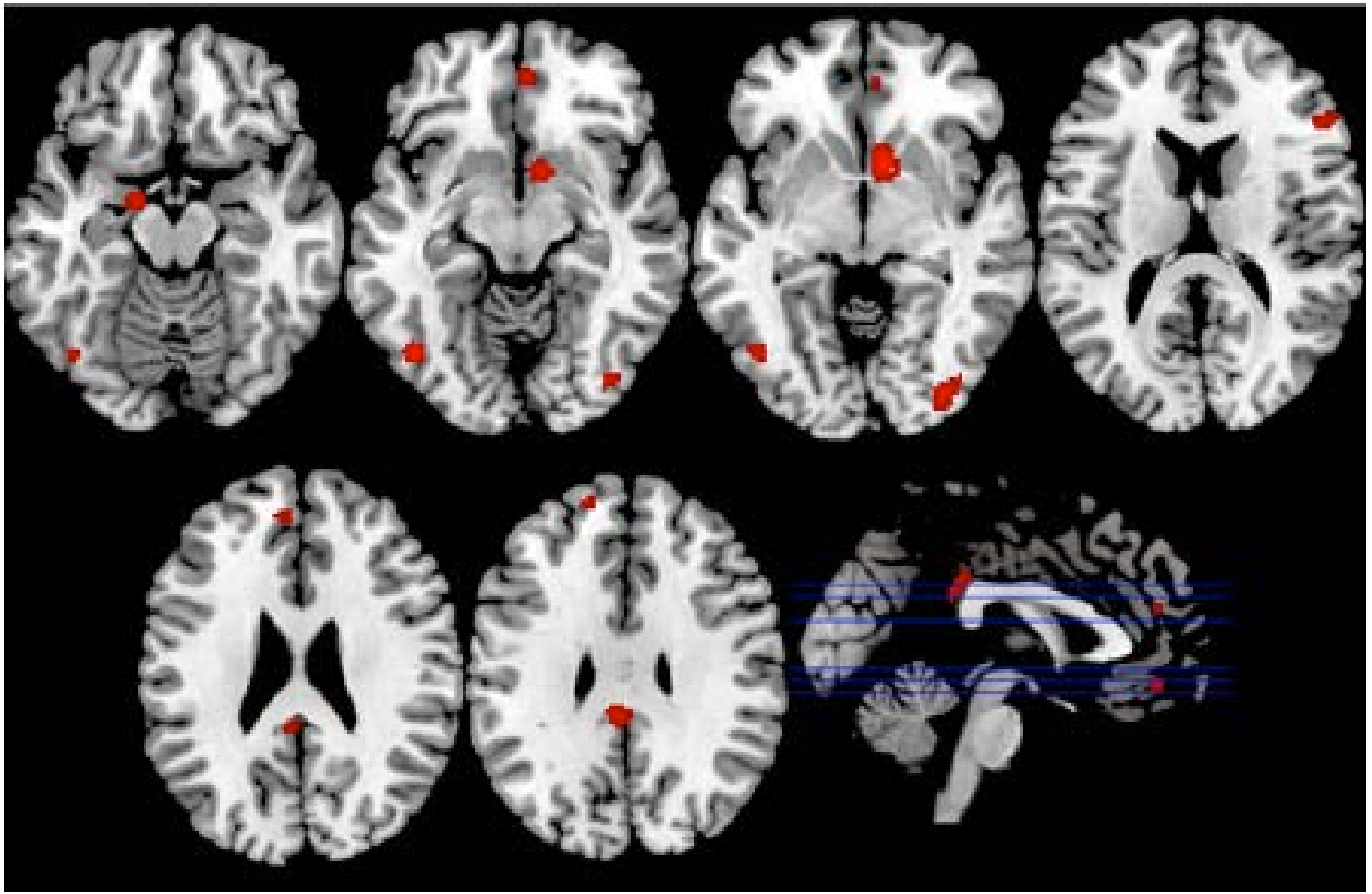


Volkow & Li *Nat Rev: Neurosci* 2004



Goldstein & Volkow *Nat Rev: Neurosci* 2011

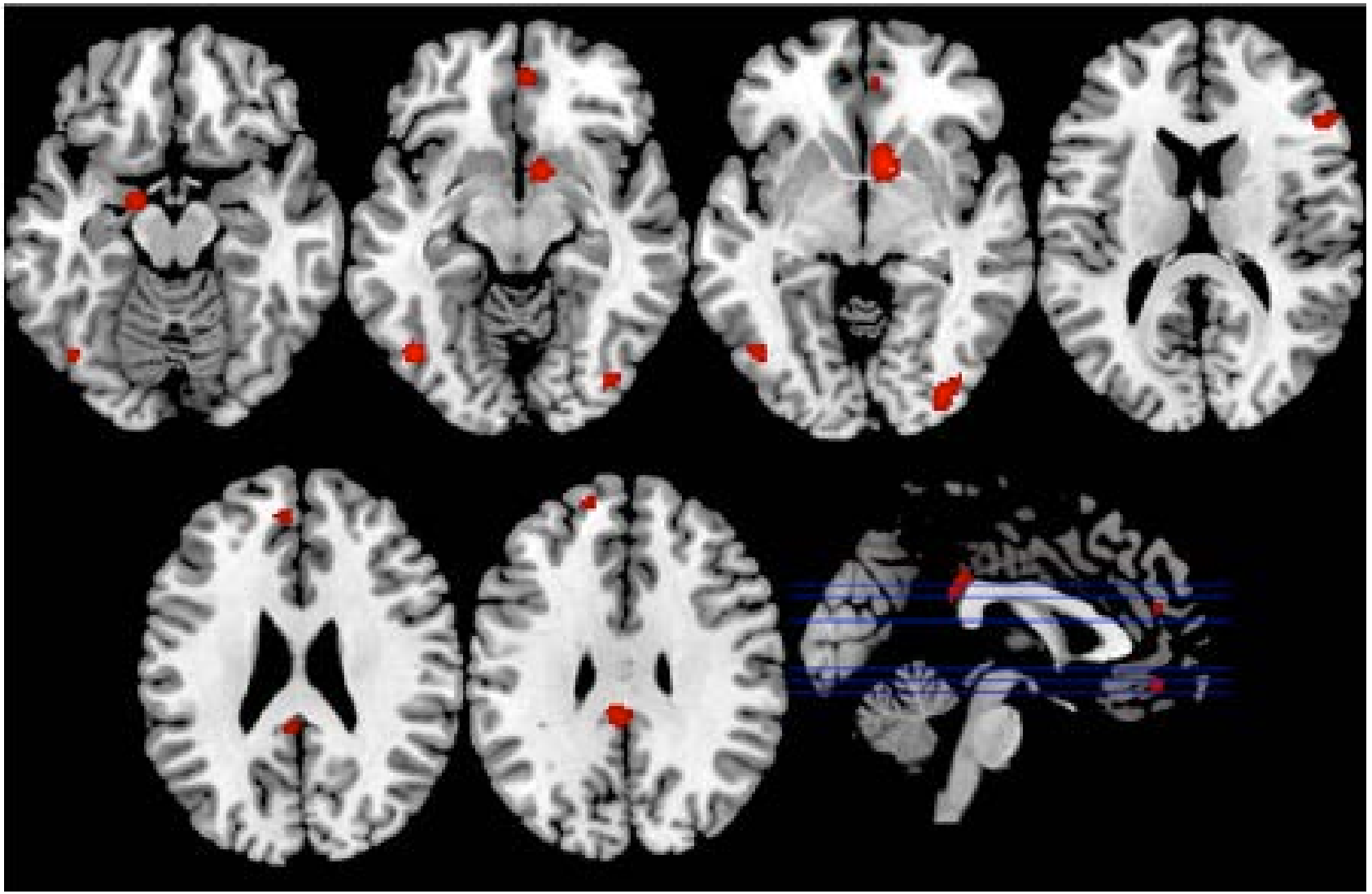
Drug Cue-Induced Activation



Hyperactive responses in orbitofrontal cortex, amygdala, and ventral striatum

Chase et al 2011 *Biol Psychiatry*

Drug Cue-Induced Activation



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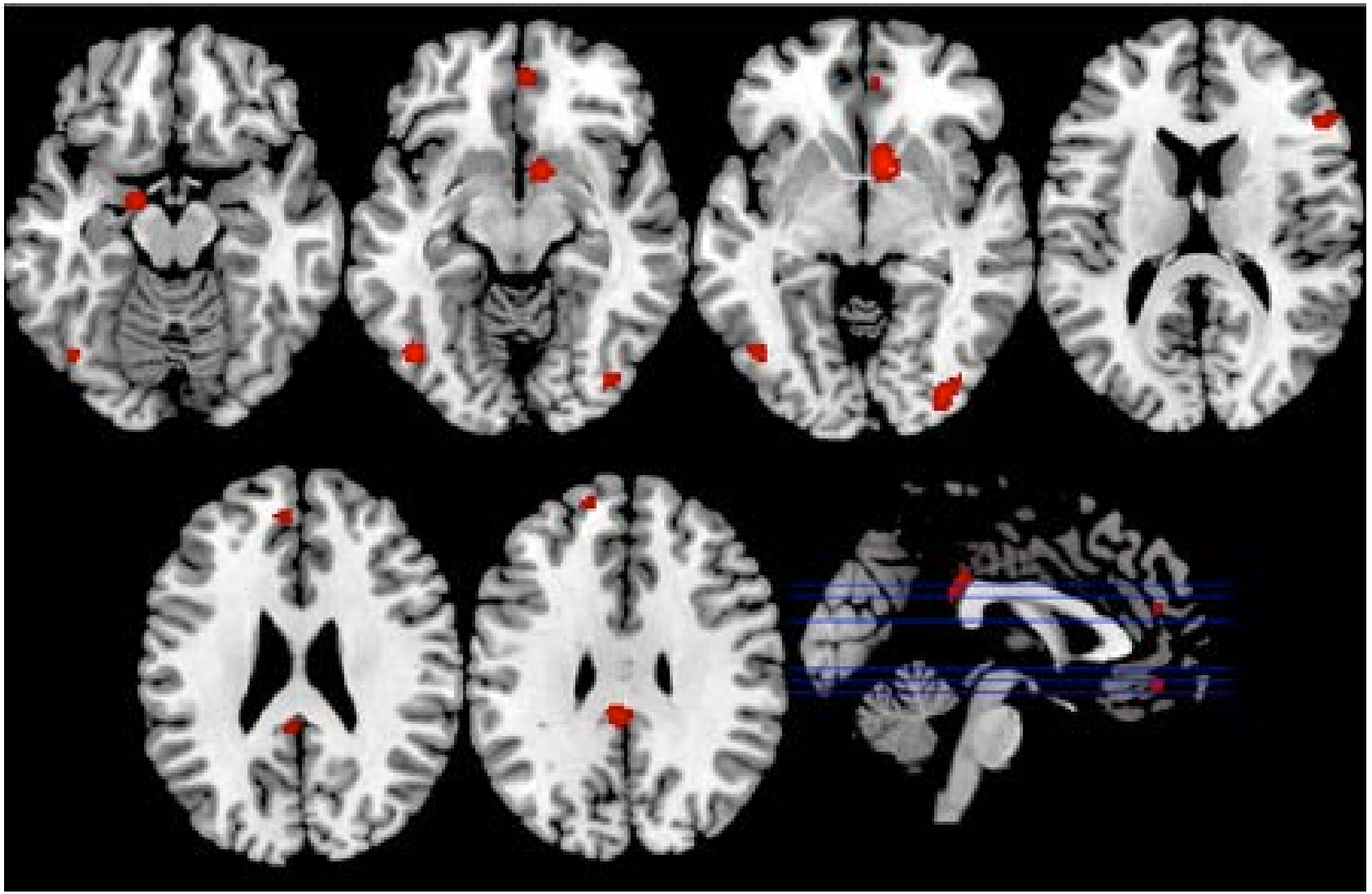

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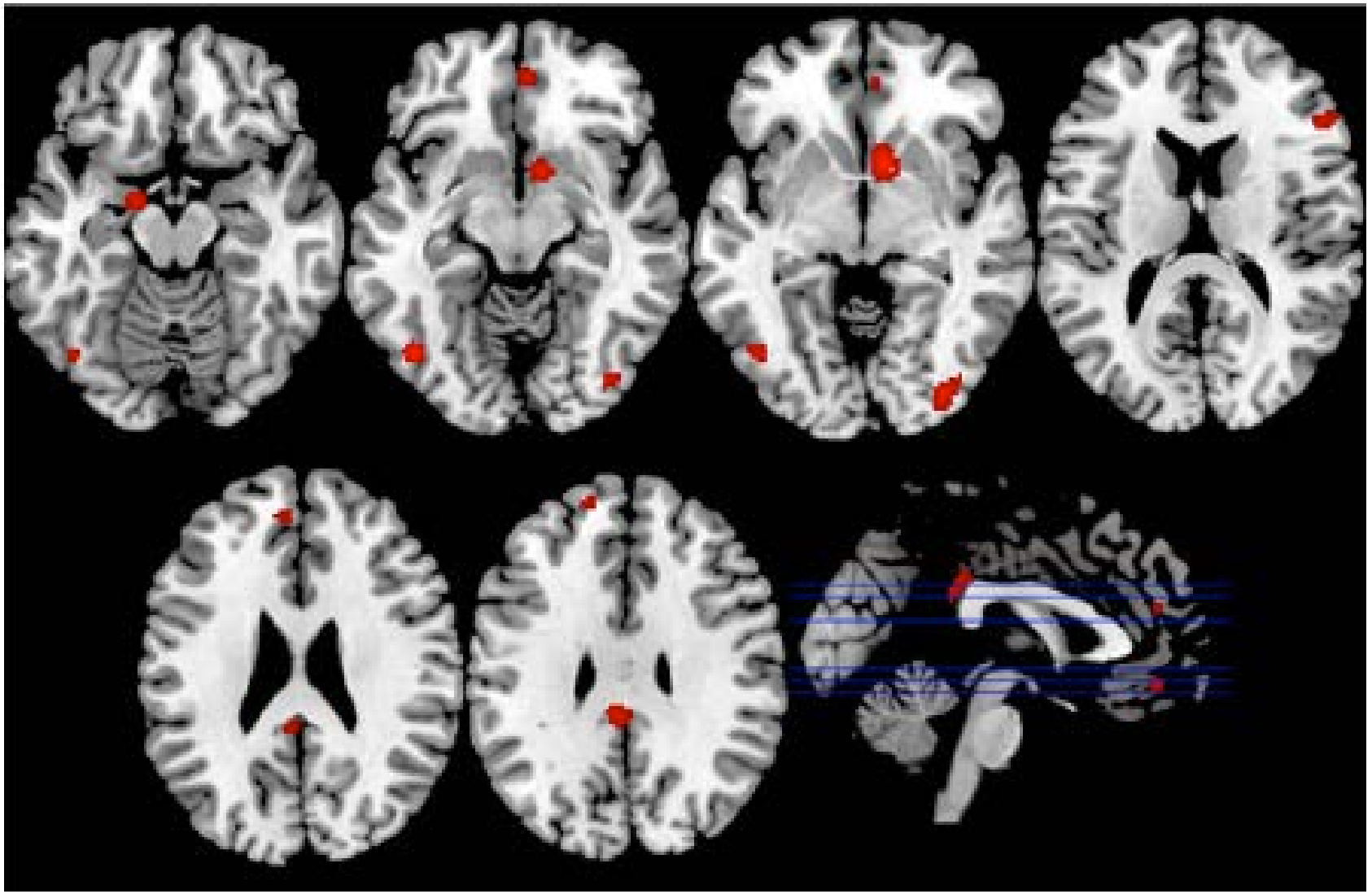
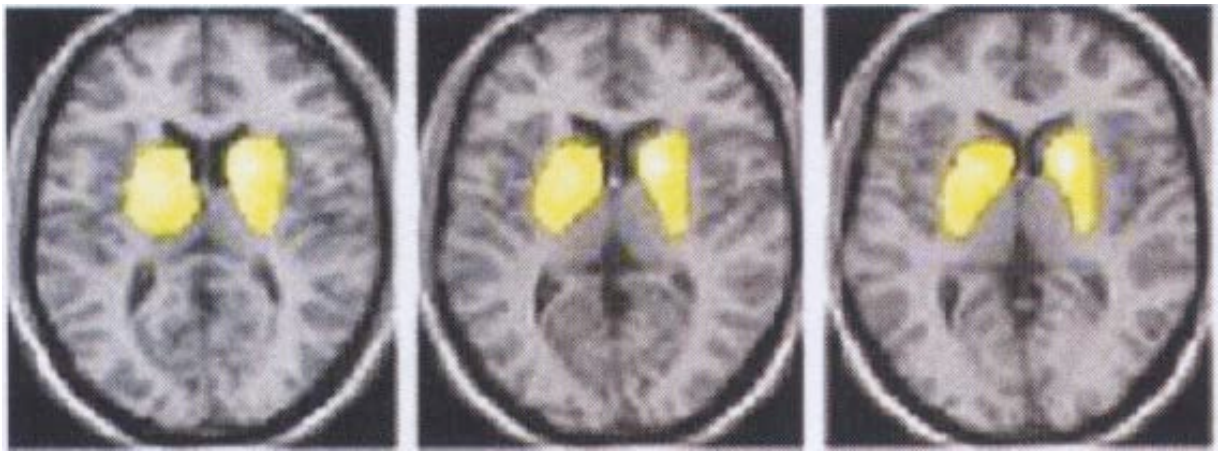


Hyperactive responses in **orbitofrontal cortex, amygdala, and ventral striatum**

Chase et al 2011 *Biol Psychiatry*

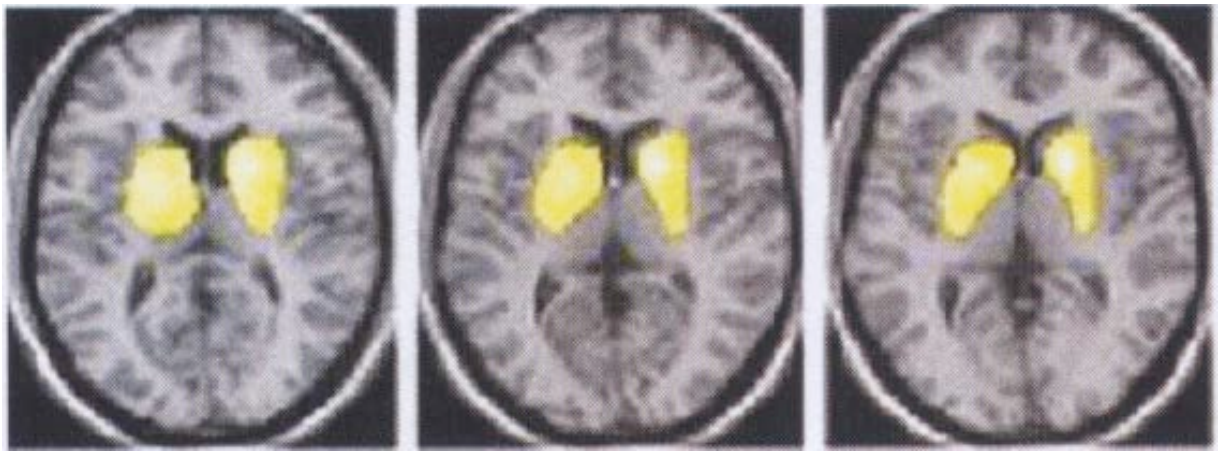
Drug Cue-Induced Striatal DA Release: Drug Dependence



Drug cue-induced DA release.

Volkow et al *J Neurosci* 2006
Wong et al *Biol Psychiatry* 2006
Fotros et al *Neuropsychopharm* 2013
Zijlstra et al *Eur Neuropsychopharm* 2008

Drug Cue-Induced Striatal DA Release: Drug Dependence



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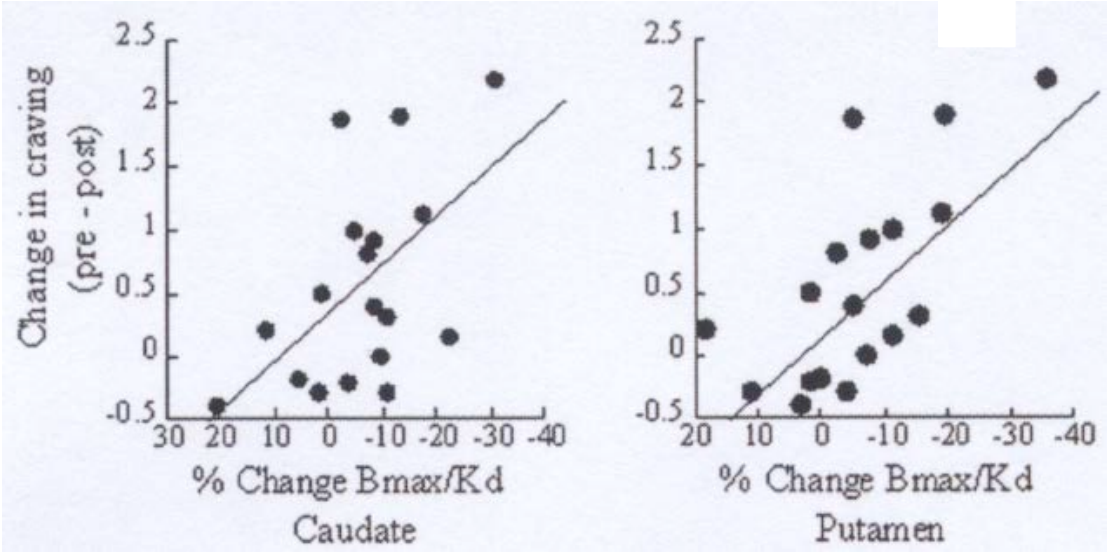

DA release co-varies with craving.

Volkow et al *J Neurosci* 2006
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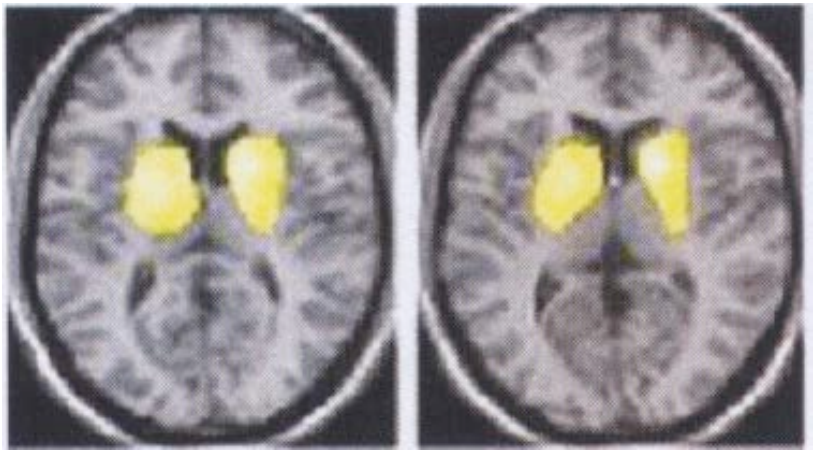
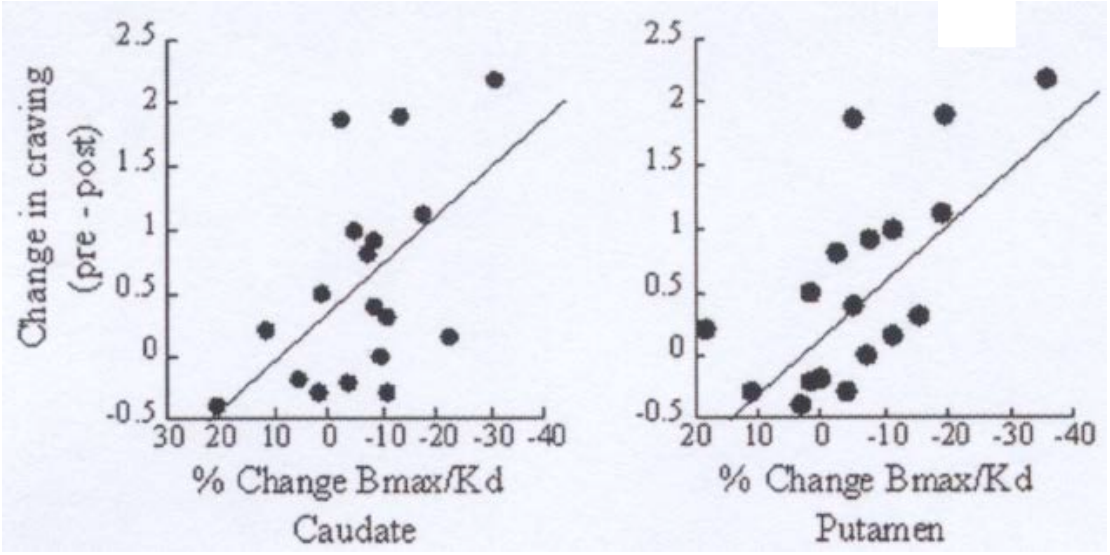


Drug Cues	DA Release	No diff
Cocaine	3 studies	0 studies
Heroin	1 study	0 studies
Total:	4	0



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Fotros et al *Neuropsychopharm* 2013
Zijlstra et al *Eur Neuropsychopharm* 2008

Substance Dependence

Low cortical activity

Substance Dependence

Low cortical activity

+

Low dopamine activity

At rest or in absence of drug cues

Substance Dependence

Low cortical activity
+
Low dopamine activity

At rest or in absence of drug cues

High cortical activity
+
High dopamine activity

In presence of drug cues

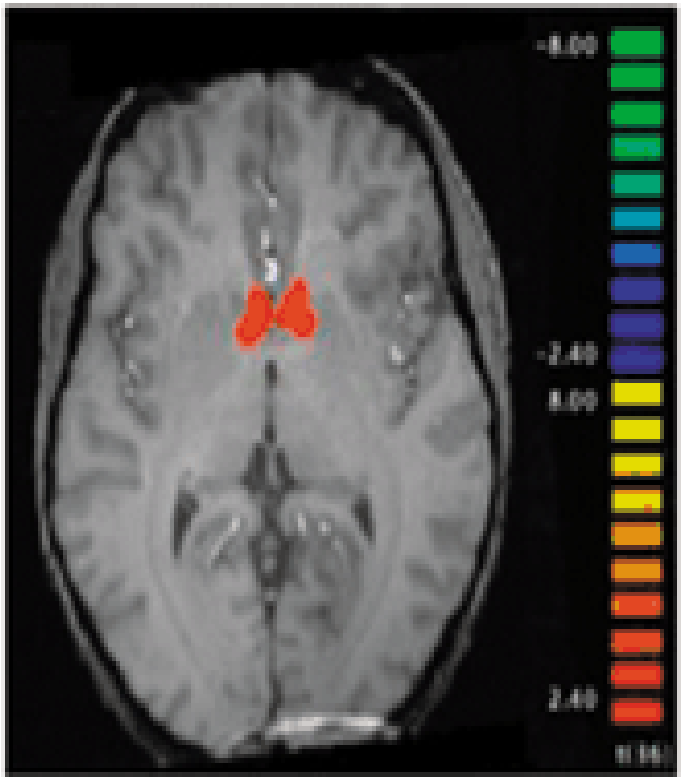
Disease Expression or Pre-Existing Traits?

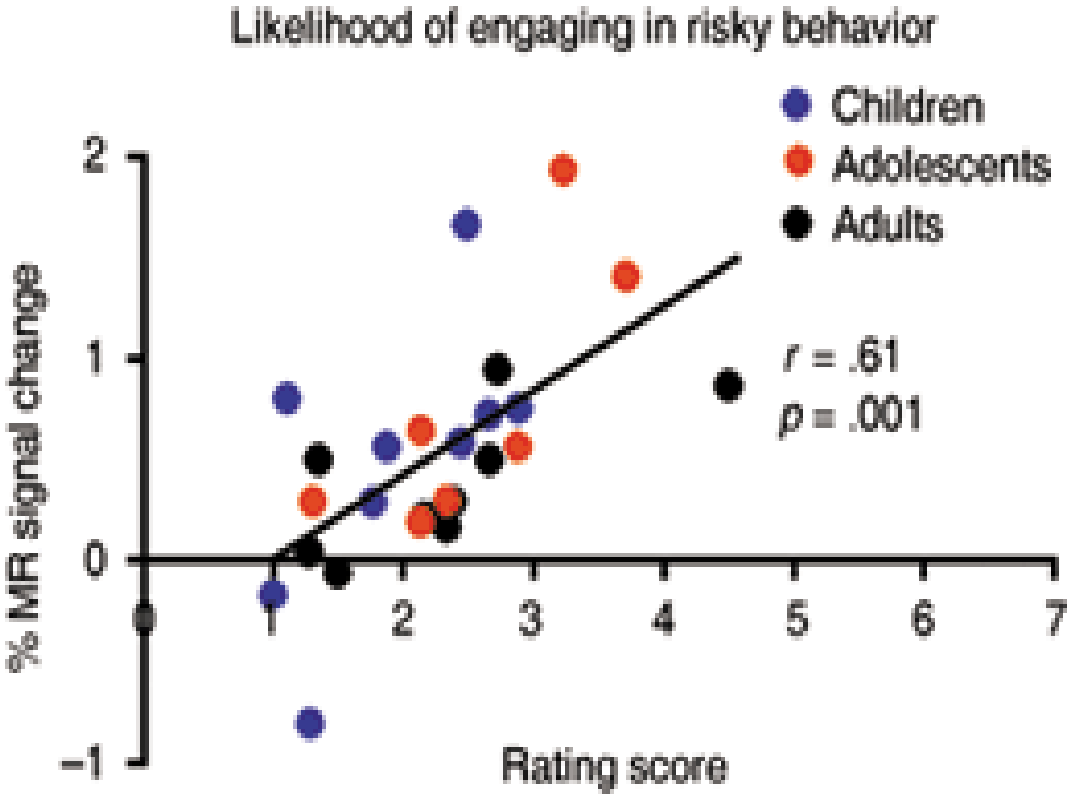
Teens Show Larger Ventral Striatum Response to Rewards

Somerville et al 2011 *J Cog Neurosci*

Happy face Go/NoGo

Larger Reward Responses in Ventral Striatum Predict More Risk-Taking

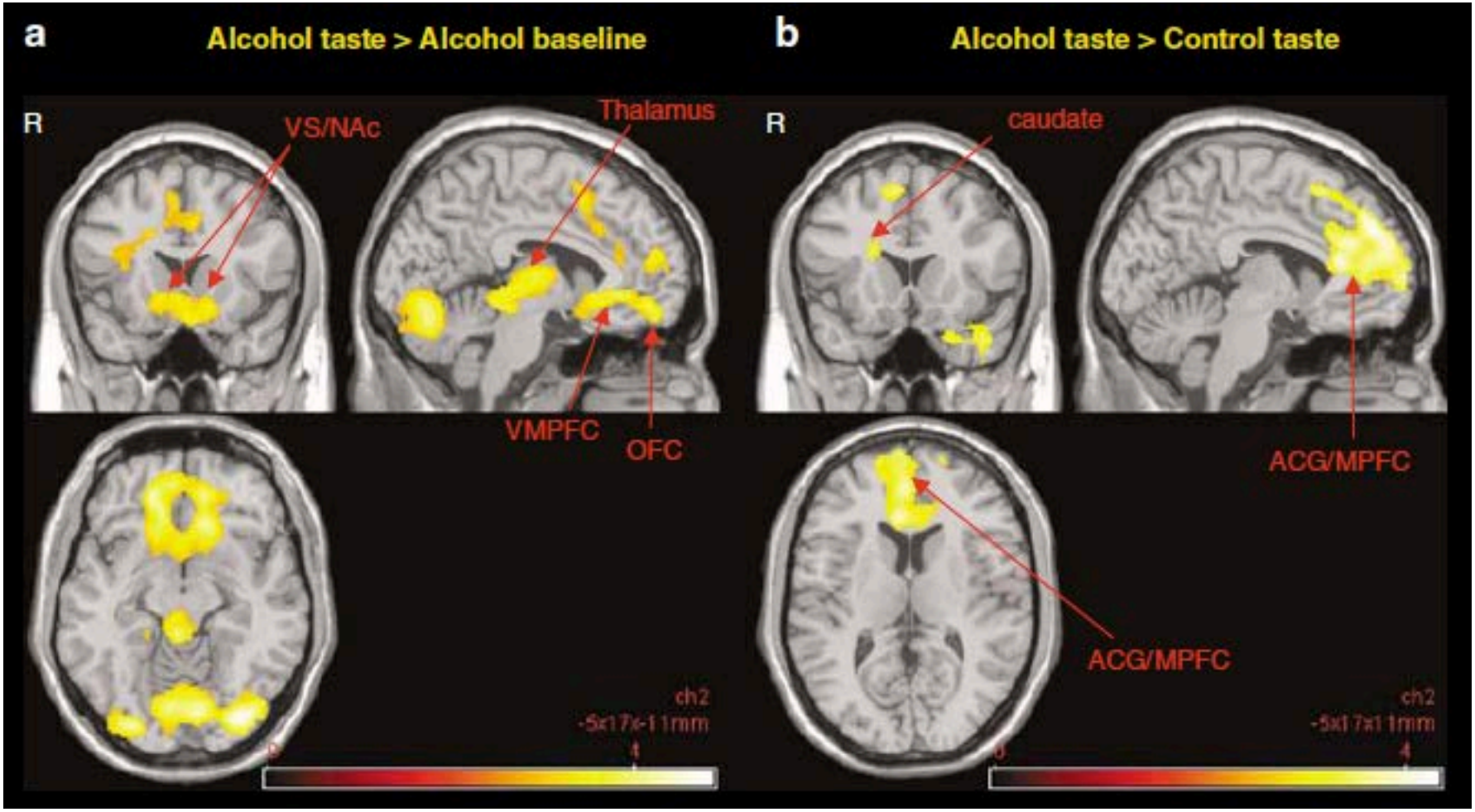




Win $

Galvan et al 2007 *Dev Sci*

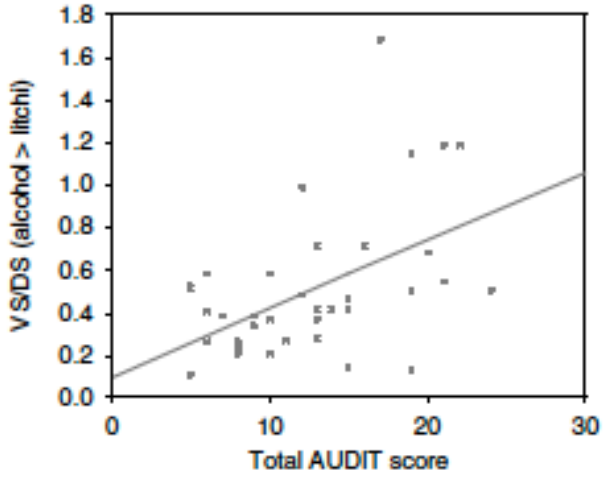
Activation Responses to Alcohol Taste

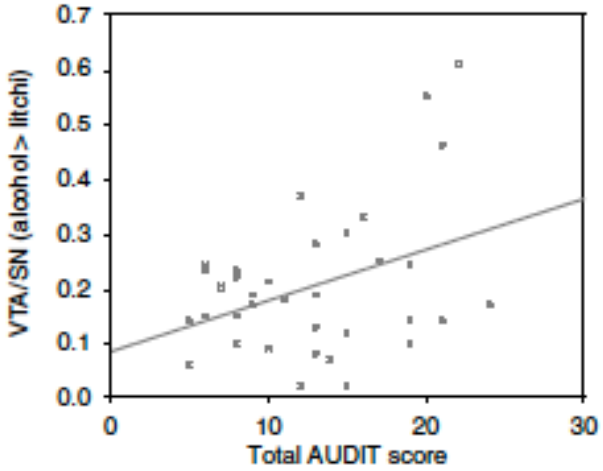


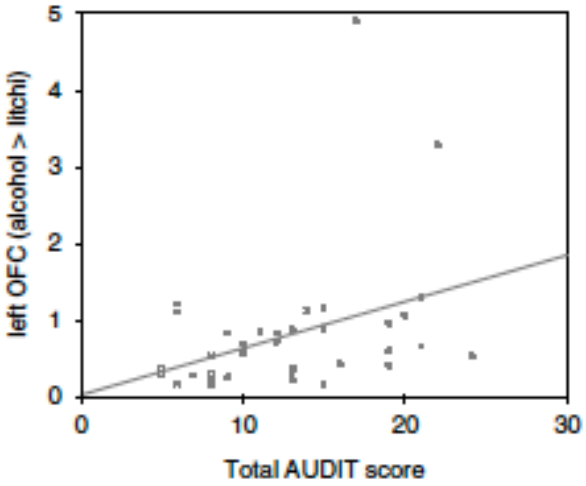
38 heavy social drinkers (15/wk)
22±2 years old

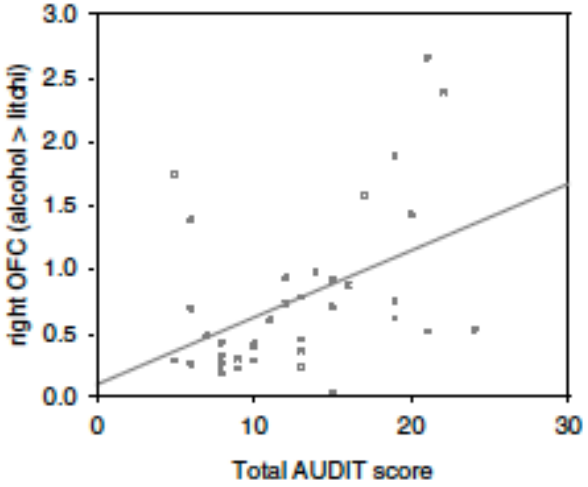
Filbey et al 2008
Neuropsychopharmacology

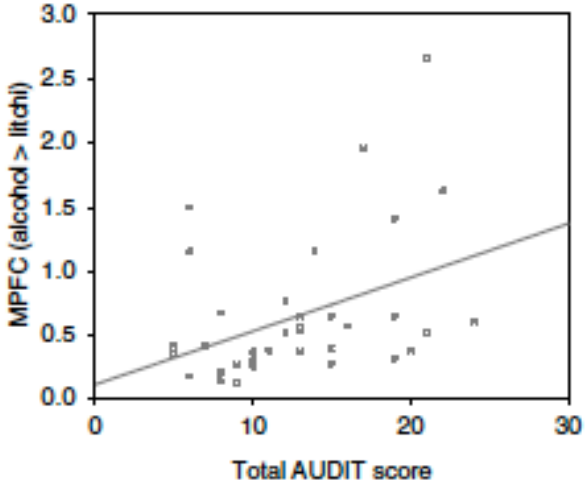
Activation Responses to Alcohol Taste Correlate with Alc Use Problems











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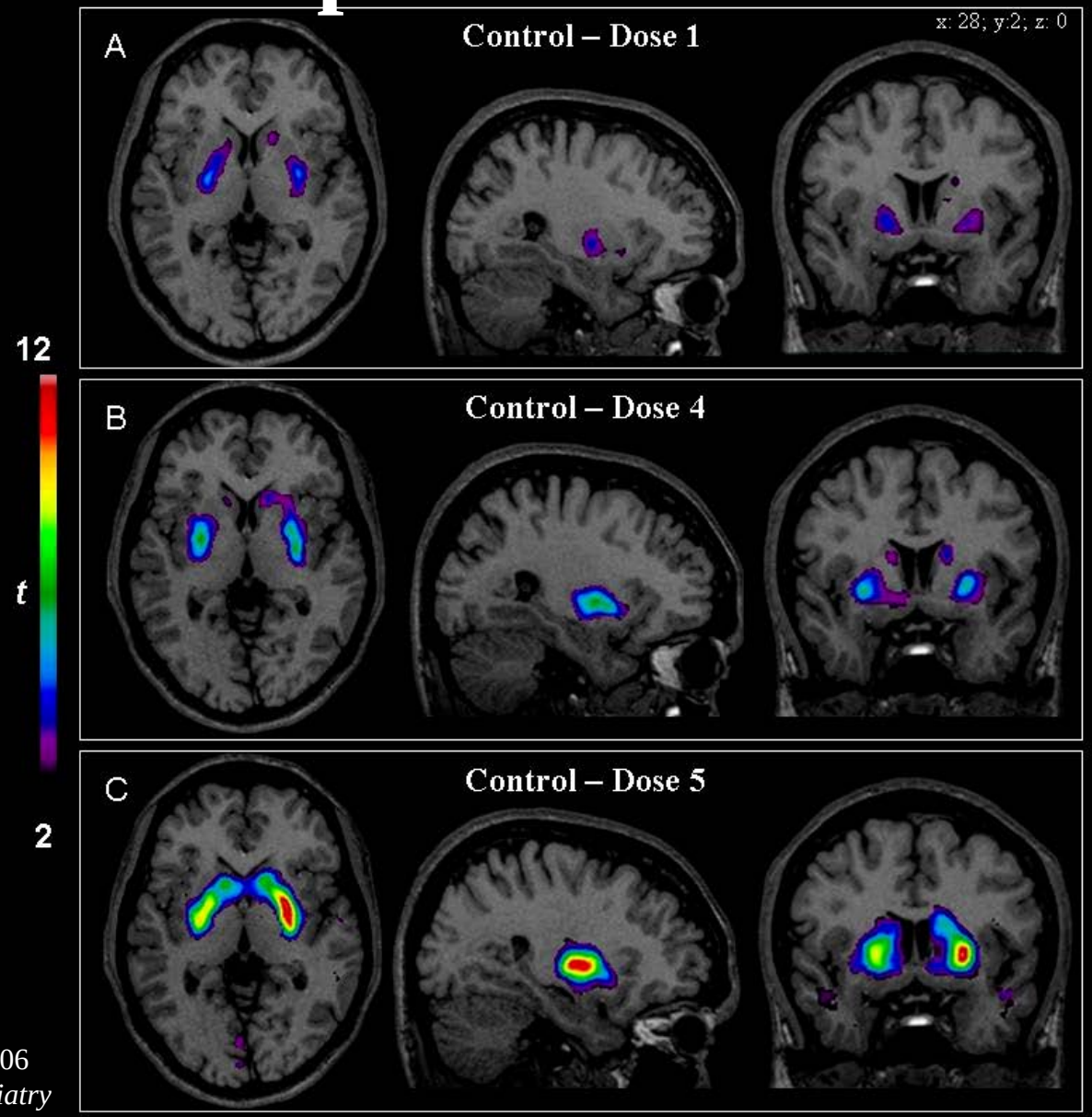
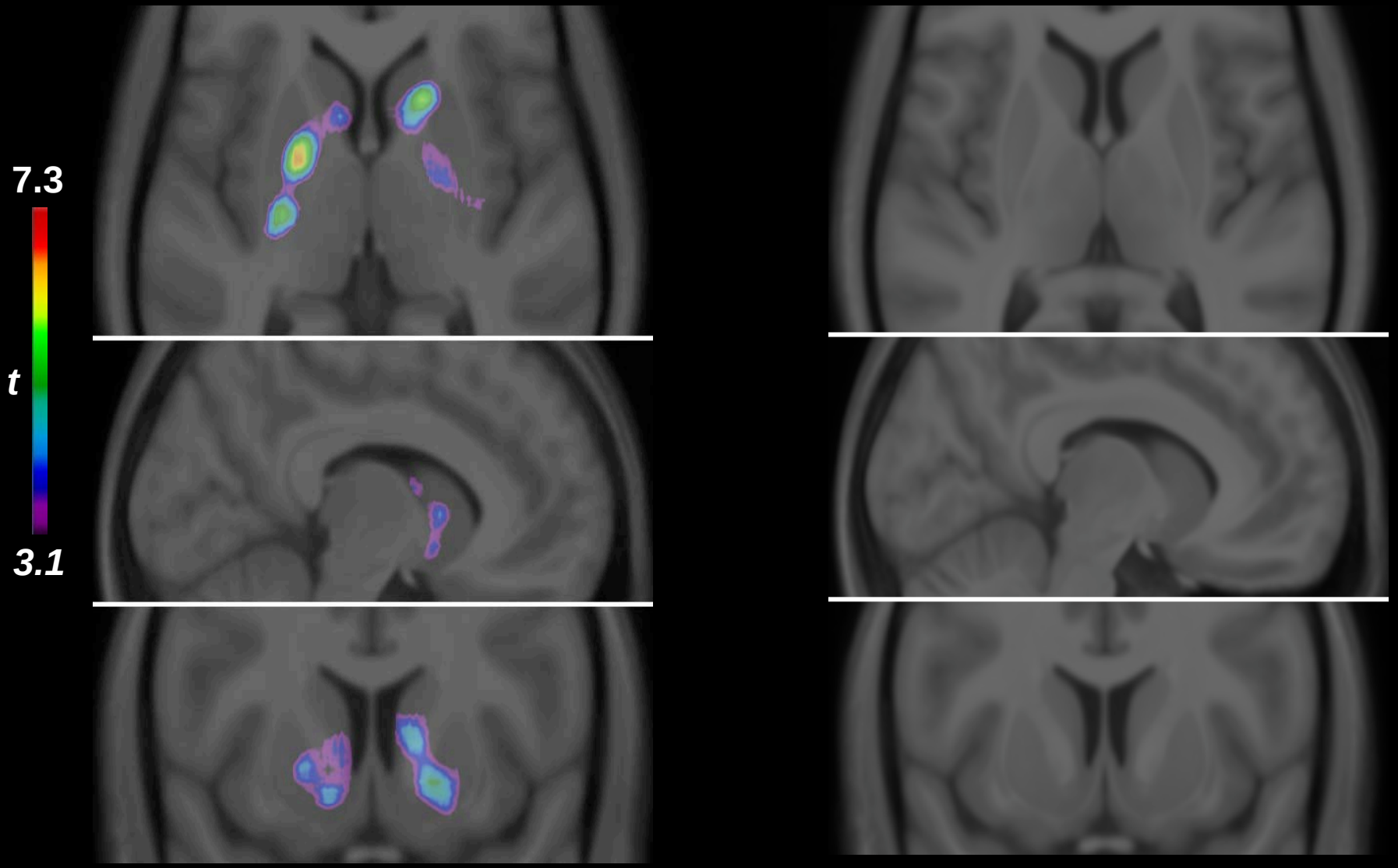
Neuropsychopharmacology

Repeat Amphetamine Administration Dopamine Sensitization



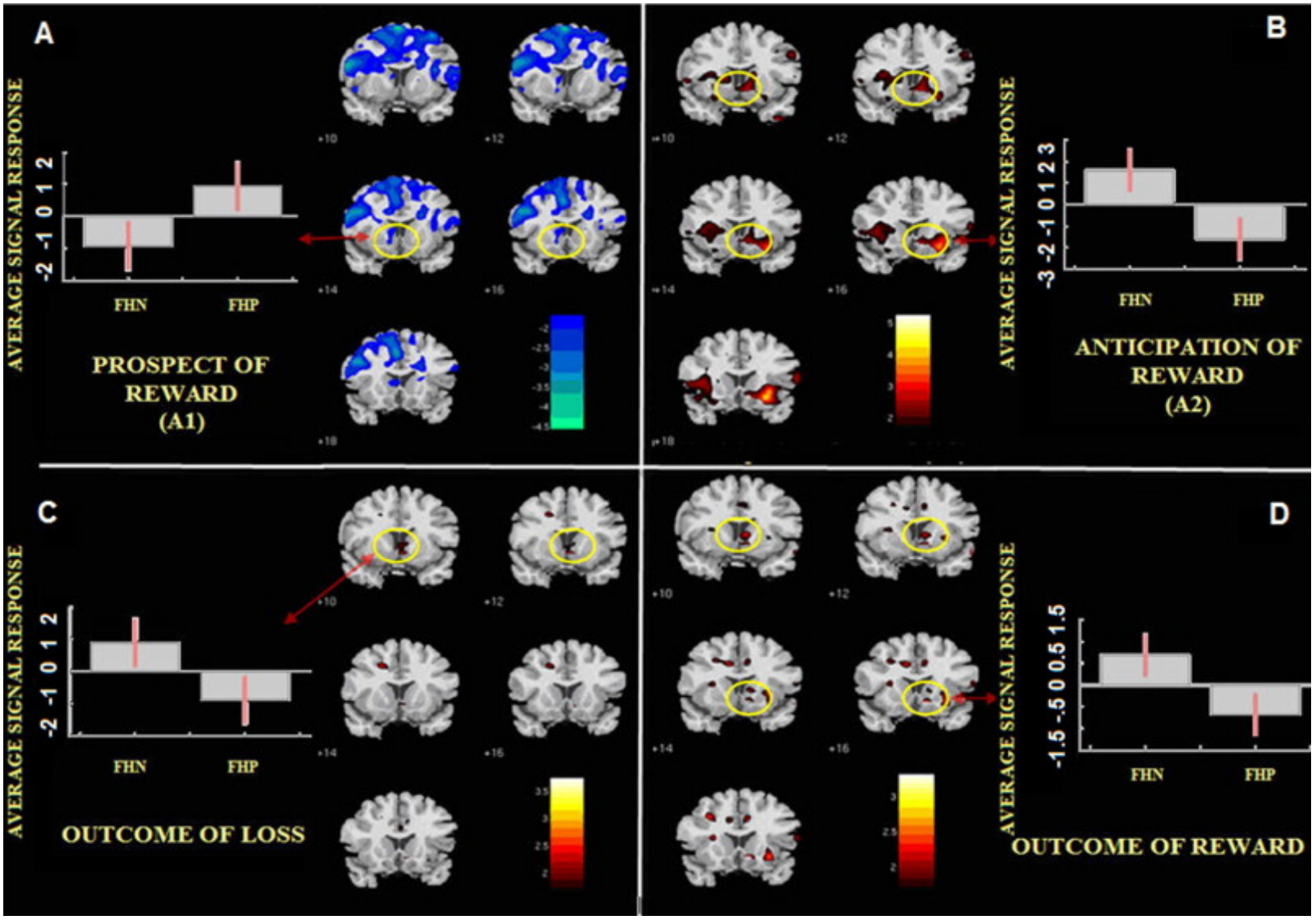
Boileau et al, 2006
Arch Gen Psychiatry

Alcohol-Induced (cues present) DA Release



Setiawan et al, *ACER*, 2013

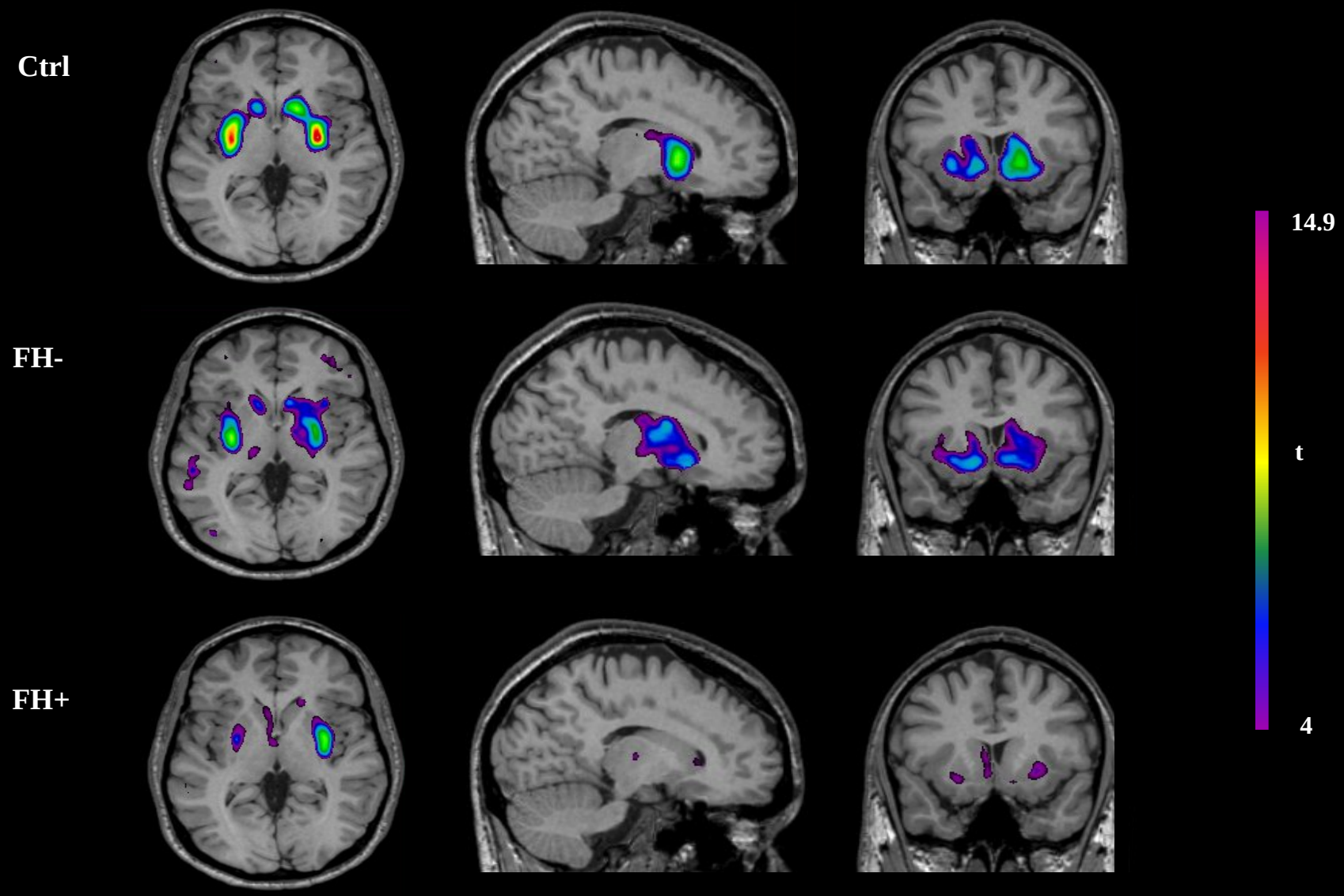
At Risk (FH+) Drug Users Decreased Response to Non-Drug Cues



MID task

Andrews et al 2011 *Biol Psychiatry*

Amphetamine (no cues) Induced Dopamine Release



Casey et al, *Biol Psychiatry*
In press

A Proposed Model of Addictions Vulnerability

Leyton *PNPBP* 2007
Leyton & Vezina *Biol Psychiatry* 2012
Leyton & Vezina *NBR* 2013

A Proposed Model of Addictions Vulnerability

Step 1: Before drug use starts, (most) high-risk subjects have increased reward circuit responses to many rewards.

Leyton *PNPBP* 2007
Leyton & Vezina *Biol Psychiatry* 2012
Leyton & Vezina *NBR* 2013

A Proposed Model of Addictions Vulnerability

Step 1: Before drug use starts, (most) high-risk subjects have increased

Step 2: Once drug use starts, reward circuit activation can become tied to drug related cues.

Leyton *PNPBP* 2007
Leyton & Vezina *Biol Psychiatry* 2012
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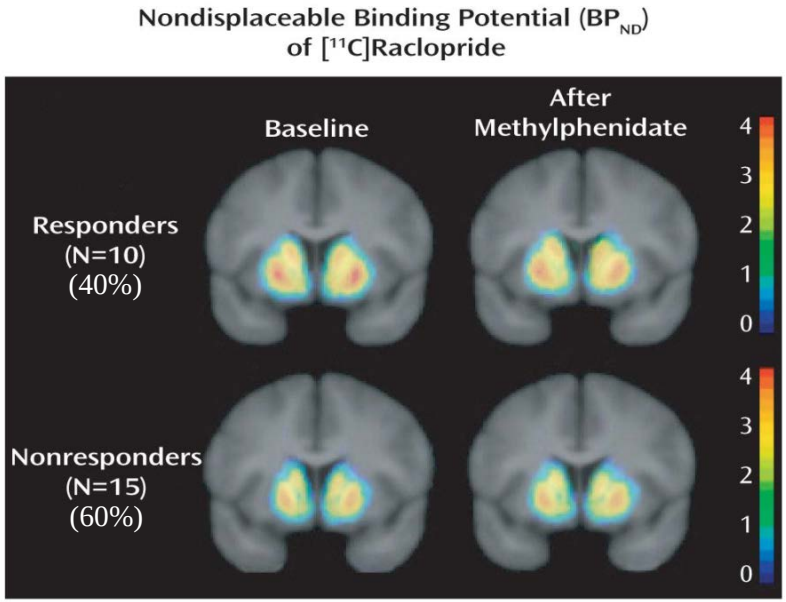
Implications for Treatment?

Low DA: Non-response to Behavioral Treatment
Normal DA: Respond to Behavioral Treatment



Martinez et al 2011 *Am J Psychiatry*
Wang et al 2012 *Mol Psychiatry*

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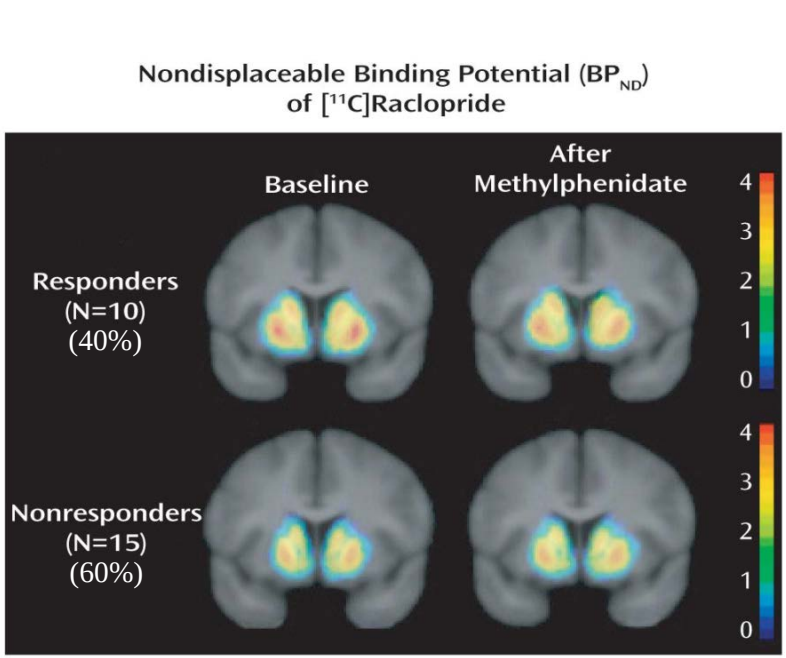

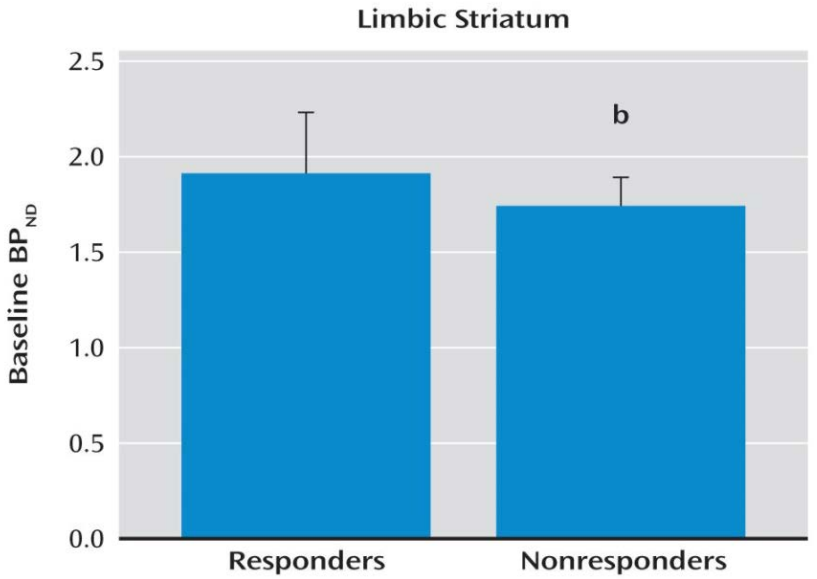

Martinez et al 2011 *Am J Psychiatry*
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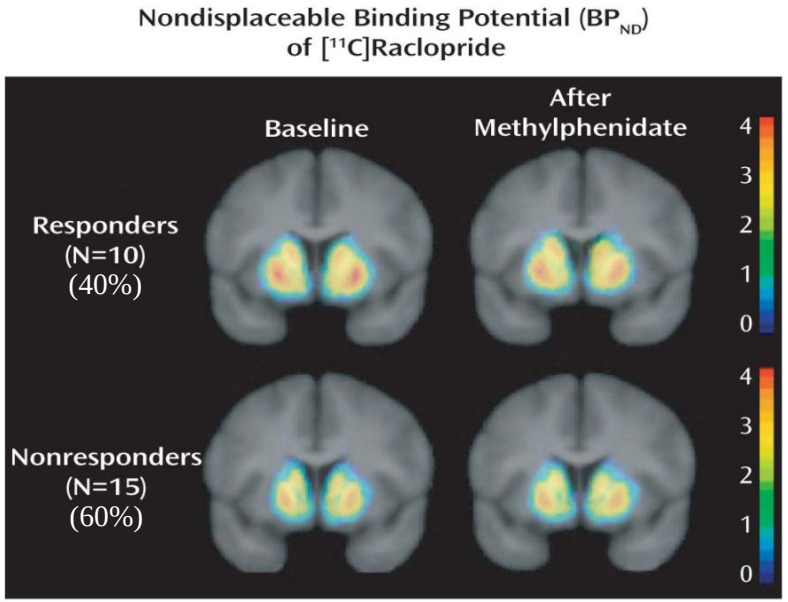

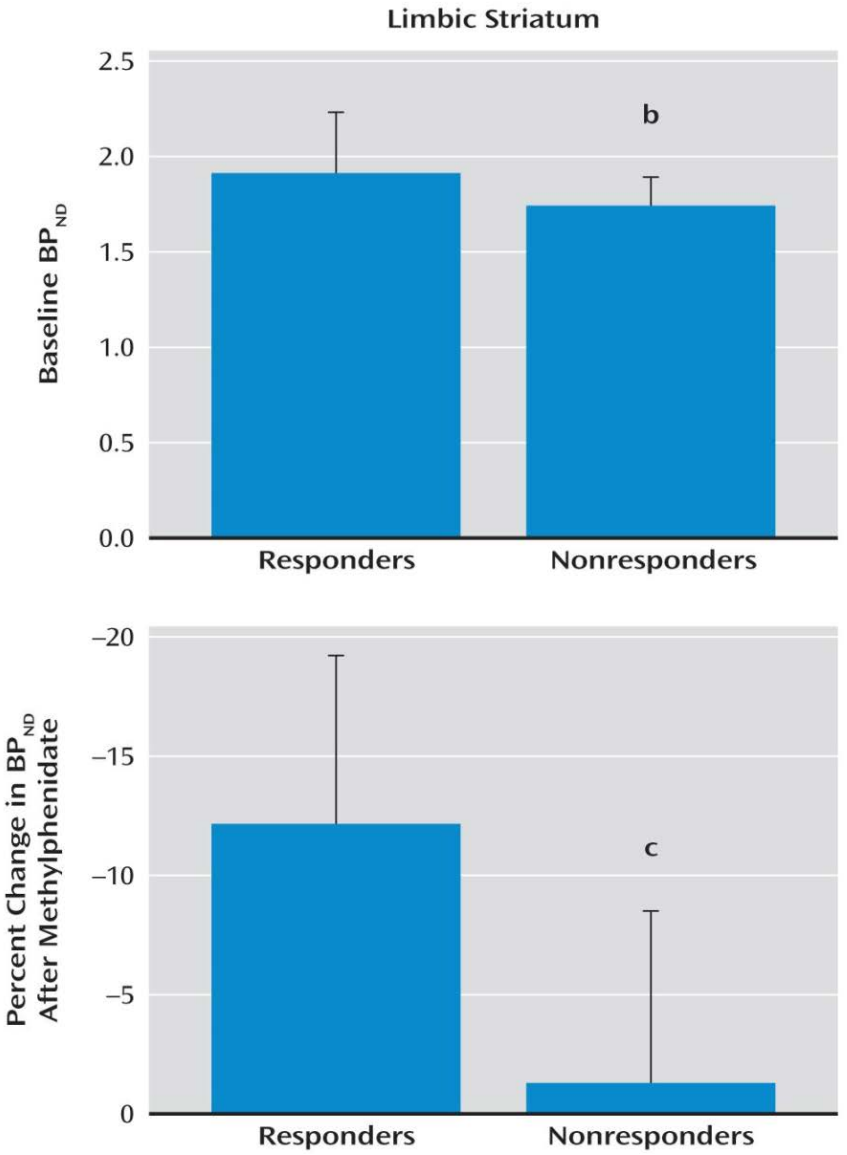

Martinez et al 2011 *Am J Psychiatry*
Wang et al 2012 *Mol Psychiatry*

Summary & Speculative Integration

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1. Before drug use starts (most) high-risk subjects have increased reward circuit responses to many rewards, influencing risk-taking.

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1. Before drug use starts (most) high-risk subjects have increased reward circuit responses to many rewards, influencing risk-taking.

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4. Those who retain the ability to activate their dopamine / reward system circuitry in the absence of drug cues can more easily develop new behaviors, and respond well to behavioral (CMT) therapies.

5. Those who lose the ability to activate their dopamine / reward system circuitry in the absence of drug cues might require other / additional treatments.