# PREDICTING SMOKING RELAPSE FROM WORKING MEMORY-RELATED NEURAL ACTIVITY

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# Collaborators

# Introduction

Tobacco dependence has far reaching health and economic consequences.

Smokers attempting to quit commonly report "difficulty concentrating".

Abstinent smokers exhibit deficits on measures of executive function, including working memory.

Working memory, a key element of executive function, is essential to maintaining goal-directed behaviors.



**The New York Times**

*Smoking's Toll on Health Is Even Worse Than Previously Thought, a Study Finds*

By DENISE GRADY    FEB. 11, 2015

Andrew Rodriguez/The New York Times

A new study adds at least five diseases and 60,000 deaths a year to the toll taken by tobacco in the United States. Before the study, smoking
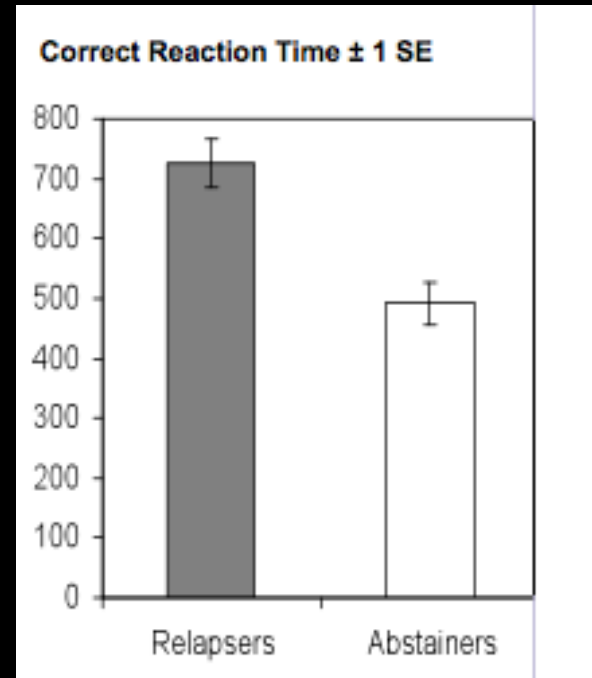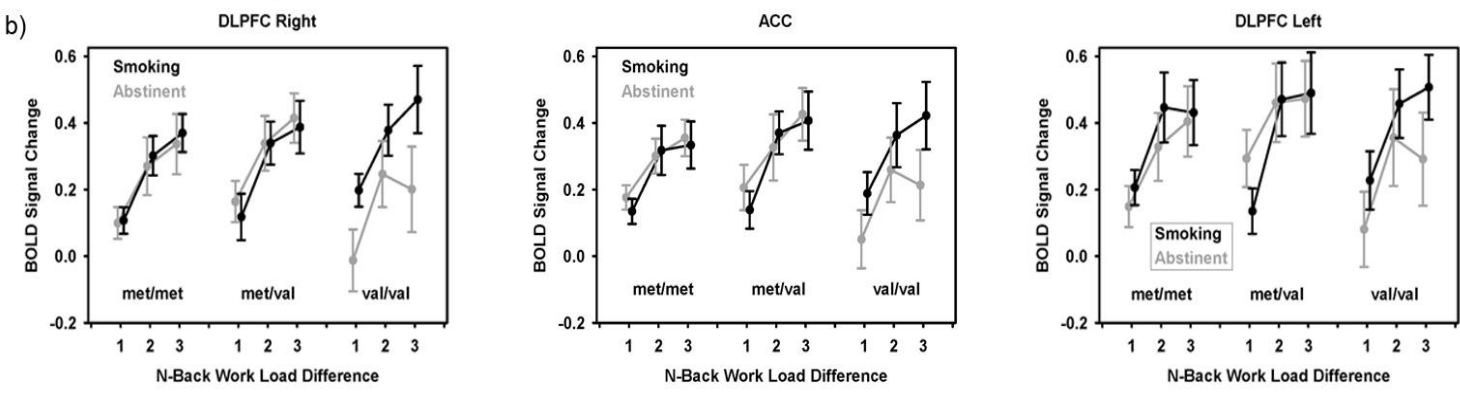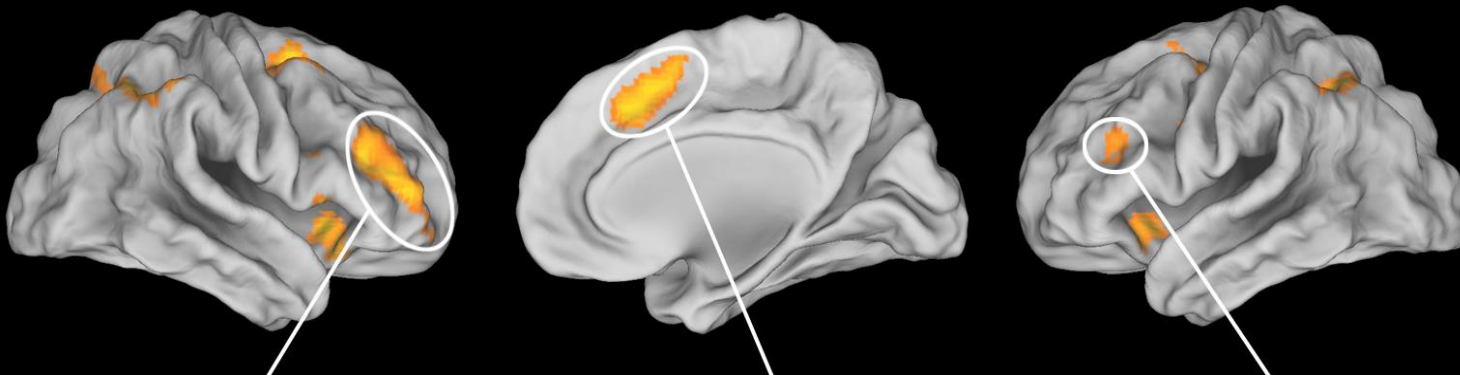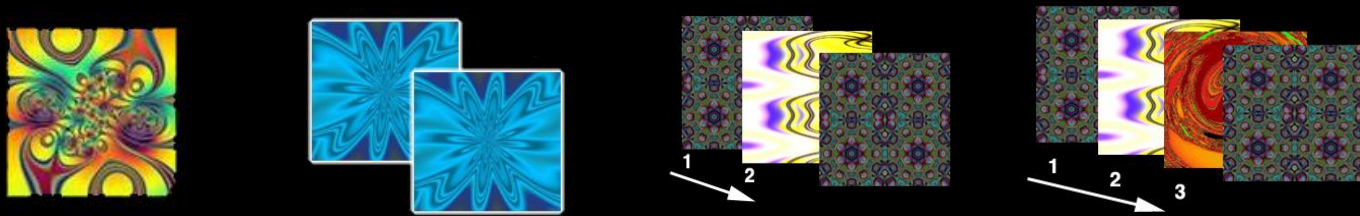
# Research Program

- **Characterize nicotine withdrawal-related working memory deficits using BOLD fMRI**

- **To evaluate the effect of a "best in class" treatment (varenicline) on abstinence induced WM deficits and underlying brain signal**

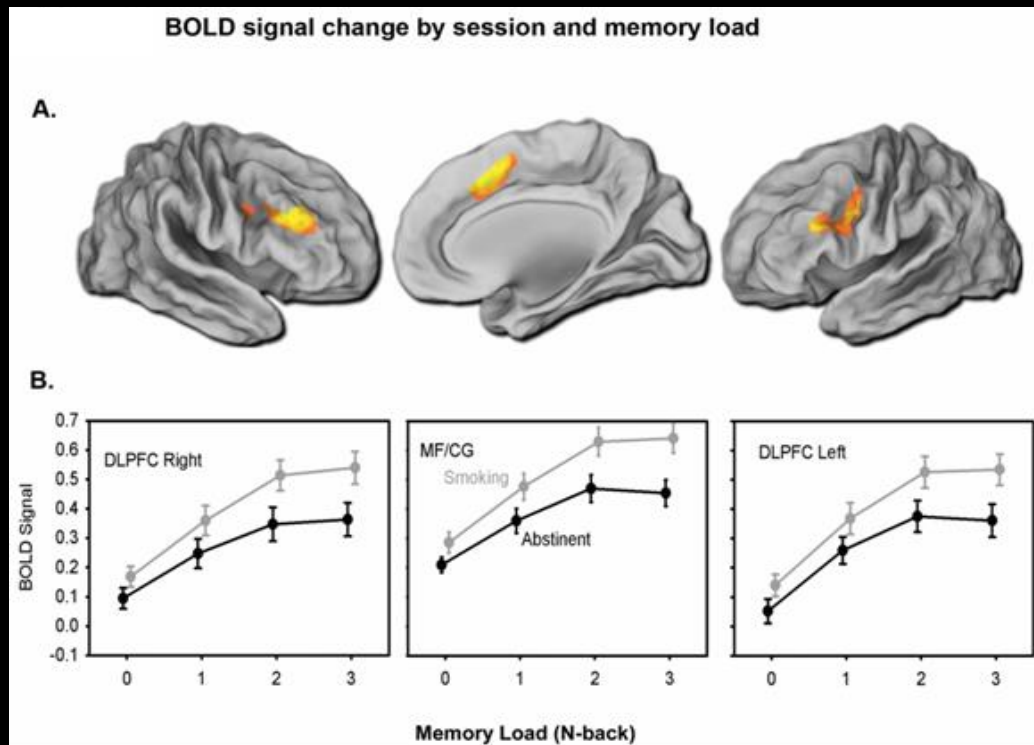- **To test whether these neural signals predict smoking relapse**

*Allenby et al., Addiction Biology, 2019; Allenby et al., Nicotine Tob Res, 2019; Ashare et al., Psychopharmacology, 2016; Loughead et al., Neuropsychopharmacology, 2015; Falcone et al., Addiction Biology, 2014; Lerman et al., JAMA Psychiatry, 2014: Loughead et al., Biological Psychiatry, 2010; Loughead et al., Molecular Psychiatry, 2009.*

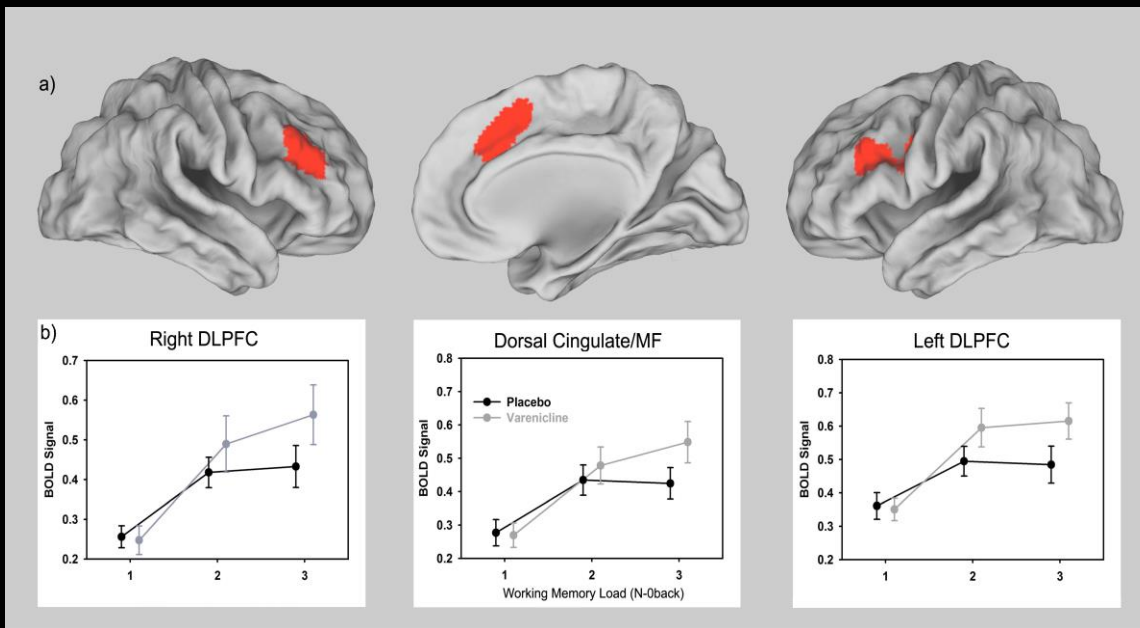# Working Memory Performance Predicts Short-Term Smoking Resumption Following Brief Abstinence

**Faster reaction time (efficiency) on the N-back working memory task after 72 hours of abstinence predicts 7-day quitting (p= 0.01; $r^2$=.15)**



**Correct Reaction Time ± 1 SE**

Patterson et al., Drug and Alcohol Dependence, 2009

Figure 2

b)

**DLPFC Right**

**ACC**

**DLPFC Left**

N-Back Work Load Difference

**BOLD signal change by session and memory load**

N=63 within-subject, session effect on WM performance and BOLD signal change p<0.001, corrected.

Falcone et al., Addiction Biology, 2013

**Visual N-Back Working Memory Task. Main effects of treatment (varenicline, placebo) observed in all three ROIs (p<0.05 corrected).**

# Abstinence challenge vs. smoking will:

**Decrease activation in DLPFC, MF/CG**

**Reduced deactivation in the PCC, vmPFC**

**Abstinence-induced changes in WM-related BOLD fMRI signal will predict the likelihood of early smoking relapse beyond standard clinical and behavioral measures.**

| Session | Eligibility Screening | Scan 1 | Scan 2 | Pre Quit | Target Quit Day | Monitoring Visits | | | | End of Tx (EOT) Survey | EOT CO Visit | Scan 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PRE QUIT ATTEMPT | | | | POST QUIT ATTEMPT | | | | | | | |
| WEEK | 0 | 1[a] | 2-3[a] | 4 | 5 | 6 | 7 | 8 | 9 | 13 | 14[b] | ~14[c] |
| Activity | Consent; Inclusion/ Exclusion; Baseline measures | fMRI Scan > 24HRS abstinent | fMRI Scan > Smoking as Usual | Complete measures & small group counseling | Complete measures & individual booster counseling | Complete measures & individual booster counseling | | | | Complete telephone survey & schedule fMRI Scan[c] | Provide CO sample | fMRI Scan |

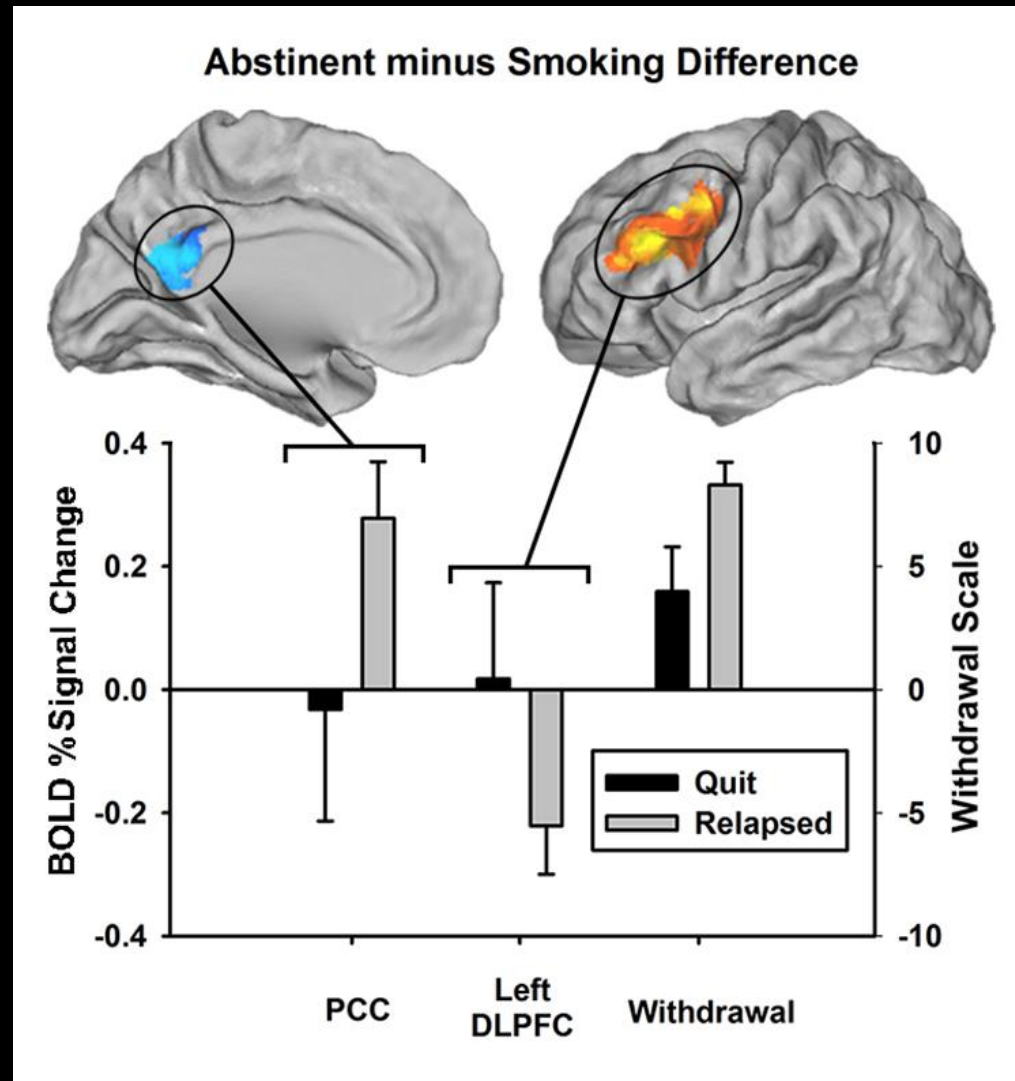# Predictors variables entered into model

**Baseline candidate predictors:
Sex, age, and nicotine dependence**

**Change scores for paired data
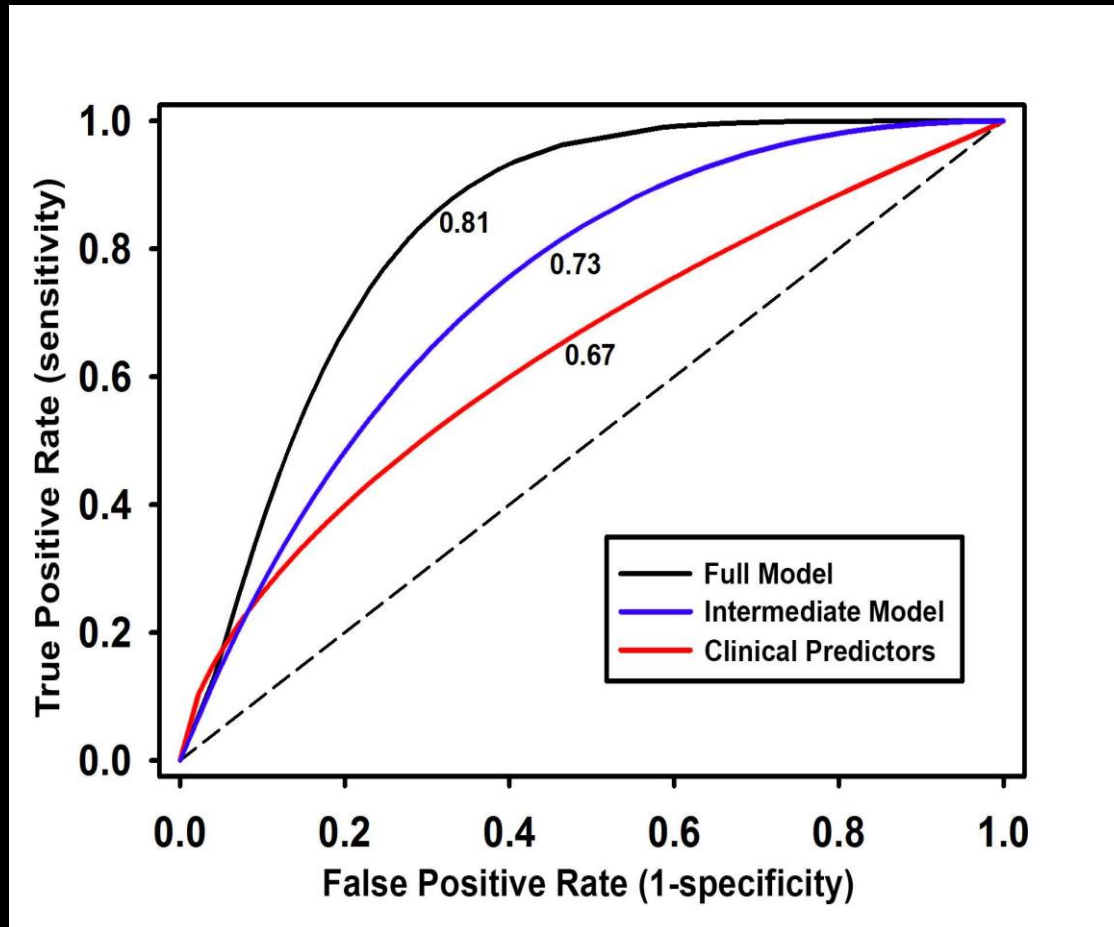collected during abstinence
challenge:**

**MNWS, QSU-Brief, PANAS Positive,
PANAS Negative, right DLPFC, left
DLPFC, MF/CG, vmPFC, and PCC**

Age and nicotine dependence entered
based on clinical relevance; sex was
non-significant, and allowed to drop out.

Using Bootstrapping procedures, PPC,
Left DLPFC, and withdrawal scale   were
most frequently retained.



Abstinent minus Smoking Difference

# ROC Analysis



Ideal cut point corresponds to 83.3% correct classification. LOOCV achieved an AUC=0.71. The 12% shrinkage observed in the LOOCV result corresponds to a 4.8% reduction in correct classification at the optimal cut-off value.

Loughead et al., *Neuropsychopharmacology*, 2015

# Summary

Altered WM-related signal in early abstinence differentiates successful vs. unsuccessful quitters.

Changes are characterized by decreased signal in left DLPFC and increased PCC (less deactivation) for abstinence vs. smoking satiety sessions

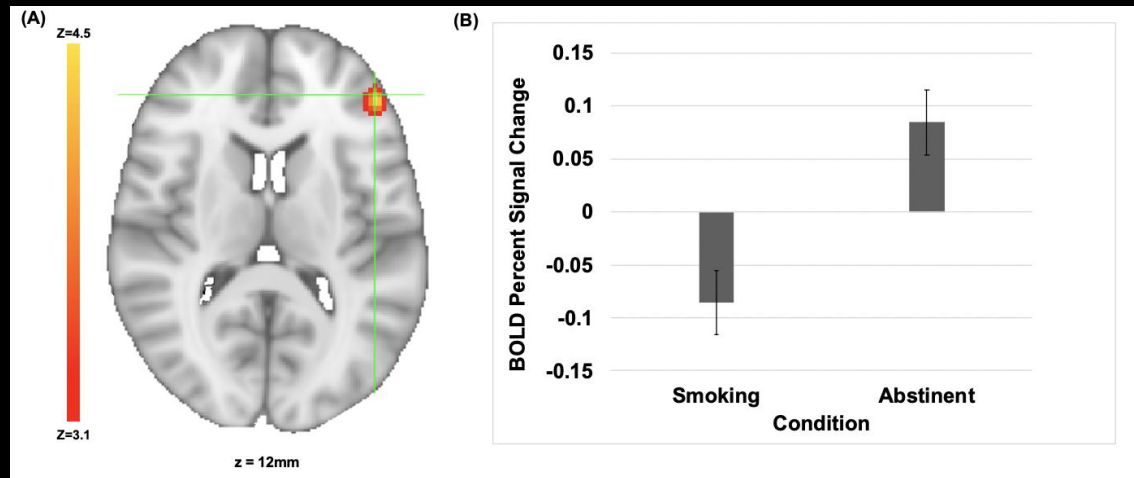81% AUC for predicting relapse, significant improvement over clinical variables only
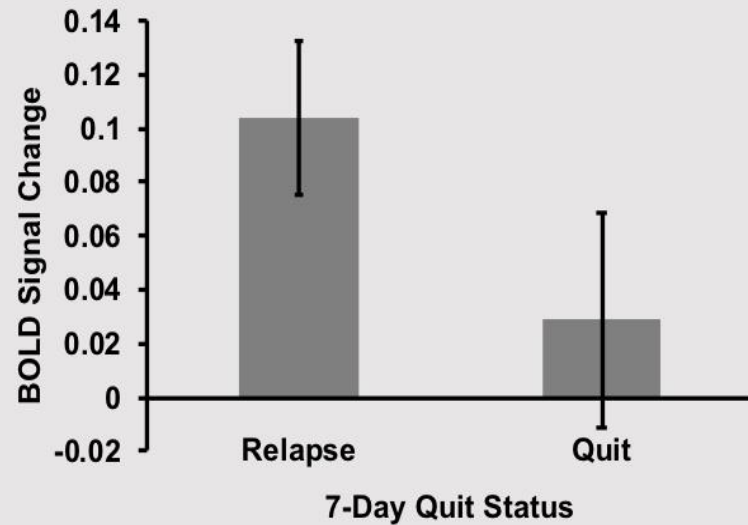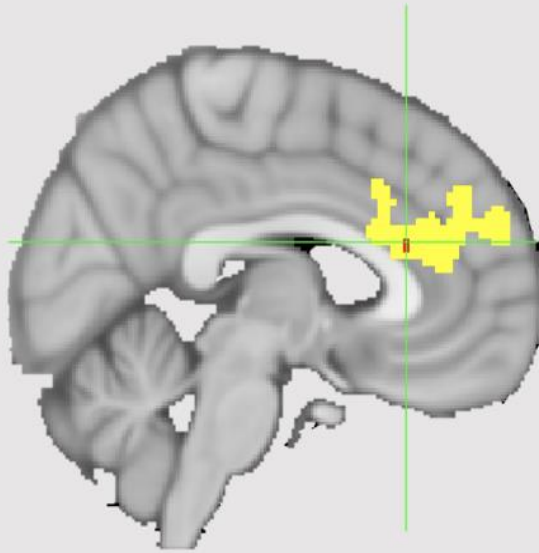
Whole brain analysis also identified left DLPFC

## Limitations:

- Model shrinkage (12%) but within expected range.

- Unaided quit attempt with low success rate.

- Short term cessation, however 7-day quit is predictive of 6-month quit (Ashare et al., 2013).

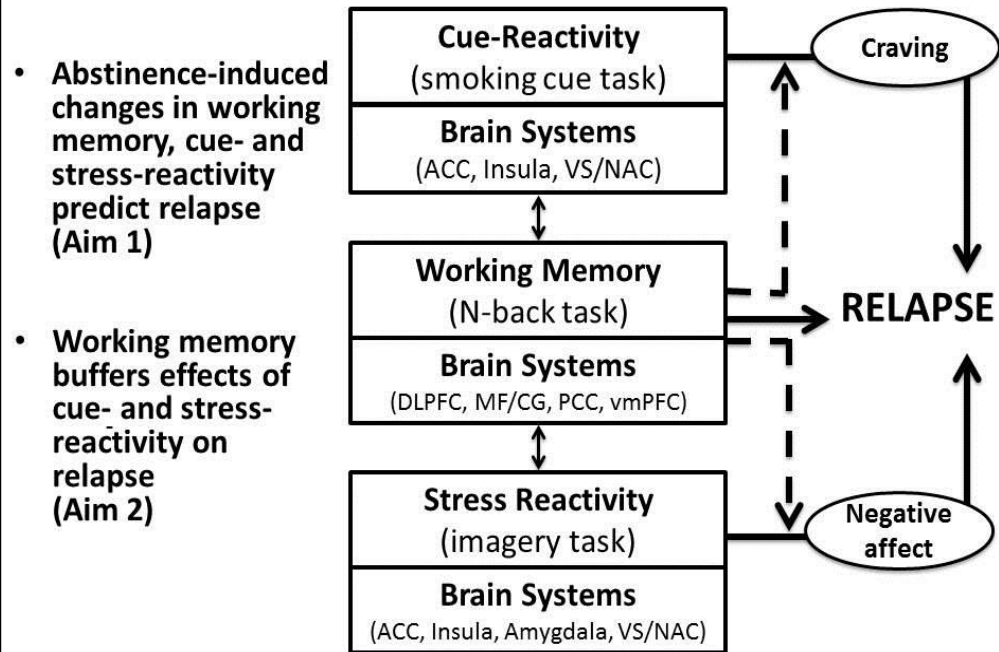# Abstinence significantly alters stress reactivity in the left inferior frontal gyrus

# Abstinence-induced change in ACC during cue reactivity

# Integrated Model



FIGURE 1: INTEGRATED BRAIN-BEHAVIOR MODEL

# Implications

Left DLPFC as a target for intervention

WM-related neural activation as a biomarker for predicting relapse risk in clinical practice?
- validate in large sample with alternate therapies and longer follow-up
- develop feasible clinical strategy (cost/benefit ratio)

Establish biomarker validation criteria
- Reproducibility
- sensitivity to intervention
- prediction threshold
- cost effectiveness    (Bough  et al, *Clin Pharm Ther*, 2013)