FMRI and Treatment Development for Addictions

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Disclosures

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- Research Gift from Mohegan Sun
- Consultant to Legal and Gambling Entities on Issues Related to Impulse Control Disorders

Changing Perspectives on Addiction

2001

Aided by brain imaging advances, scientists are looking for evidence that compulsive nondrug behaviors lead to long-term changes in reward circuitry

'Behavioral' Addictions: Do They Exist?

ADDICTION

The concept of addiction is changing, as this special news package describes: There's more emphasis on how drugs and even behaviors may wreak long-term damage to the brain.

COMPULSIVE BEHAVIORS

LONG-TERM CHANGES

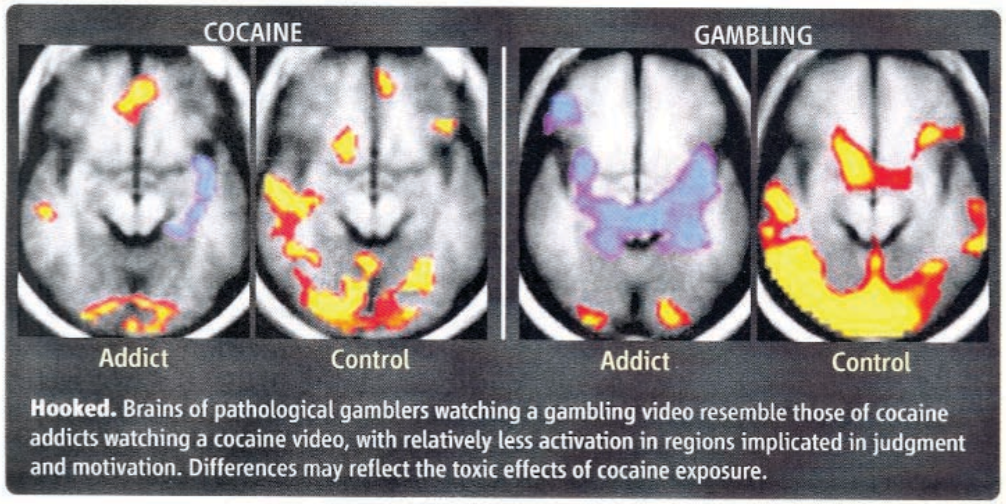
Verona, Nov 13, 2012

2010

Shared brain vulnerabilities open the way for nonsubstance addictions: Carving addiction at a new joint?

Joseph Frascella,[1] Marc N. Potenza,[2] Lucy L. Brown,[3] and Anna Rose Childress[4,5]

Behavioral Addictions Debut in Proposed *DSM-V*

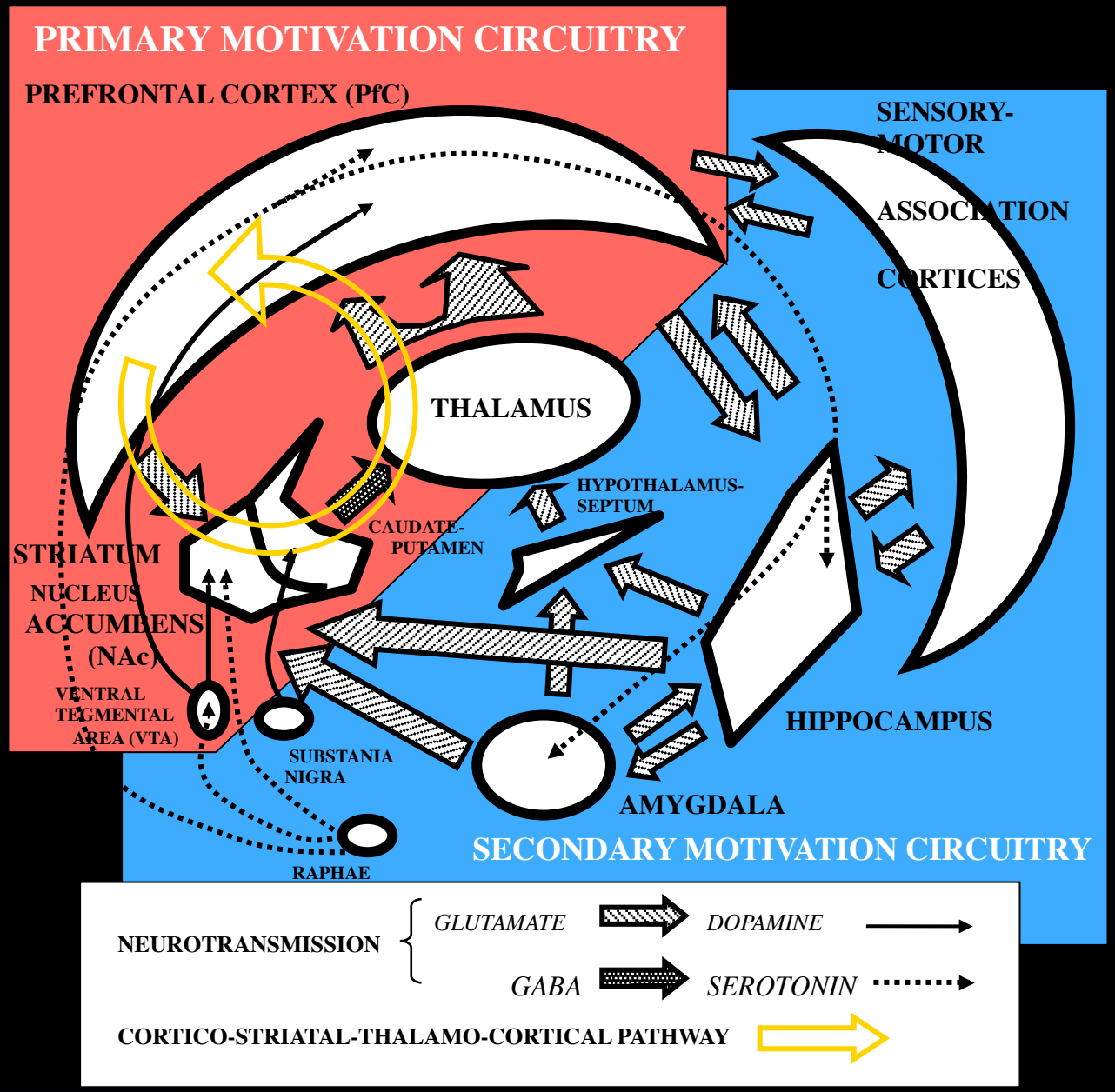


Hooked. Brains of pathological gamblers watching a gambling video resemble those of cocaine addicts watching a cocaine video, with relatively less activation in regions implicated in judgment and motivation. Differences may reflect the toxic effects of cocaine exposure.

Holden, Science, 2001, 2010; Frascella et al, Ann NY Acad Sci, 2010

Addiction as a Disorder of Misdirected Motivation

- In Addiction, Priority is Given to Specific Motivated Behaviors (e.g., Drug Use) That Are Associated with Immediate or Short-Term Reward
- Less Priority is Given to Other Motivated Behaviors (e.g., Occupational or Familial) That Are Arguably Less Associated with Immediate Reward
- Understanding the Neurobiology Underlying Motivated Behaviors and How the Biology May Go Awry in Addiction Should Help Develop More Effective Approaches for Addiction Treatment



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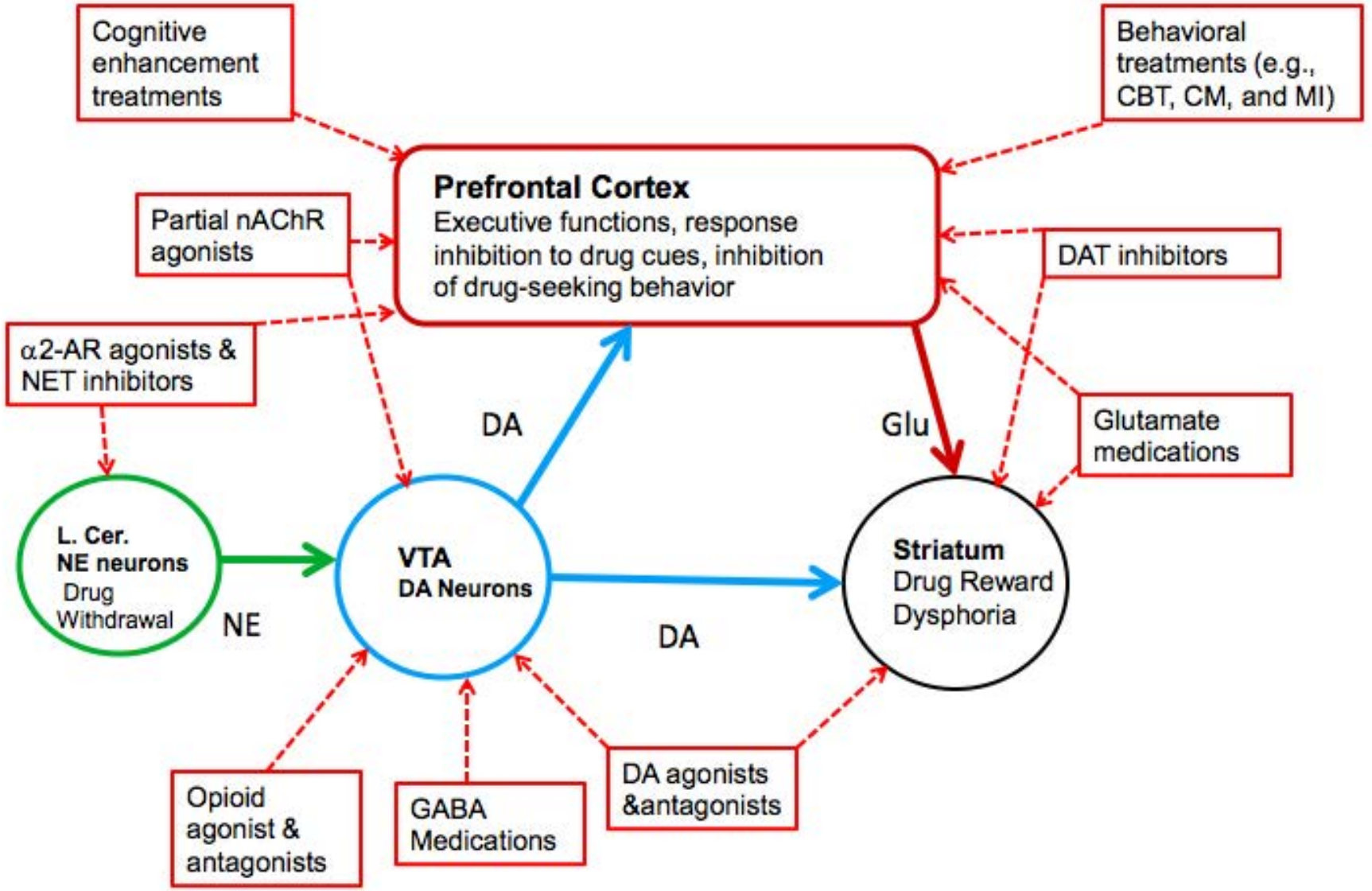
Chambers, Taylor & Potenza, Am J Psychiatry, 2003

Targets of Behavioral and Pharmacological Treatments for Addictions



Potenza, Sofuoglu, et al 2011

Verona, 2012

Intermediary Phenotypes in Addictions

- Common Elements (e.g., Impulsivity, Compulsivity, Other Aspects of Self-Control) May Be Shared Among Groups of Individuals with Addictions
- These Features May Represent Intermediary Phenotypes or Endophenotypes that More Closely Align with Clinical Measures Than Do Heterogeneous Diagnostic Categories
- Identifying Clinically Relevant Intermediary Phenotypes Has Significant Potential in Treatment Development and Matching

Impulsivity and Compulsivity in Addictions

- Impulsivity and Compulsivity Have Both Been Found to Be Elevated in Behavioral and Drug Addictions (Tavares et al, 2007; deWit and Potenza, 2010)
- Self-Report and Behavioral Measures of Impulsivity and Compulsivity Have Been Linked to Tx Outcomes in Addictions (Blanco et al, 2009; Grant et al, 2010)
- Identifying Tx-Relevant Neural Correlates of These Intermediary Phenotypes (Ones that Can Be Readily Assessed in Clinical Settings) May Help in Tx Development and Tx Matching

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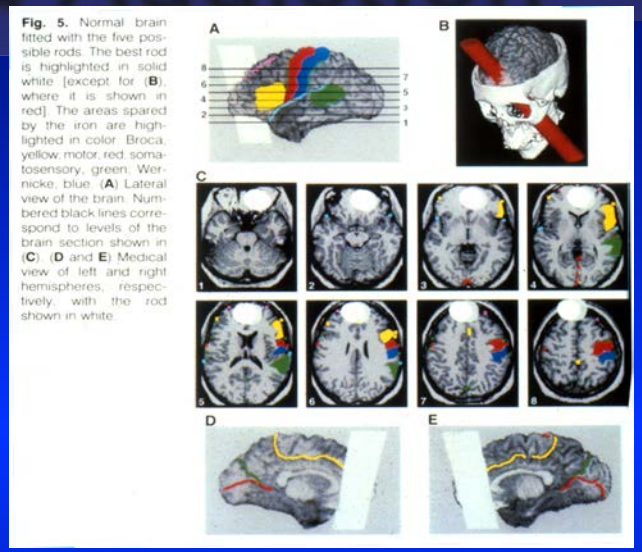
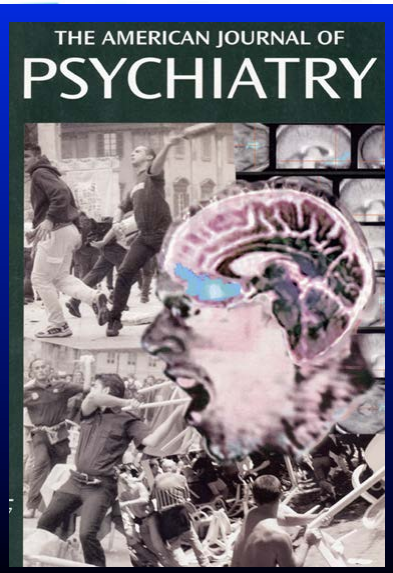
Risk/Reward Decision-Making, Reward Processing & Addiction

- Subjects with PG or SUDs Perform Disadvantageously on Gambling Tasks (Petry et al, 2001; Bechara, 2003)
- Rapid Discounting of Rewards (Bickel et al, 1999; Petry et al, 2001)
- Given Links with Treatment Outcome (Krishnan-Sarin et al 2007), it is Important to Understand Neurobiological Factors Underlying These Processes in Addiction





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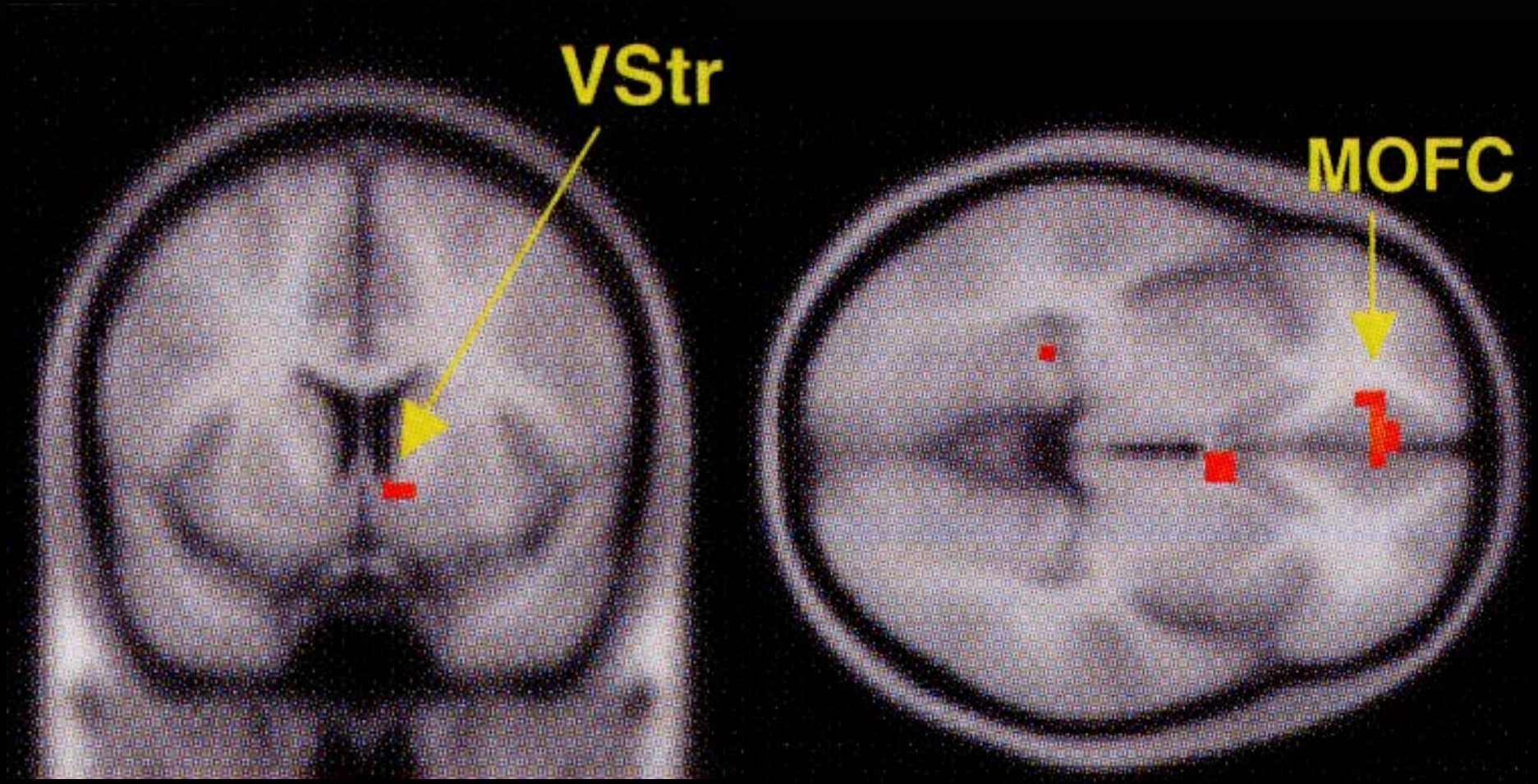
Small, Immediate Rewards Preferentially Activate Ventral Striatum and vmPFC



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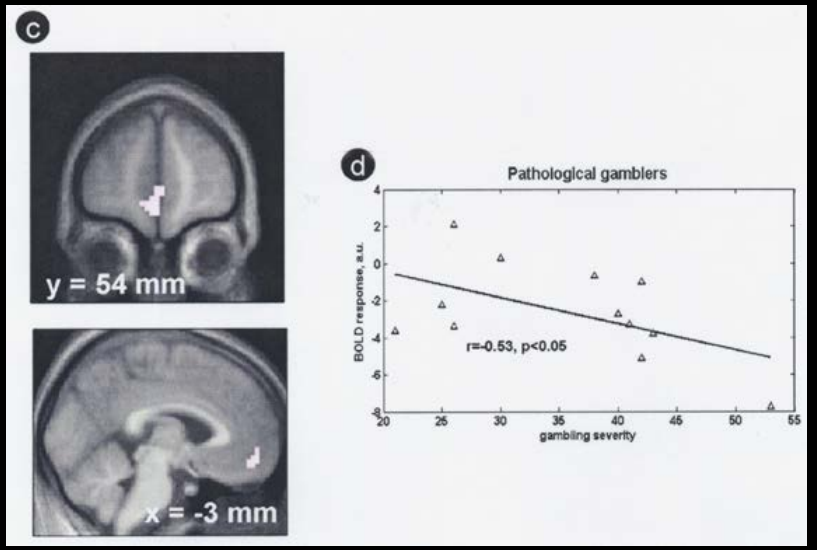
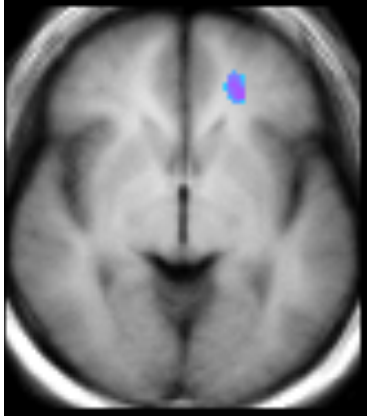
McClure et al, 2004

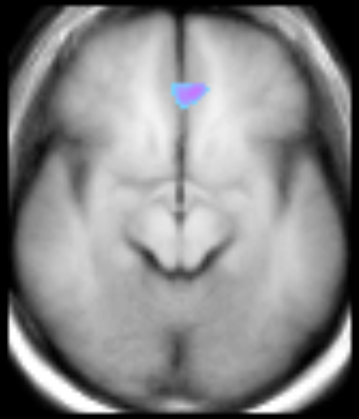
vmPFC, PG and SUDs



Simulated Gambling
Reuter et al, 2005, *Nat Neurosci*

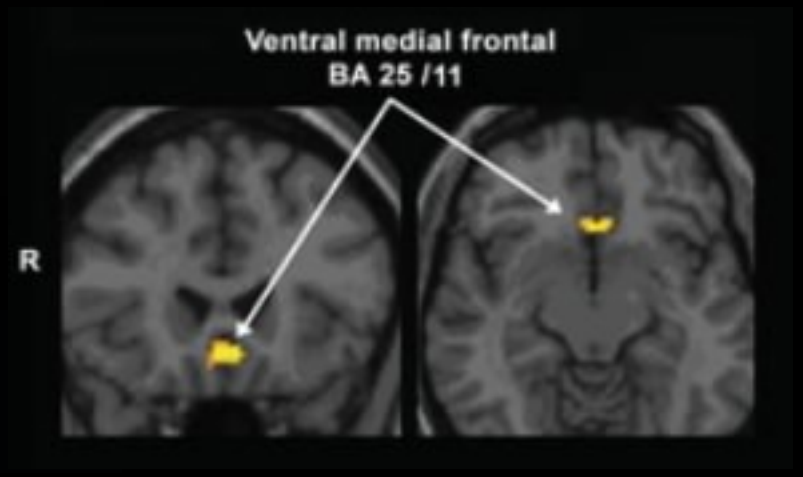


Stroop
PG - Control
(Potenza et al, 2003, *Am J Psychiatry*)



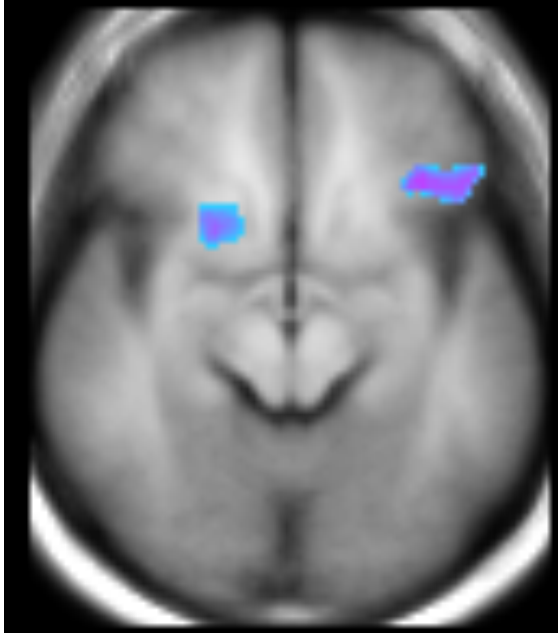
Gambling
Tape
PG-Control
(Potenza et al, 2003, *Arch Gen Psychiatry*)

Reward OC
PG-Control
(Balodis et al, 2012, *Biol Psych*)

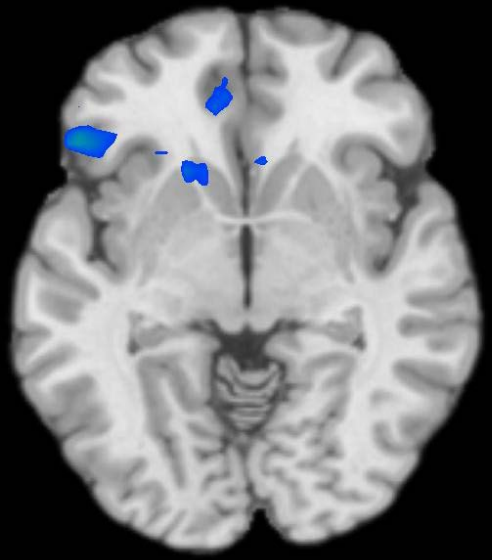


Controls > SUD/PG in vmPFC on IGT
Tanabe et al, 2007, *Hum Brain Mapp*

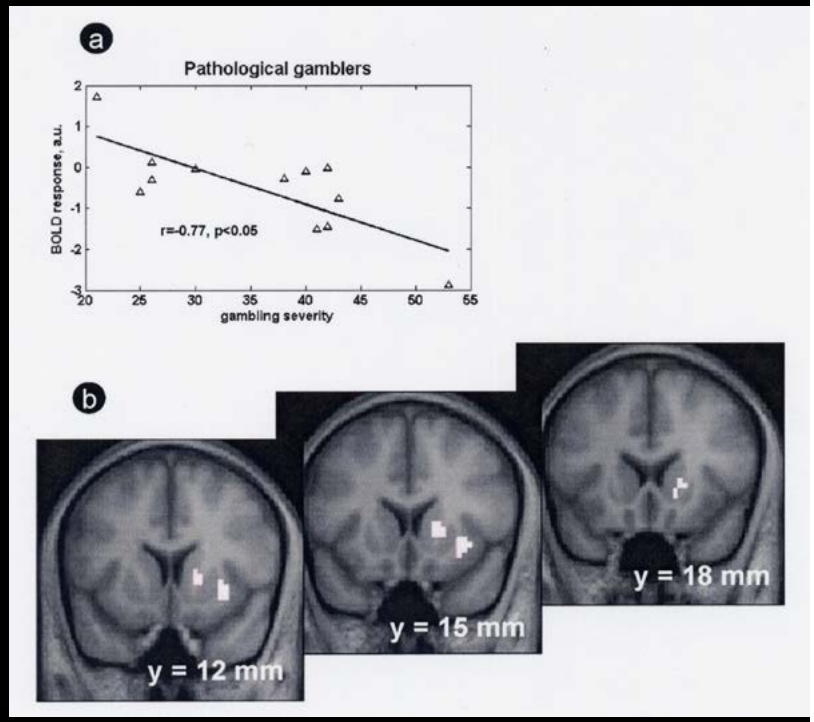
Less Ventral Striatal Activation in PG



Addiction Tapes
(PG-C_{PG})+(CD-C_{CD})
(Potenza, 2008)



Reward Anticipation
PG-Control
(Balodis et al,
2012)



Simulated Gambling
(Reuter et al, 2005)

Reward Processing in Addiction

- Adults w/ AD vs Those w/o AD Show Less Activation of VS in Anticipation of Working for Monetary Reward (Hommer et al, 2004; Wrase et al, 2007)
- Similar Findings in Adolescents and Adults FH+ Vs. FH- for AD and Adolescent Smokers (Hommer et al, 2004; Bjork et al, 2008; Andrews et al, 2011; Peters et al 2011)
- In AD and PG, Diminished VS Activation Correlates with Impulsivity (Back et al, 2009; Balodis et al, 2012) and Measures of Addiction Severity in PG and ND (Reuter et al, 2005; Peters et al, 2011)

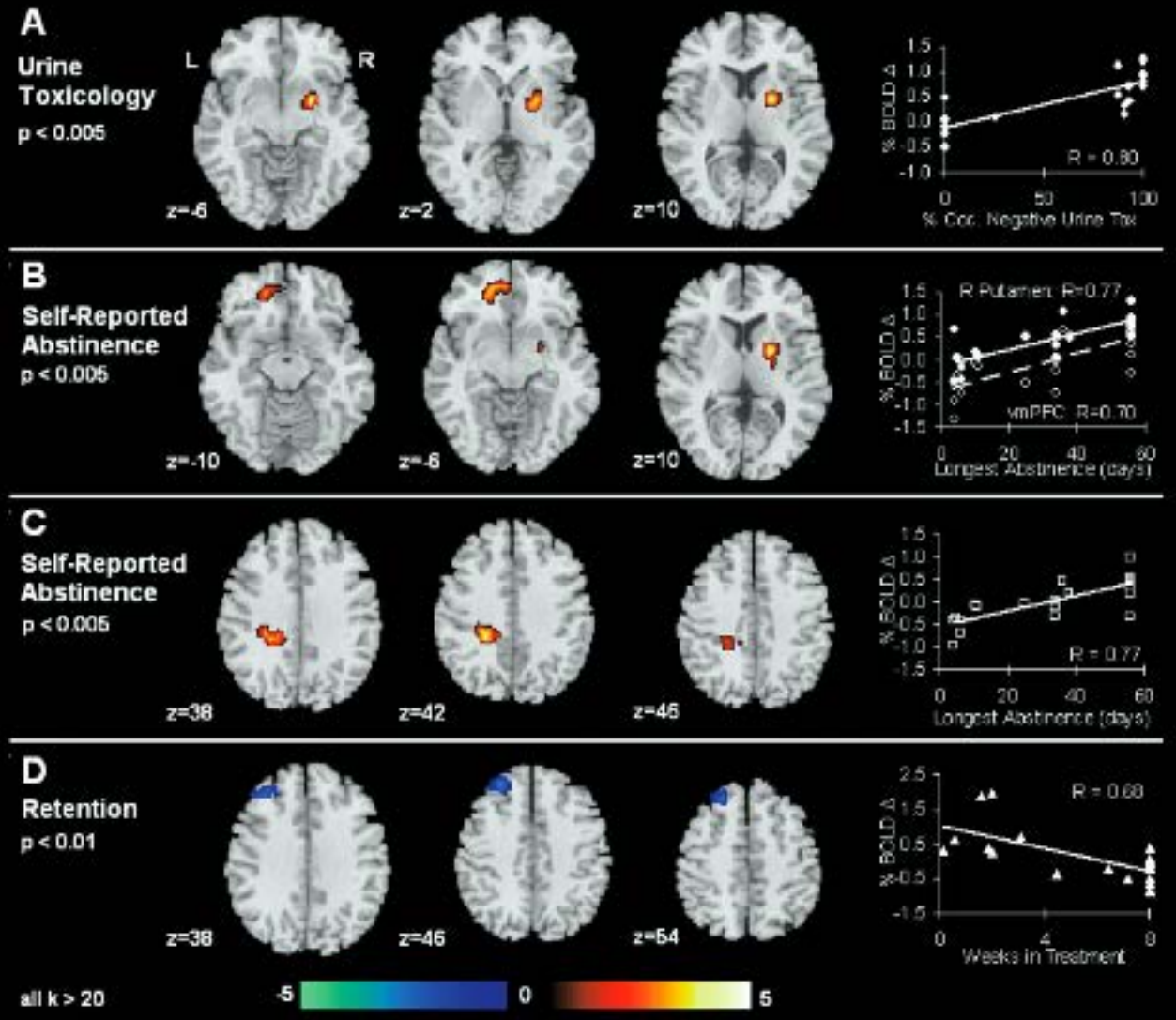
Integrating MRI Into RCTs

- A Recent Major Effort of Our Group Has Been to Investigate the Neural Predictors and Correlates of Therapies for Addictions
- Investigations Have Significant Potential for Understanding How Therapies Work and For Whom They May Work Best
- Our Approach Has Involved Incorporating fMRI Tasks that are: 1) Associated with Neural Circuitry Underlying Motivated Behaviors (Assessing Reward Processing (Drive), Cognitive Control); and 2) Theoretically Linked to the Proposed Mechanisms of Actions of the Therapies

Behavioral Therapies in Addiction

- Behavioral Therapies for Drug Addiction Are Efficacious and Widely Used (Carroll et al, 2008)
- Despite Their Widespread Use, Little is Known Regarding Brain Changes Associated with Treatment Outcomes in Behavioral Treatments for Addictions
- Specific Treatments May Demonstrate Efficacy Through Changes in Different Brain Circuits
- Specific Aspects of Outcome (Retention vs. Abstinence) May Differentially Relate to Specific Aspects of Brain Function

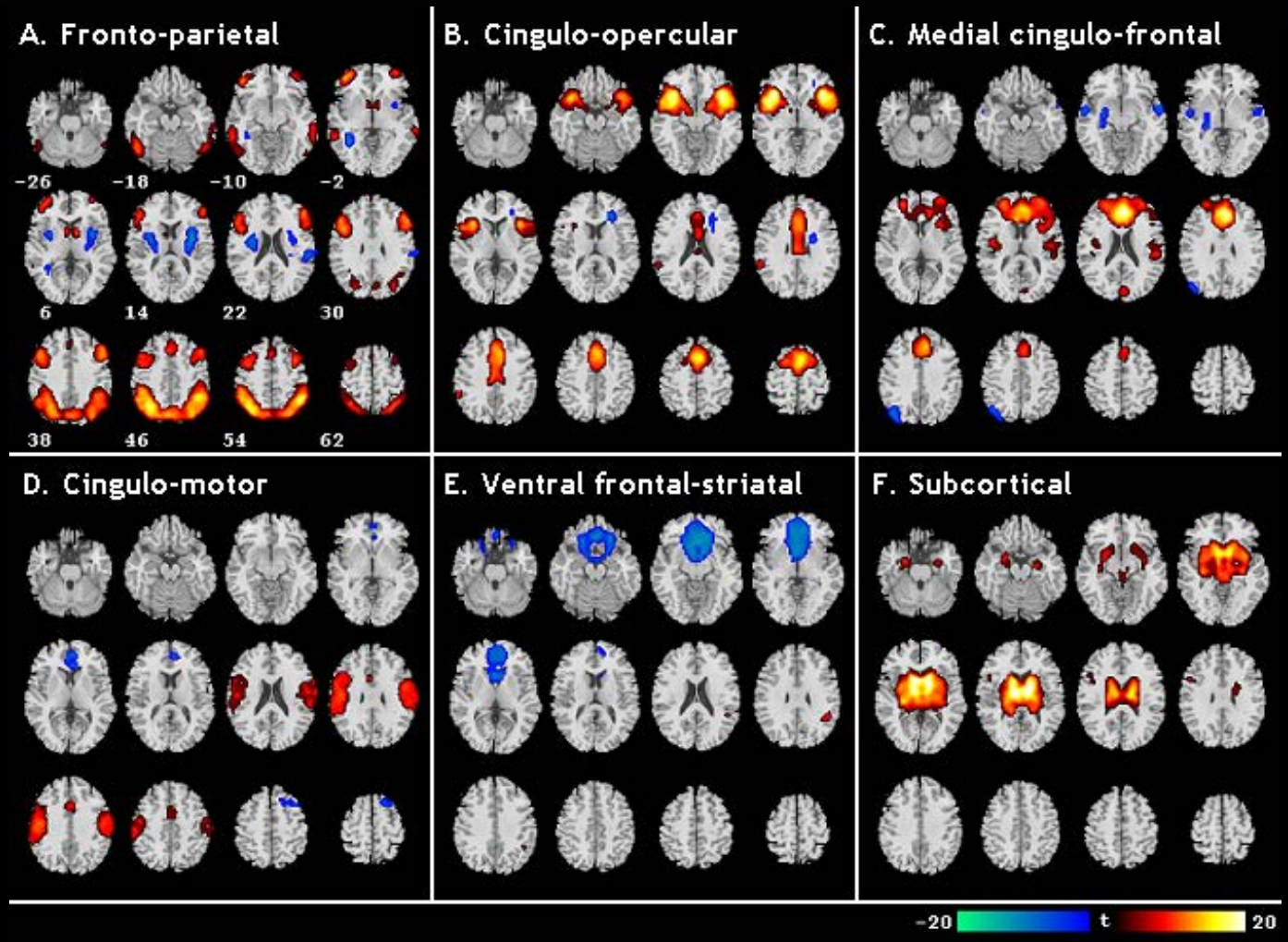
Pre-Treatment fMRI Stroop Measures Associated with Tx Outcomes



Verona, 11/12

Brewer et al, 2008

ICA of Incongruent Vs. Congruent Stimuli in CD and Control Subjects



B, D Show CD Vs. Control Differences

C Relates to Retention in CD Group

E, F Relate to Abstinence (Urine Toxicology) in CD Group

n=40 subjects, p<0.001, FWE

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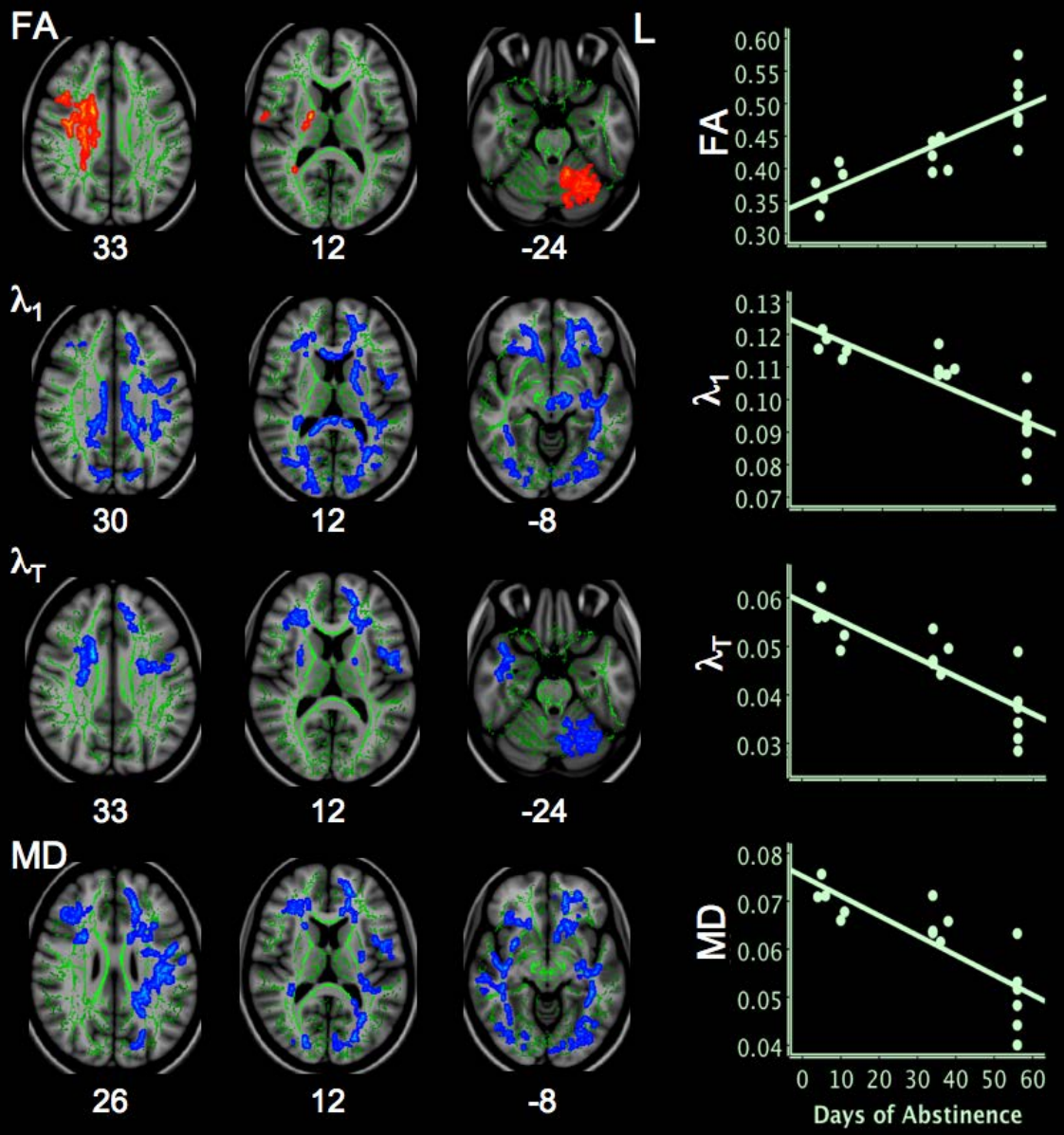
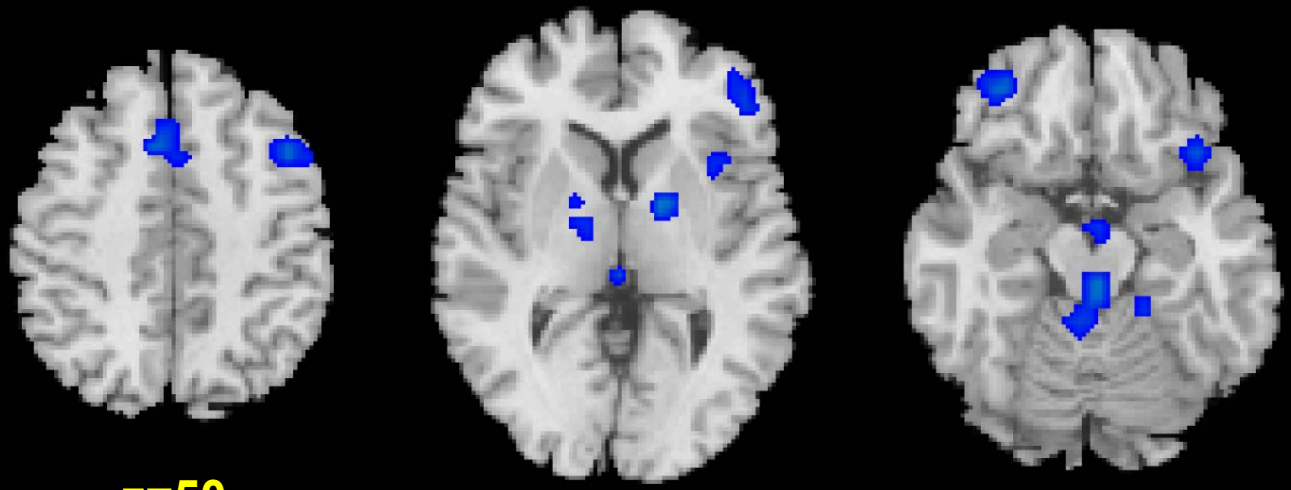
Worhunsky et al, in press, PAB

Poorer WM Integrity Associated with Shorter Duration of Cocaine Abstinence in CD Subjects



Xu et al, 2010

fMRI Stroop Measures Change After Behavioral Tx (CBT and TAU) for SUDs



z=50 z=6 z=-14

Post-Tx Vs. Pre-Tx Contrast of Incongruent Vs. Congruent Stroop Stimuli

n=12 subjects, p<0.005; k>20

DeVito et al, 2012

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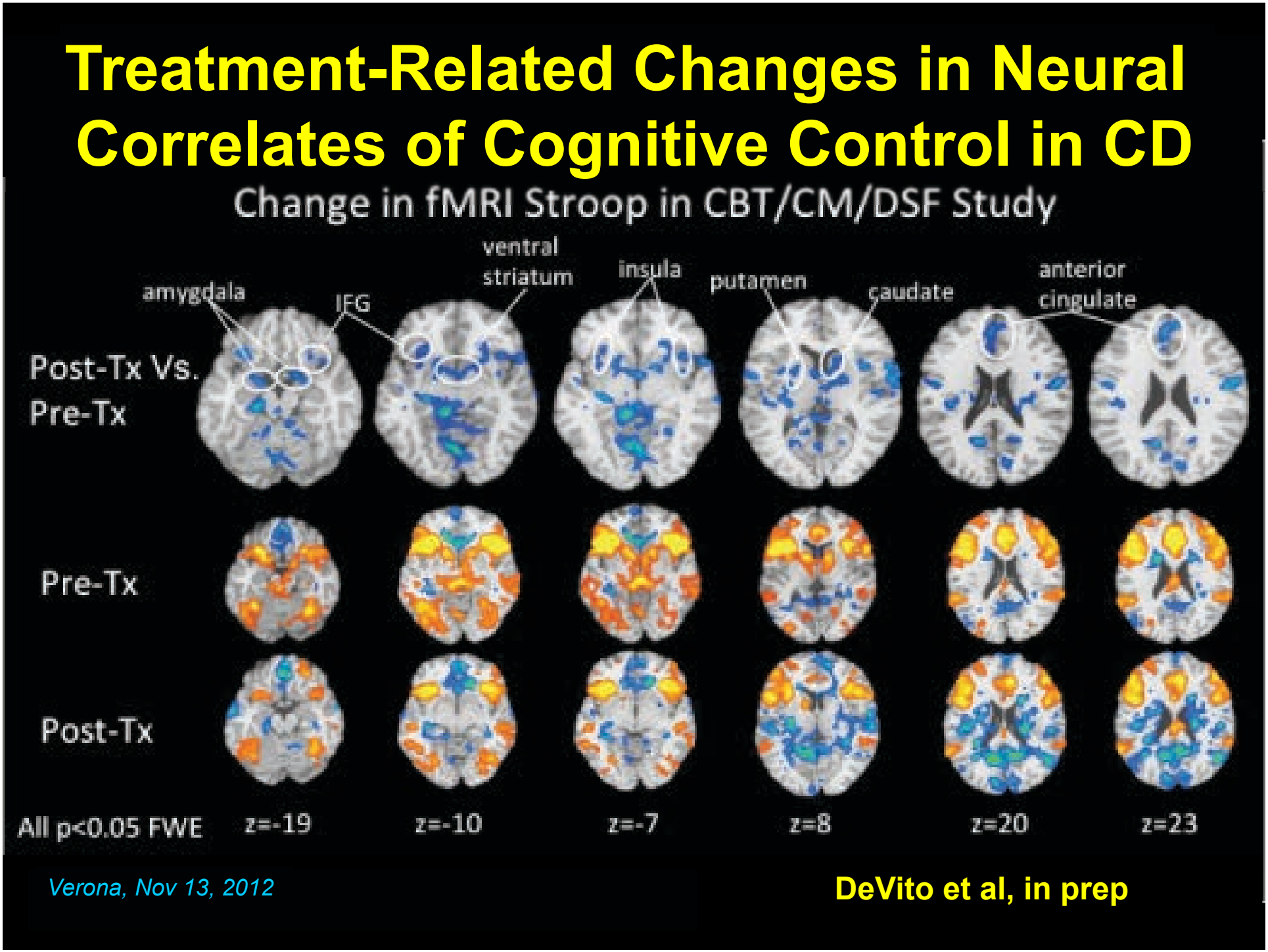
Treatment-Related Changes in Neural Correlates of Cognitive Control in CD



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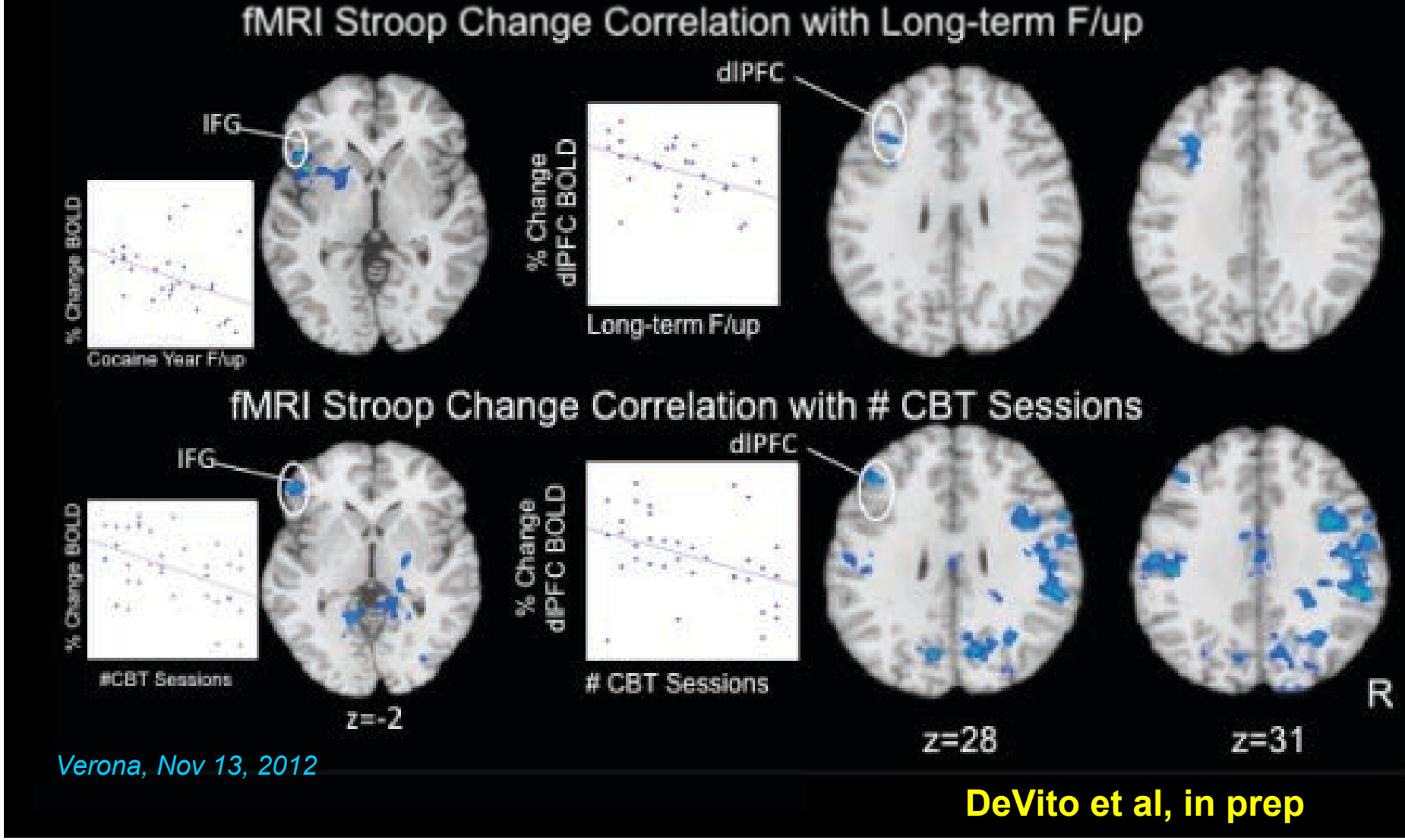
DeVito et al, in prep

Changes in Neural Correlates of Cognitive Control Correlate with Outcome and CBT Measures



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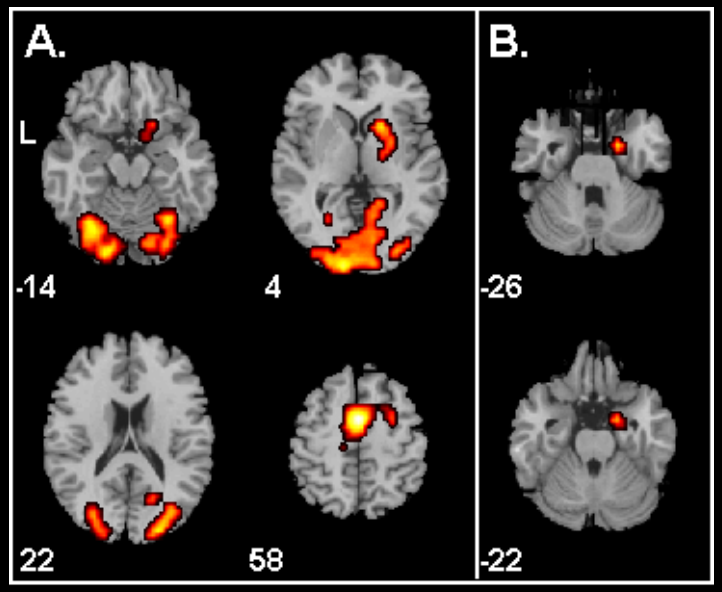
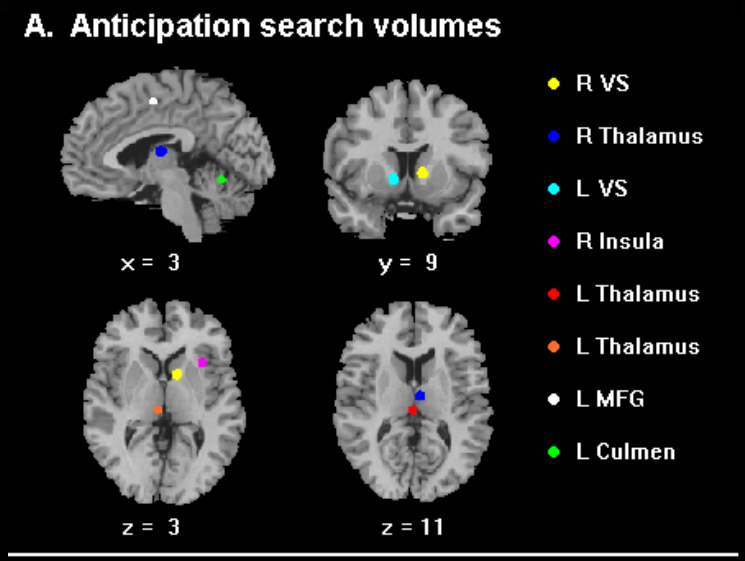
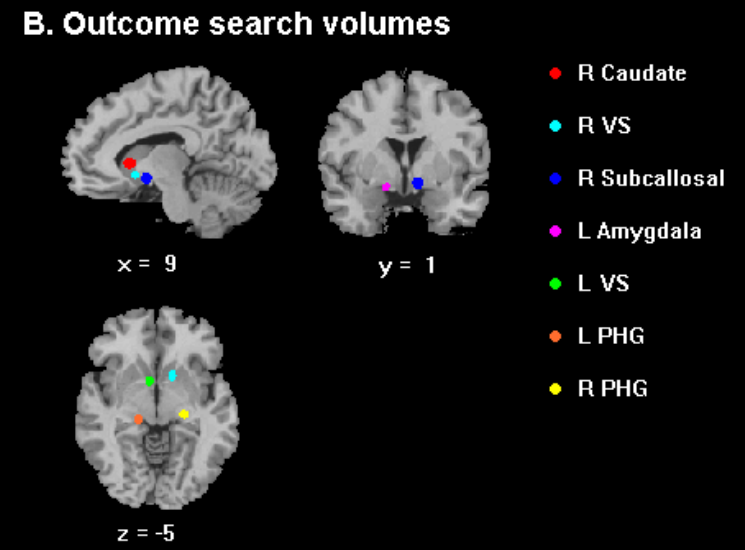
DeVito et al, in prep

Reward Processing & CD Tx Outcome







1. CD Subjects Show Relatively Increased Activation of Reward Circuitry, Particularly in OC Phase

2. Increased Activation in OC Phase Associated with Poorer Treatment Outcome

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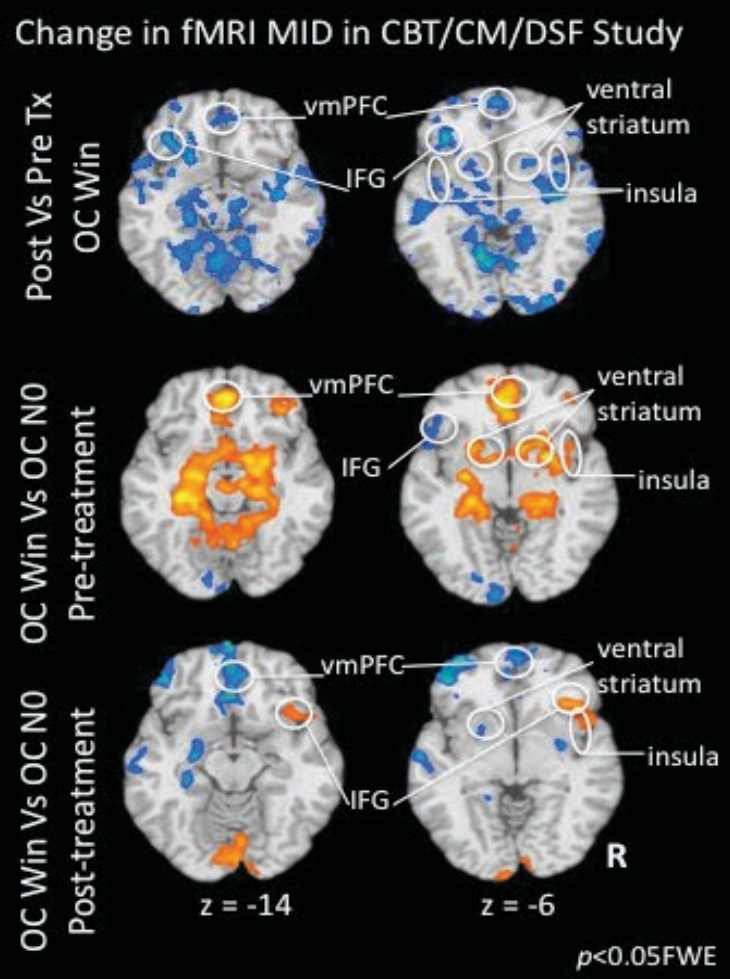
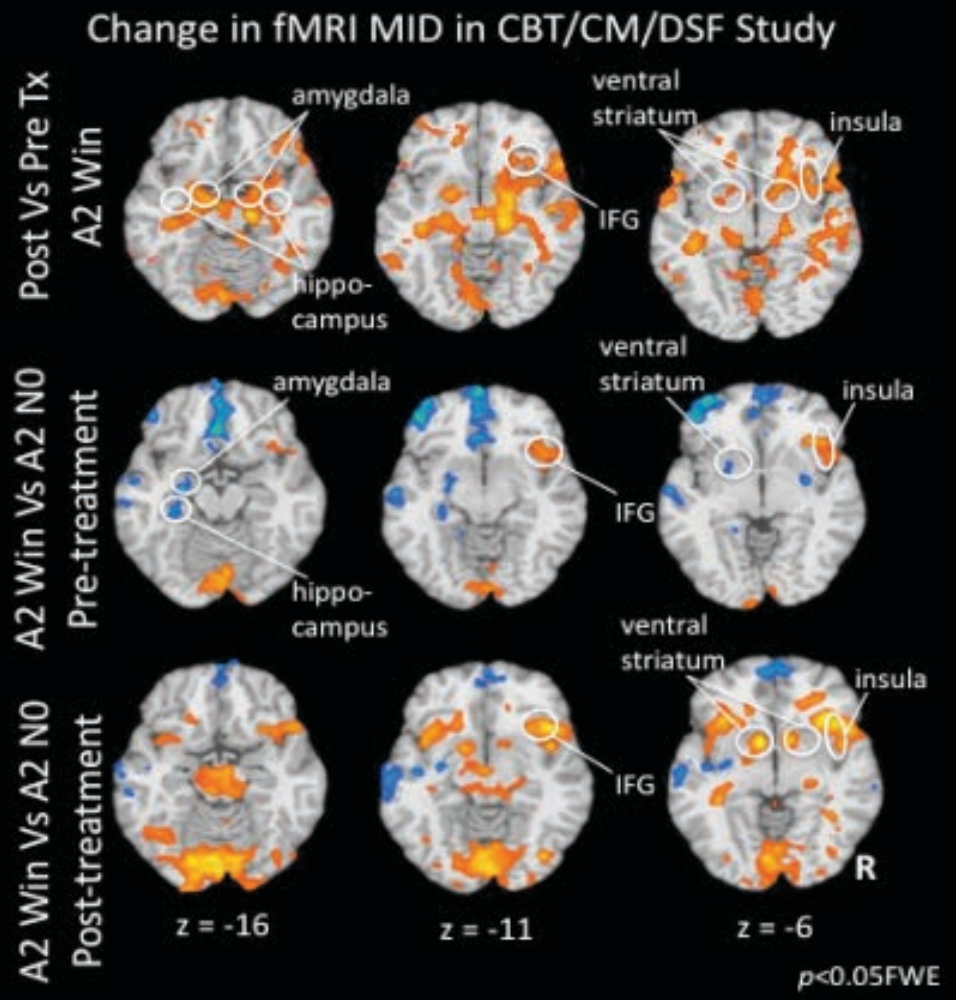
Jia, Worhunsky et al, 2011

Treatment-Related Changes in Neural Correlates of Reward Processing in CD





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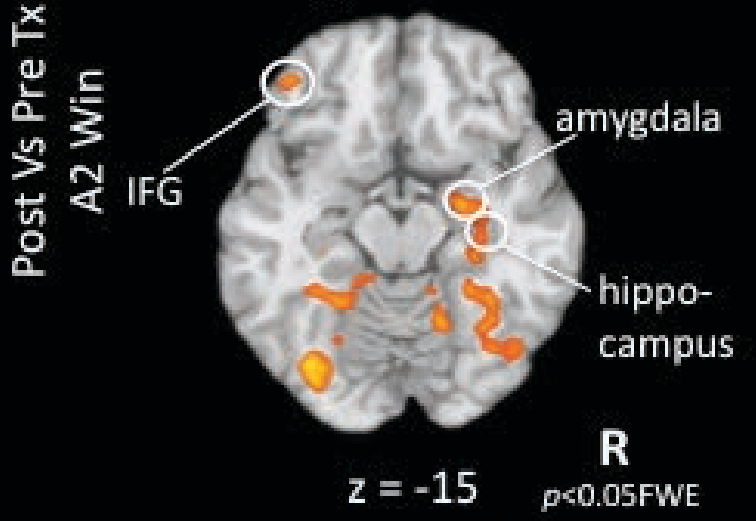
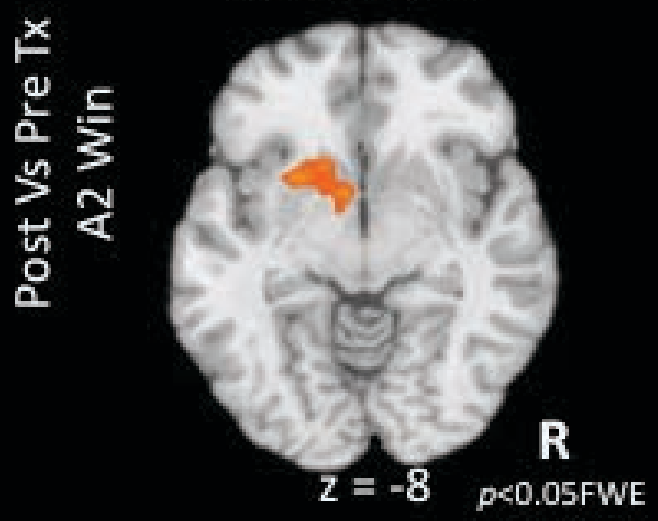
Balodis et al, in prep

Changes in Neural Correlates of Reward Processing Correlate with Outcome and CBT Measures

Days Abstinent During CBT/CM/DSF Study Follow Up Correlated with Change fMRI MID



Change fMRI MID in Homework Completers vs Homework Non-Completers



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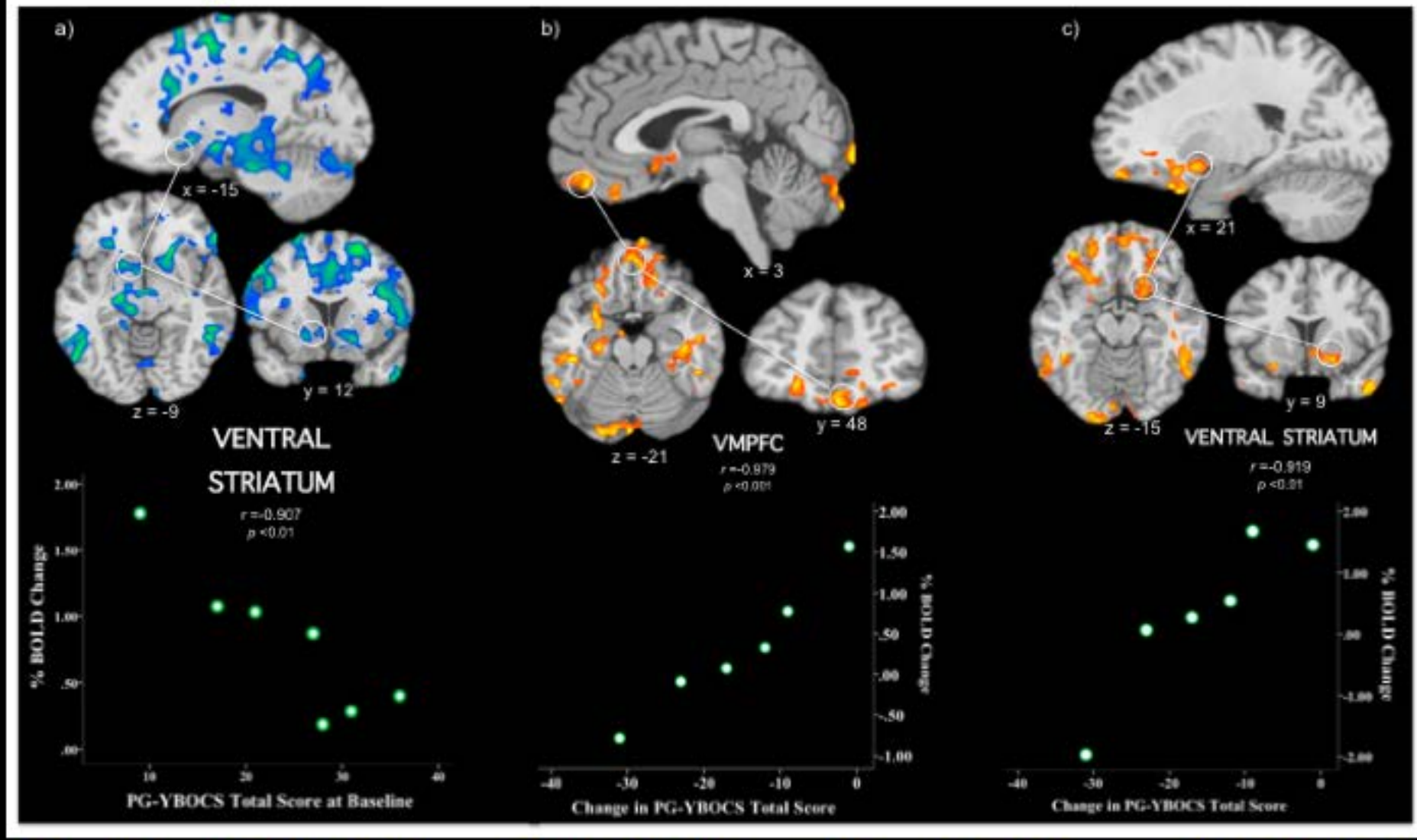
Balodis et al, in prep

Stroop Activation and Tx Outcome in PG



Baseline PG-YBOCS

VMPFC Change & PG-YBOCS

VS Change & PG-YBOCS

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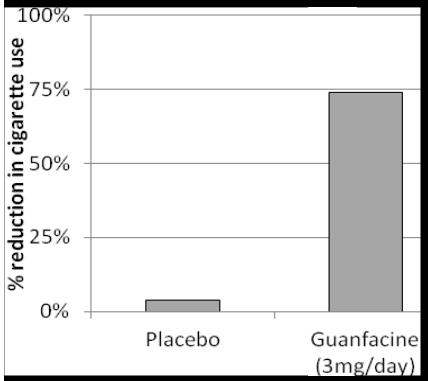
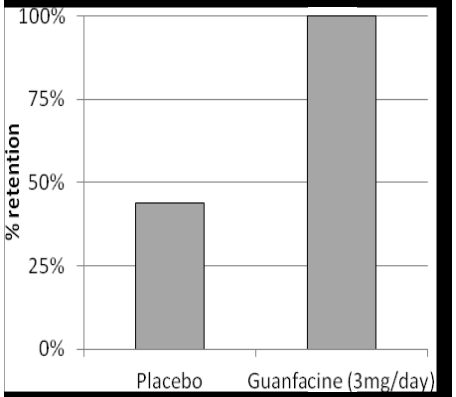
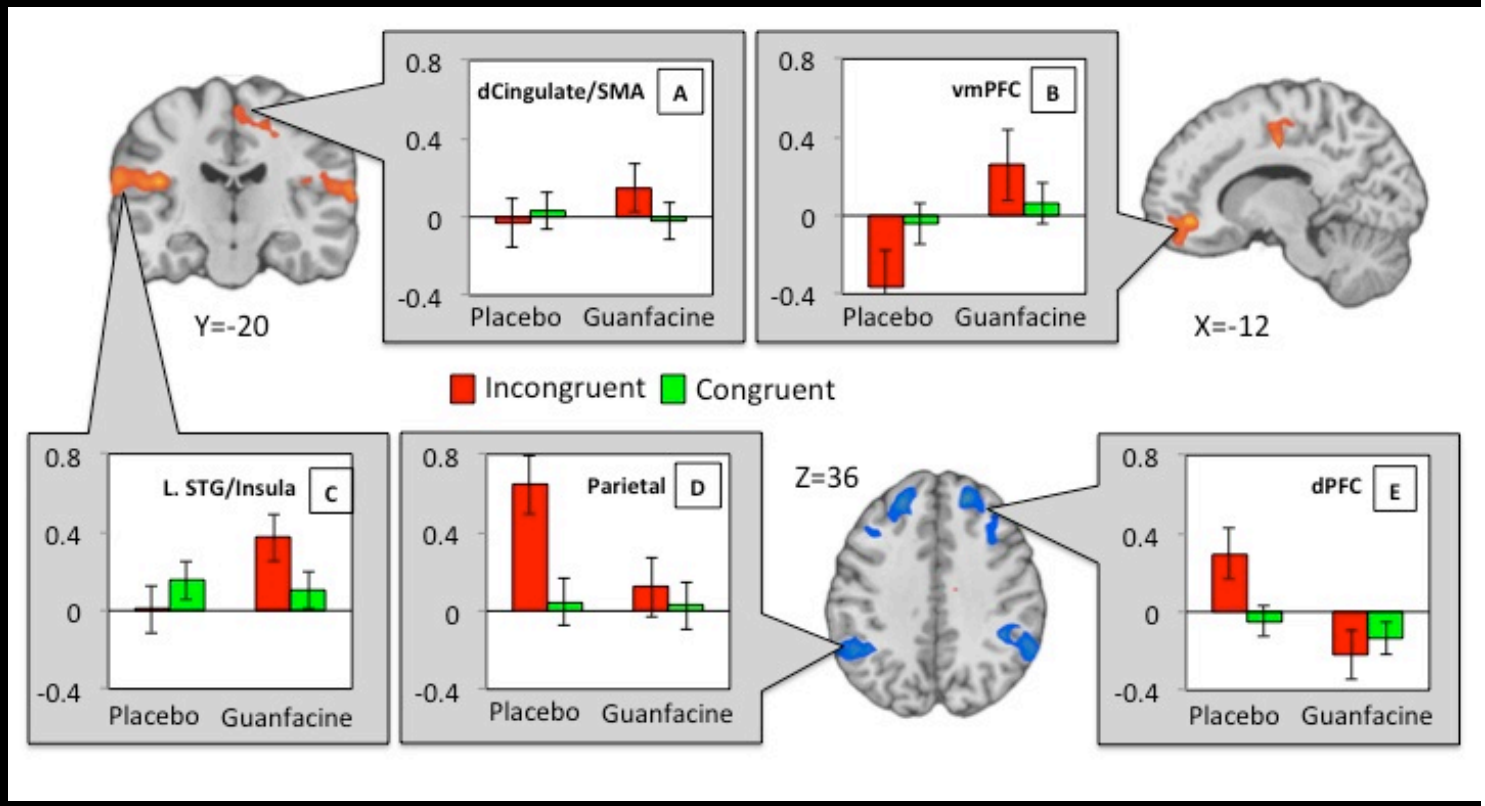
Potenza et al, rev & res

Guanfacine Tx Associated with Reduced Tobacco Use, Increased Retention and Altered Stroop-Related Neural Processing







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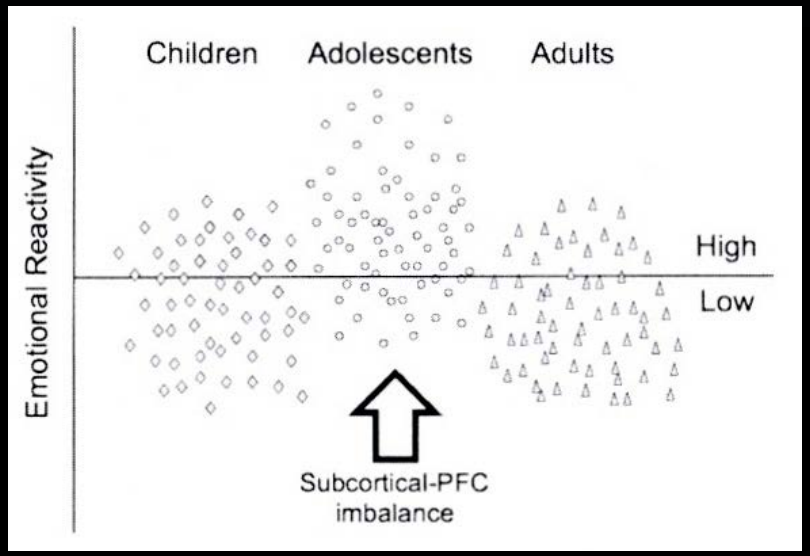
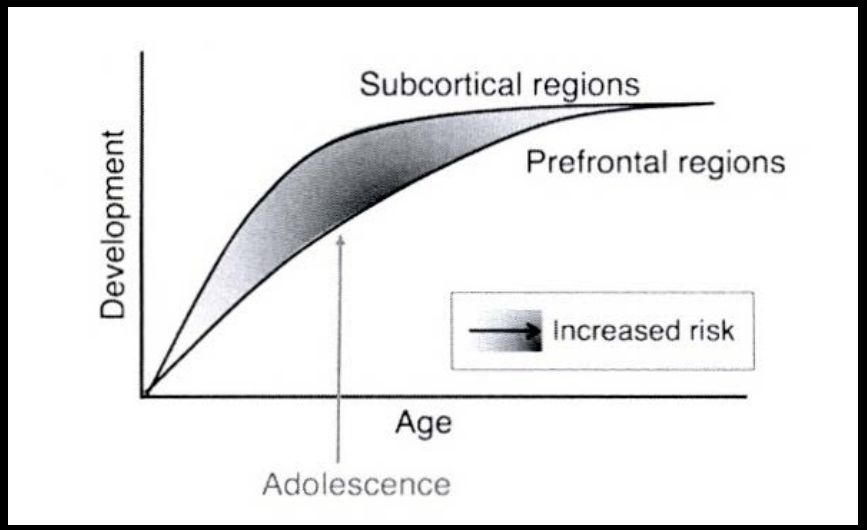
p<0.05 FWE

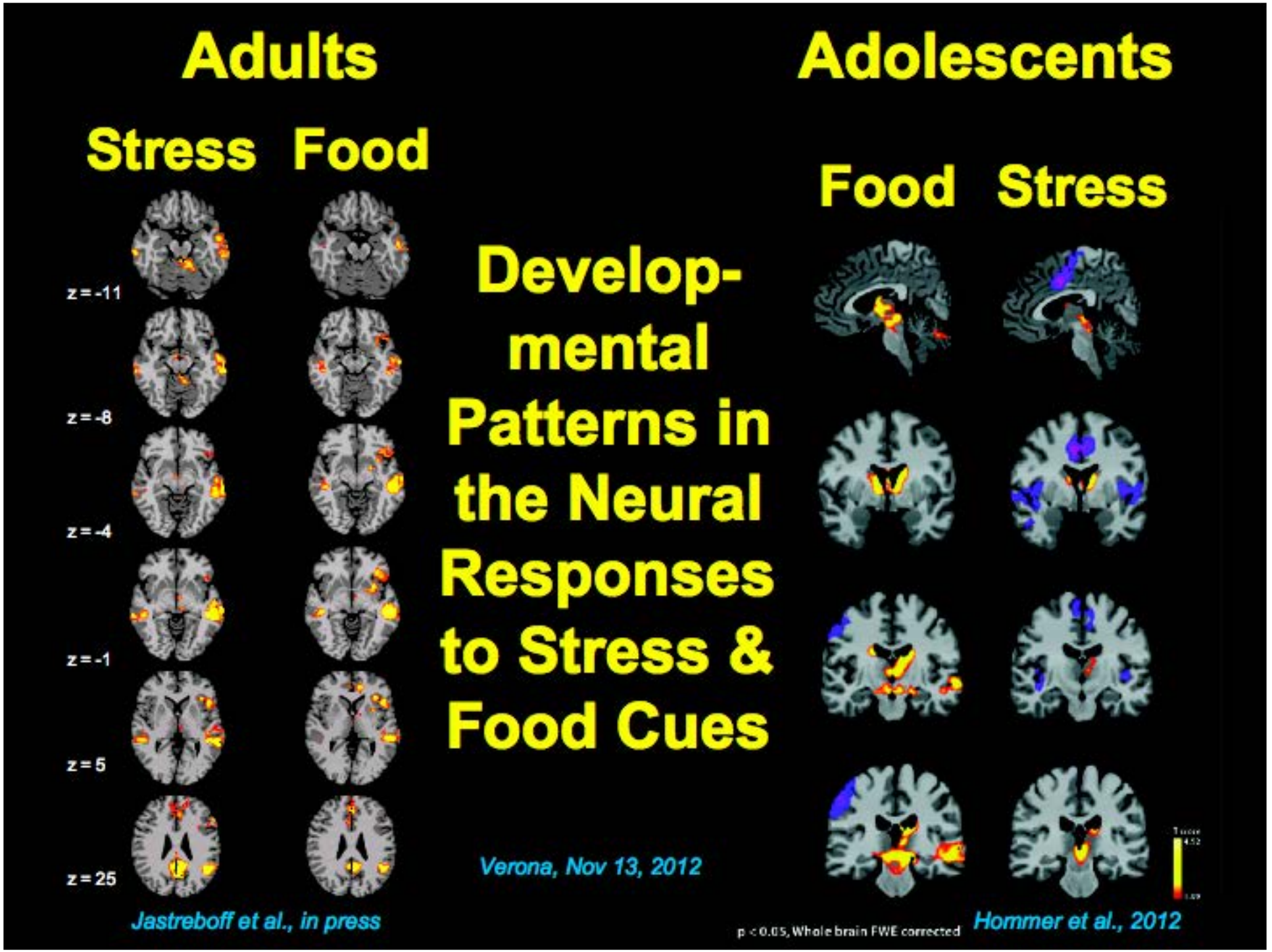
McKee et al, submitted

Behavioral and Brain Changes in Adolescence: Tx Considerations

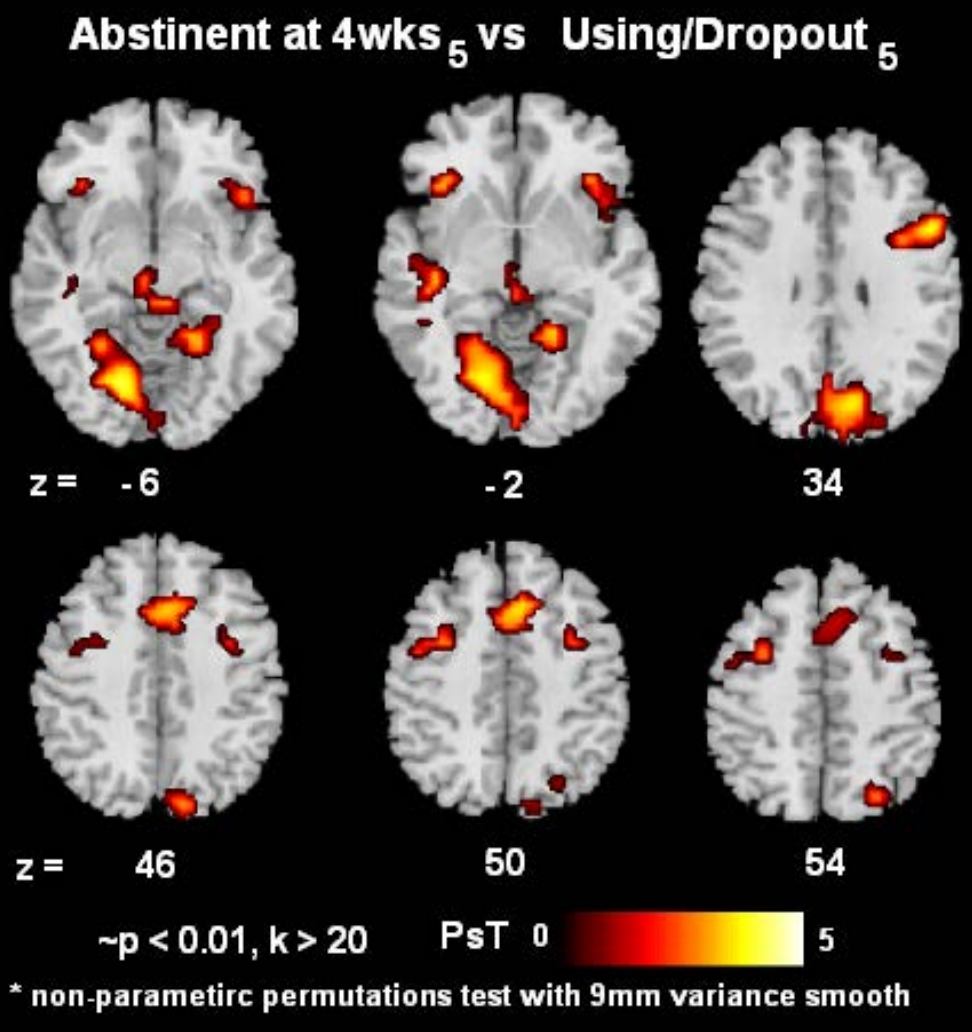


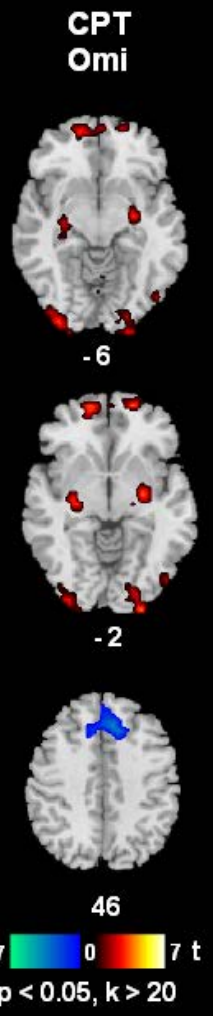


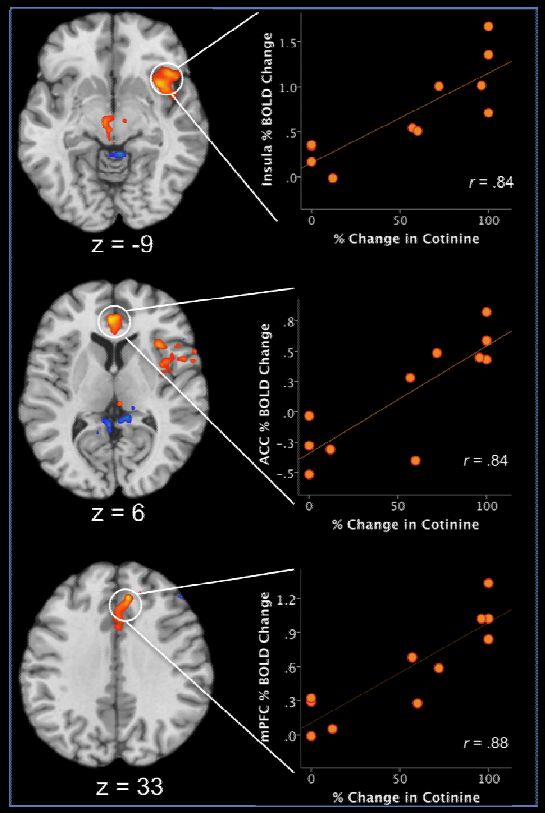
Verona, Nov 13, 2012 *Somerville et al., 2010* *Counselor cover (June, 2011)*


Adults
Adolescents
Stress
Food
Food
Stress
z = -11
z = -8
z = -4
z = -1
z = 5
z = 25
Develop-
mental
Patterns in
the Neural
Responses
to Stress &
Food Cues
Verona, Nov 13, 2012
Jastreboff et al., in press
p < 0.05, Whole brain FWE corrected
Hommer et al., 2012

fMRI Stroop in Adolescent Smokers: Relationship with Tx Outcome, Attention







p<0.05, FWE

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Krishnan-Sarin et al, rev and resub, PAB

Binge Eating Disorder As A Food Addiction?

Current Drug Abuse Reviews, 2011, *4*, 201-207

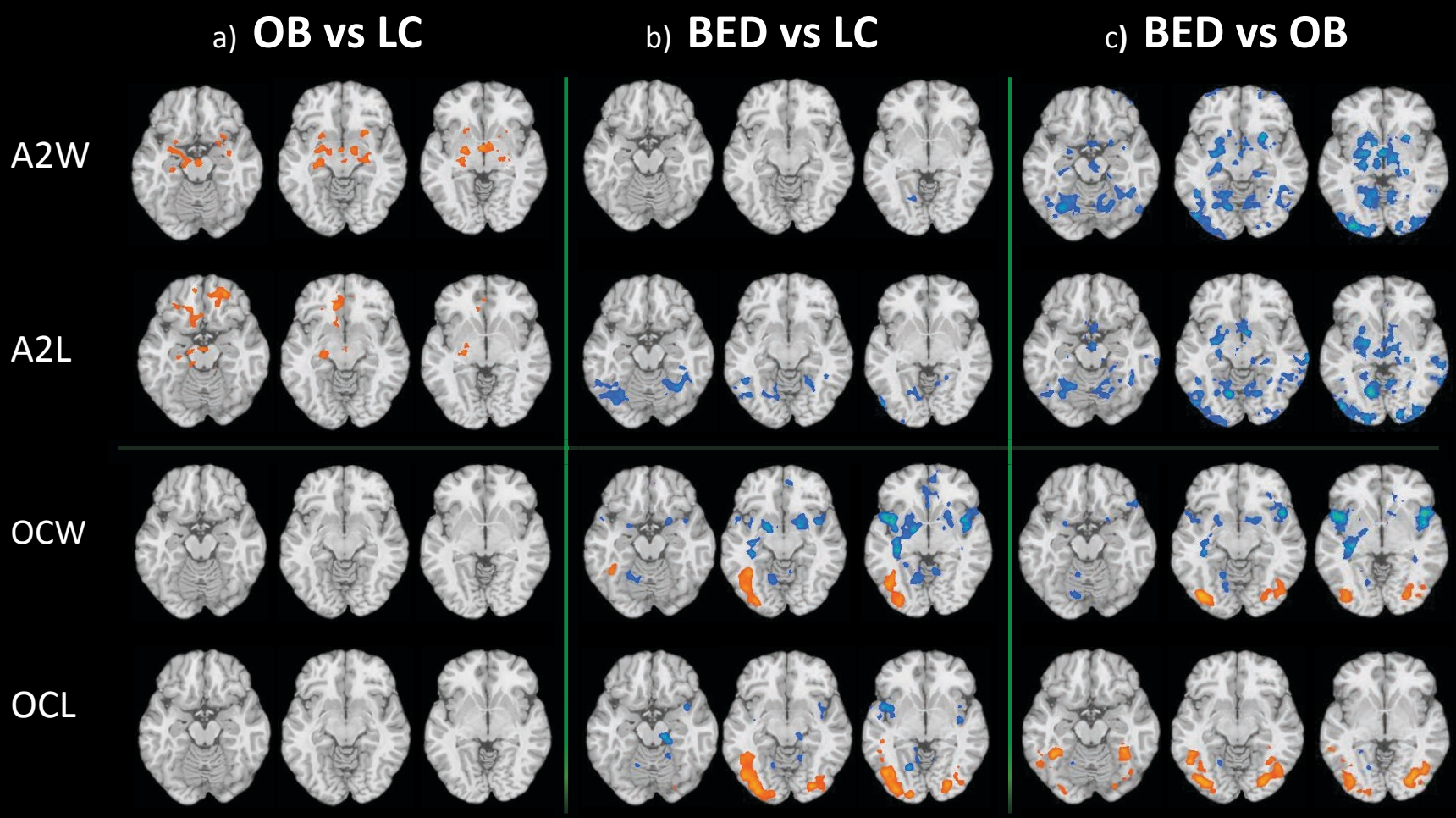
Binge Eating Disorder and Food Addiction

Ashley N. Gearhardt[*,1], Marney A. White[2] and Marc N. Potenza[2,3]

Similarities Between BED and Substance Dependence	
1.	Diminished control over consumption
2.	Continued use despite negative consequences
3.	Diminished ability to cut down or abstain from problematic substance
4.	Elevated levels of impulsivity
5.	Elevated comorbidity with mood/anxiety disorders
6.	Triggered by cravings and negative affect
7.	Similar patterns of neural activations

Differences Between BED and Substance Dependence	
1.	BED is associated with elevated concerns with shape or weight, but substance dependence is not
2.	BED diagnosis specifies that consumption must occur during a discrete period of time, but substance dependence does not
3.	Substance dependence diagnosis assesses withdrawal, tolerance, amount of time spent on substance-focused activities and activities given up due to substance use, but BED does not
4.	Substance dependence diagnosis places a greater emphasis on the contribution of the substance (e.g., addictive potential of substances), BED diagnosis does not consider specific types or properties of food consumed (merely the amount)
5.	Substance dependence treatments typically focus on abstaining from the problematic substance, but BED treatments do not

Reward-Related Between-Group Differences in BED and Obesity



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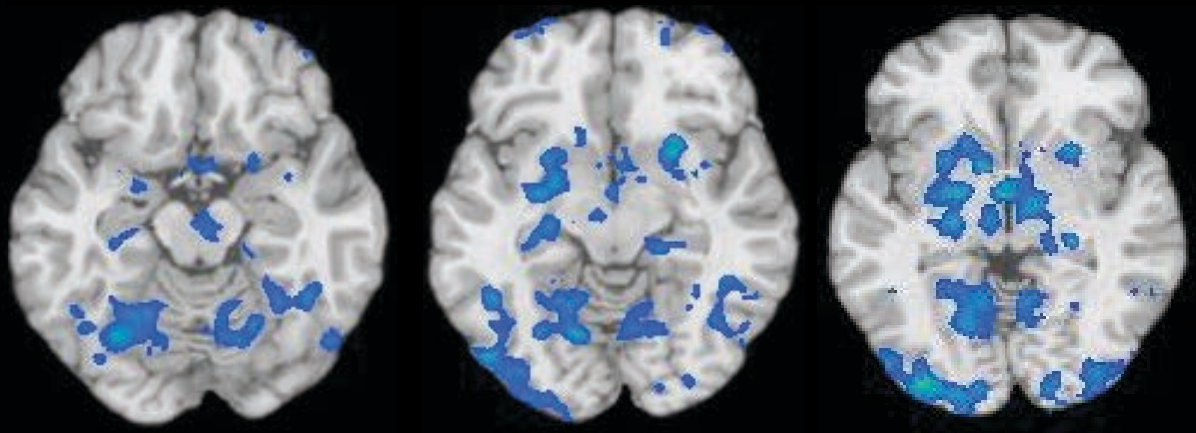
Balodis et al, rev and resub

A2Win Reward-Related Between-Group Differences in BED and Obesity

BED vs OB



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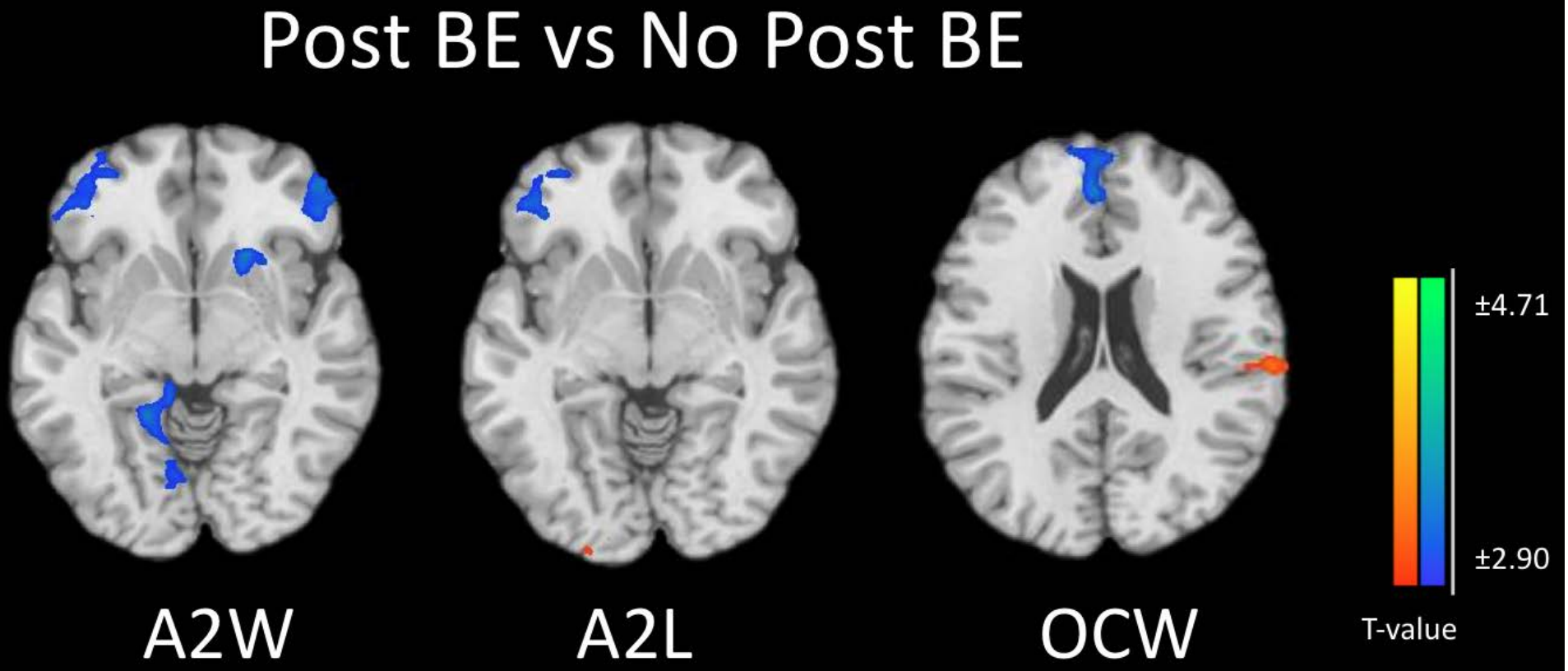
Post-Tx Binge Eating Associated with Diminished Reward-Related Activation at Treatment Onset



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Balodis et al, rev and resub

Conclusions & Future Directions

- Although Empirically Validated Treatments for Addictions Exist, Many Individuals with Addictions Experience Relapses and Significant Drug-related Problems in Multiple Domains
- Investigating Clinically Relevant Intermediary Phenotypes Like Impulsivity and Compulsivity Have the Potential to Better Understand the Mechanisms Underlying Effective Therapies and Implement Treatment Matching Strategies
- Understanding the Biological Mechanisms Underlying Specific Components of Therapies May Further Facilitate Treatment Development and Matching

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ICD Trials
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