



ATHS 2015

Workshop and Discussion:

*Should “Food / Eating Addiction” replace
current Eating Disorders?*

**Brain imaging during
(drug and non-drug) reward cues:**

**“PROGNOSTIC” vs. “DIAGNOSTIC” roles in the
understanding and treatment of
reward “over-pursuit”**

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We humans are exquisite reward detectors!





ADDICTION



Q 1: Can fMRI distinguish cue responses related to.... **“reward”** vs. **“addiction”** ?

[[[**“DIAGNOSTIC”** role ?]]]

Q 2: ((If not ‘diagnostic’)) → can fMRI (still) be powerful in parsing **phenotypic subgroups**, **predicting future vulnerability / outcome**, and thus... **providing treatment targets?**



[[[**“PROGNOSTIC”** role ?]]]



ADDICTION

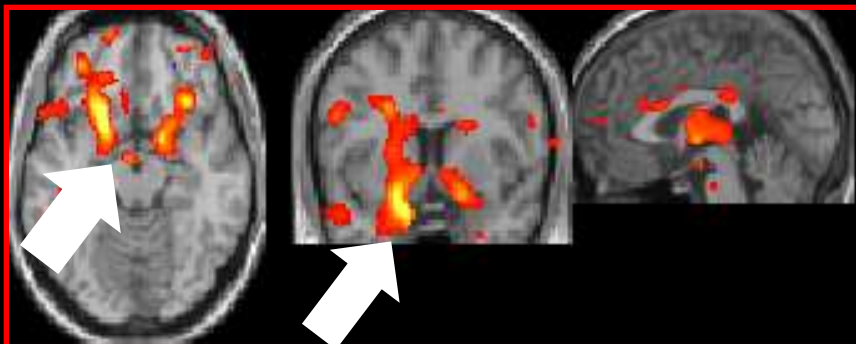
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Q 2: ((If not ‘diagnostic’)) → can fMRI (still) be helpful in parsing phenotypic subgroups, predicting outcome, and providing treatment targets?

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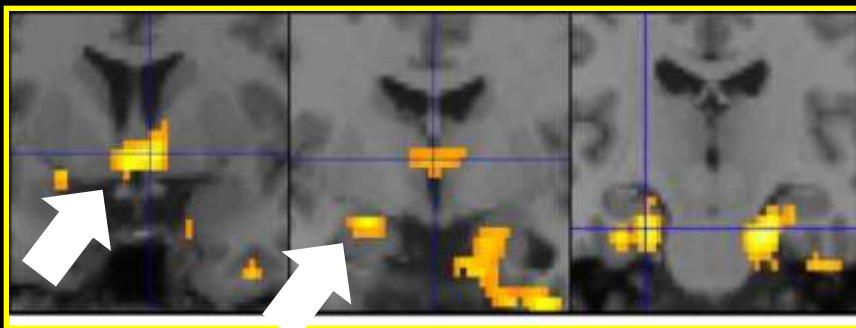
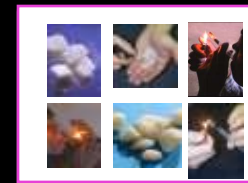
Which cue-image is from an “addicted” brain?



COCAINE

(33 msec. cues *)

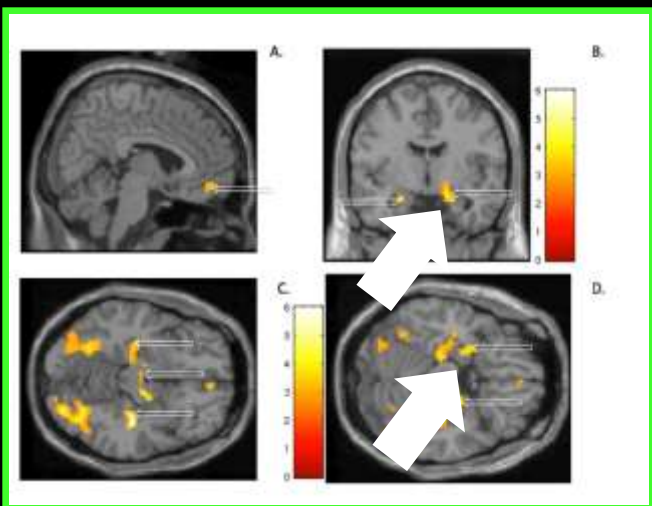
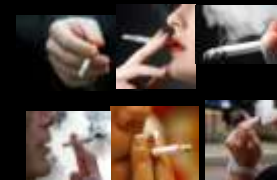
Kimberly Young et al. J. Neuroscience 2014



CIGARETTES

(10 min. video cues *)

Teri Franklin, et. al, Neuropsychopharm. 2007



MARIJUANA

(20 sec. cues *)

Marina Goldman, et al. JAM 2013.



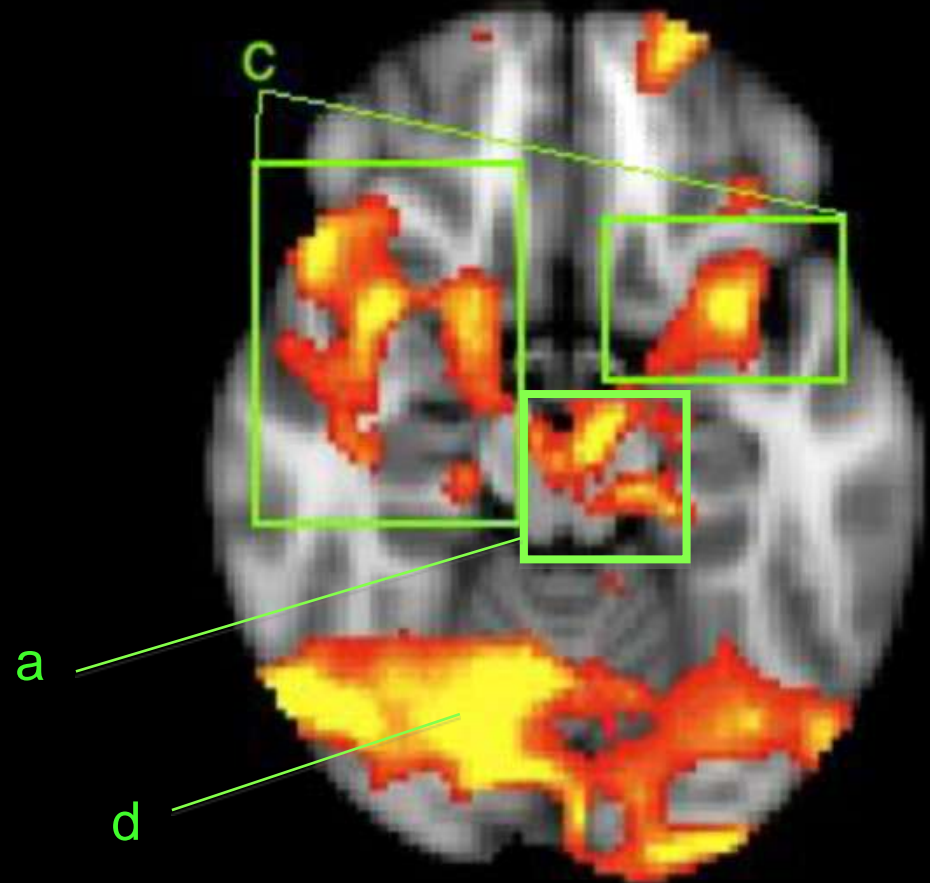
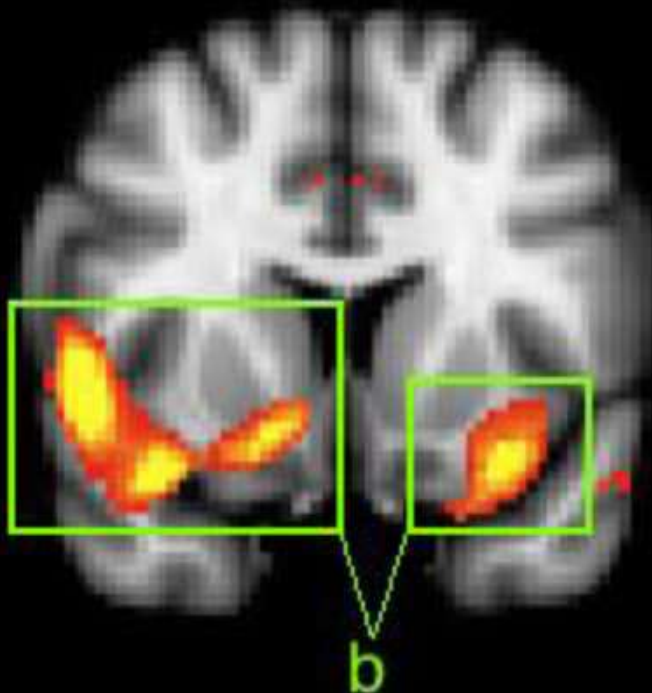
(* v. neutral cues)

Which image is from an “addicted” brain?



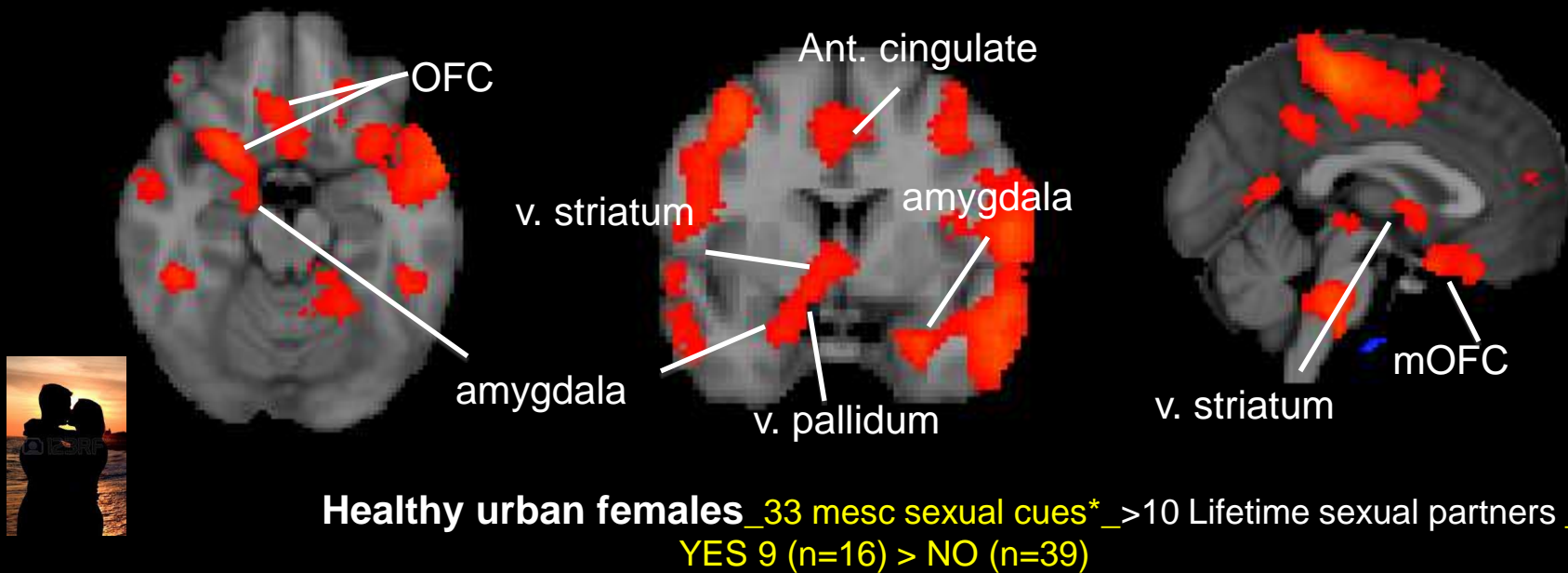
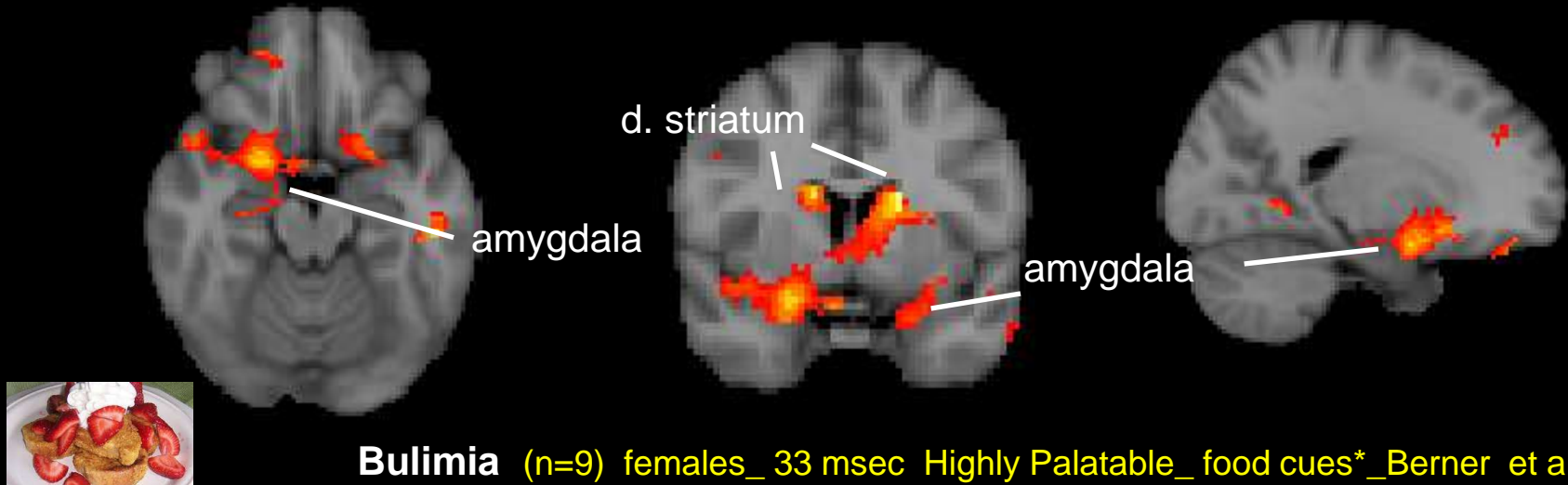
Highly palatable 500 msec **FOOD cues** * trigger reward-motivational circuitry in healthy young women at-risk for weight gain (“historical dieters”, but **currently normal weight**) .

Ali Ely, et al. Obesity 2013



(* v. neutral cues)

Which cue-image is from an “addicted” brain?



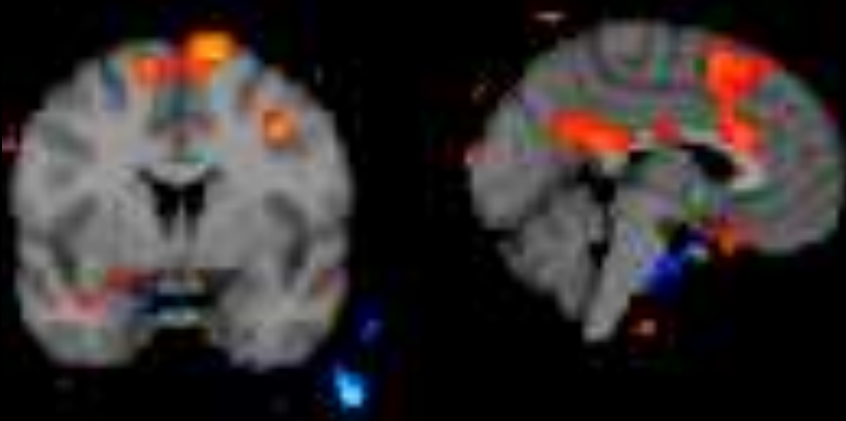
(* v. neutral cues)

Which cue-image is from an “addicted” brain?

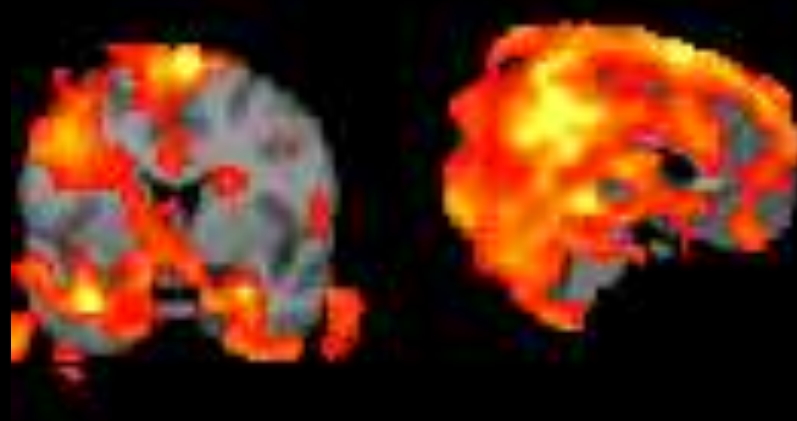


Male Cocaine Patients

(6 sec cocaine video cues * ; first half)



GOOD Clinical Outcome sub-group
(<30% cocaine positive urines), n=9



POOR Clinical Outcome sub-group
(>90% cocaine positive urines) , n=12

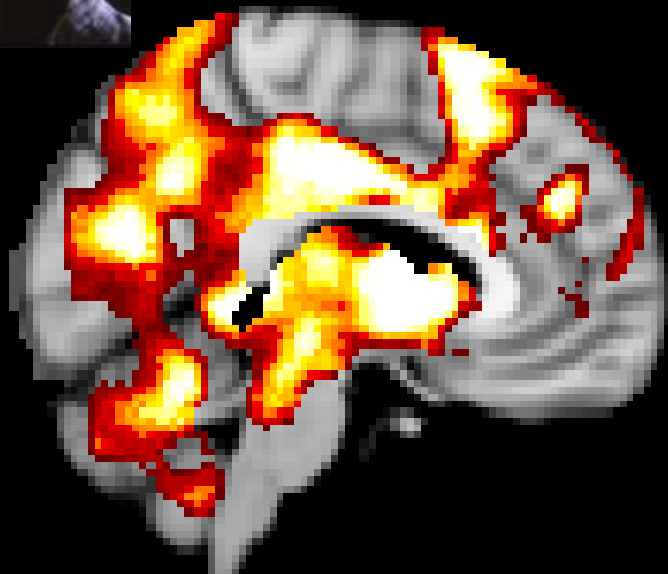
(v. neutral cues)

Which cue-image is from an “addicted” brain?



Male Cocaine Patients

(500 msec cocaine cues *)



Abuse Group (N = 11)



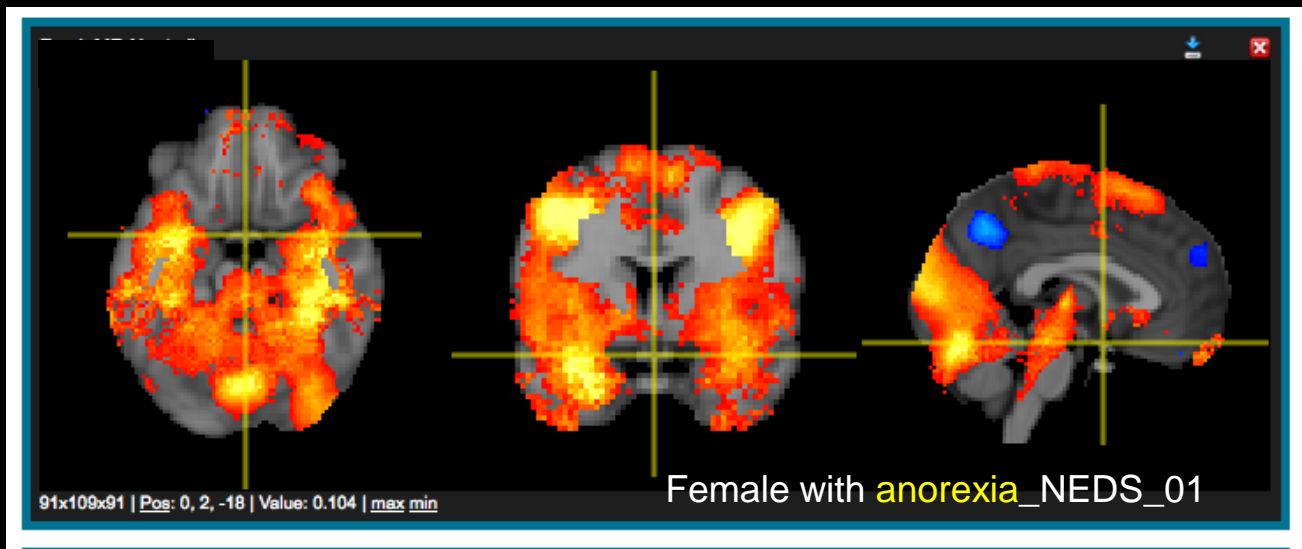
No Abuse Group (N = 14)

(* v. neutral cues)

Which cue-image is from an “addicted” brain?



33 msec



500 msec

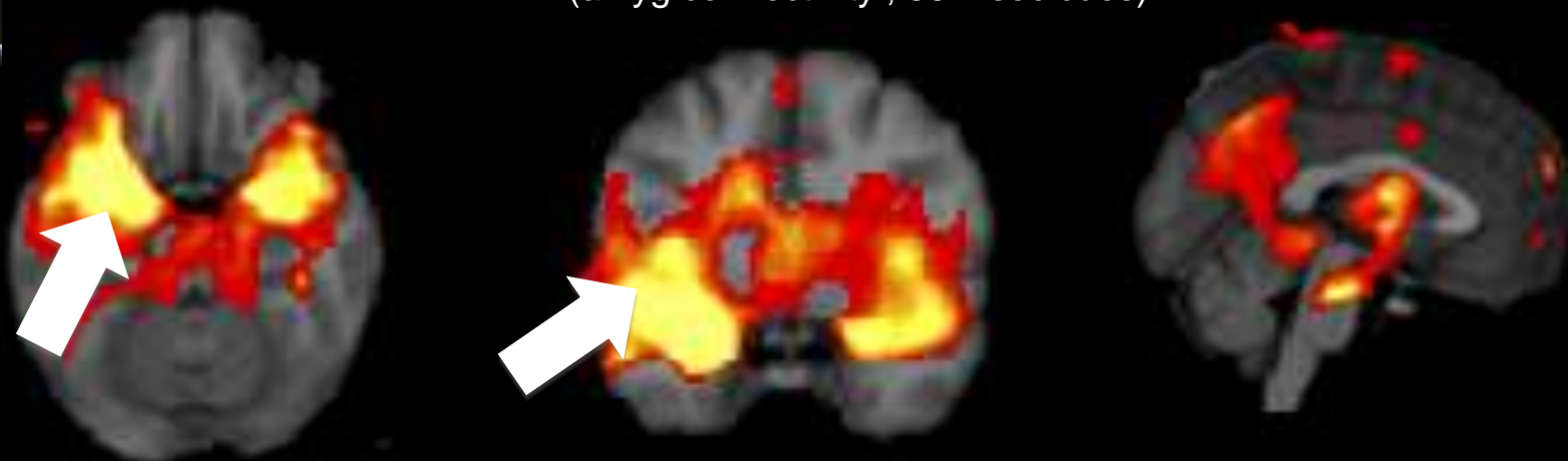


(* v. neutral cues)

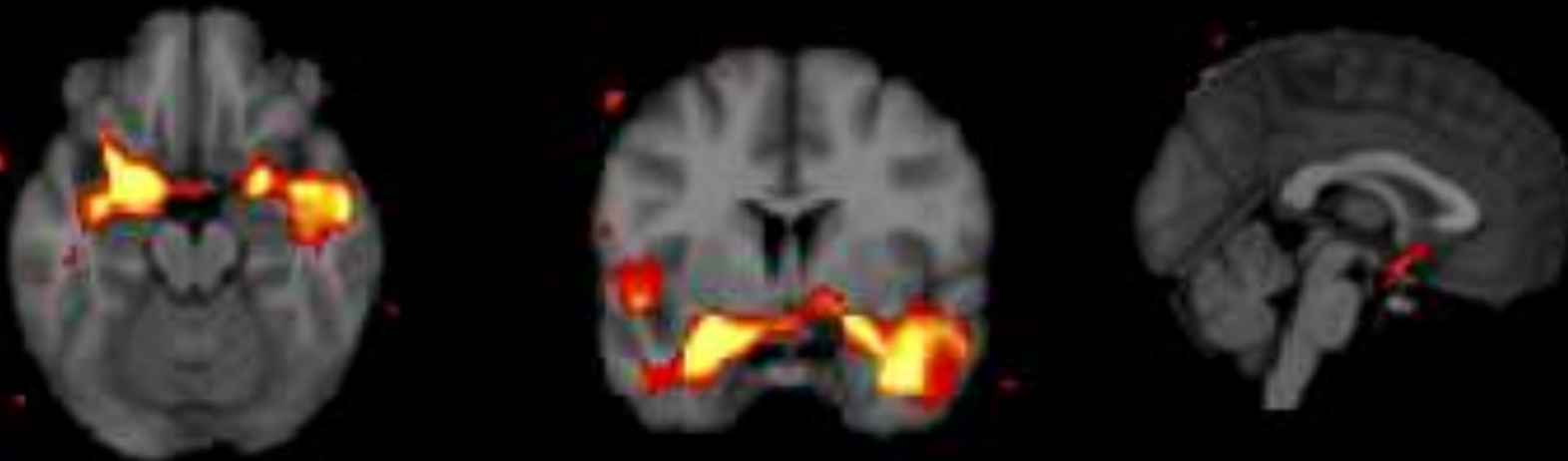
Which cue-image is from an “addicted” brain?



Male Cocaine Patients
(amyg connectivity , 33 msec cues)



POOR Clinical Outcome sub-group (>90% cocaine positive urines) , n=12

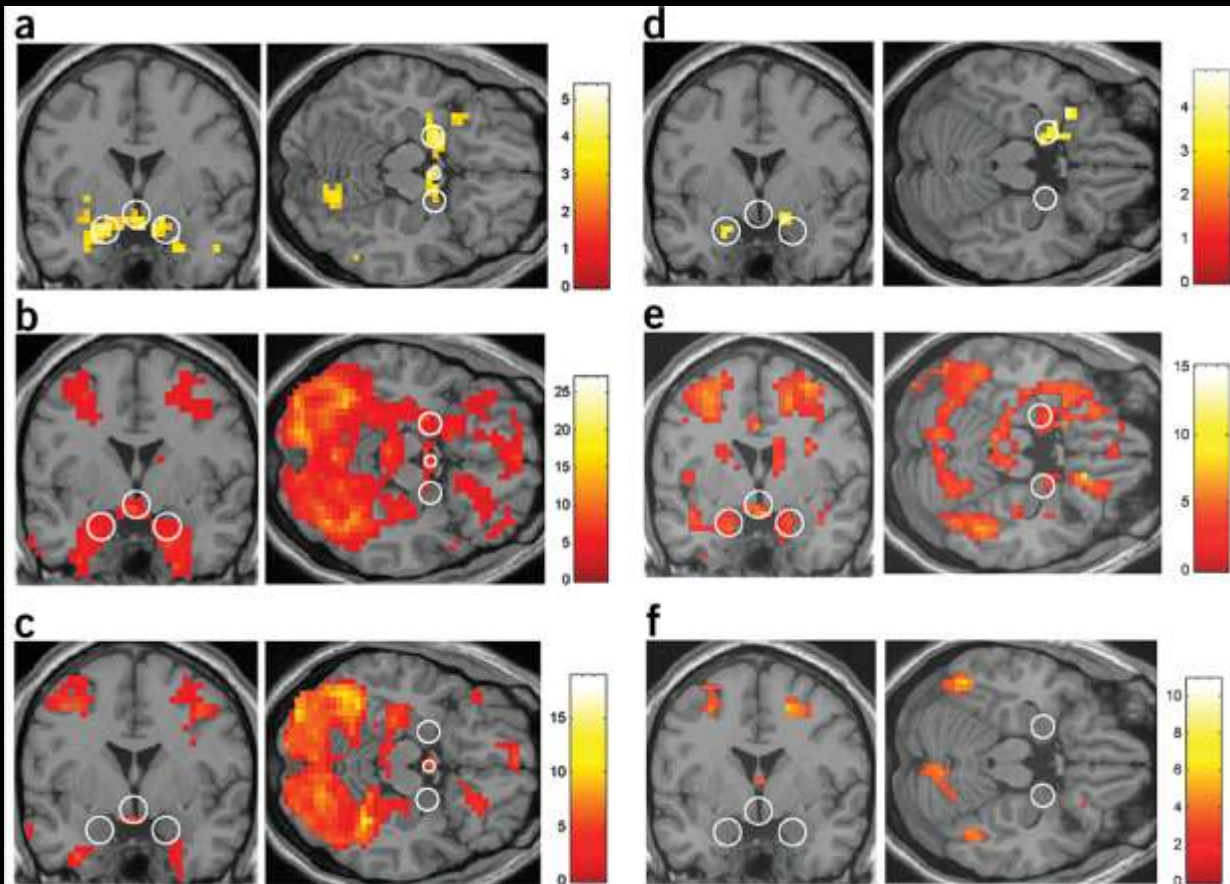


GOOD Clinical Outcome sub-group (<30% cocaine positive urines), n=9

Which cue-image is from an “addicted” brain?

Healthy males > healthy females in arousal to sexual cues):
amygdala, v. striatum, hypothal (Hamann, et al. NN 2004)

Men >
Women



Healthy
men

Healthy
women

Naked couple vs. fixation

Naked couple vs. neutral

(5 x 3.75 sec stimulus block)





ADDICTION



Q 1: Can fMRI distinguish cue responses related to.... **“reward”** vs. **“addiction”** ?

[[[**“DIAGNOSTIC”** role ?

]]]

NO, at least not yet →>> Though a lot of very interesting population variability in the brain response to reward cues, the colorful images are not currently helpful for **DIAGNOSTICS** – for determining **whether** someone is “addicted” or not – (neither the location, nor the magnitude, of the brain response to reward cues is ‘diagnostic’ of addiction to drugs, food, sex, etc.)

....OK....but what about a **PROGNOSTIC** role, for identifying treatment targets across problematic reward pursuit ?





ADDICTION



Q 1: Can fMRI distinguish cue responses related to....”reward” vs. “addiction” ?

[[[“DIAGNOSTIC” role ?

]]]

Q 2 : ((If not ‘diagnostic’)) → can fMRI (still) be powerful in parsing **phenotypic subgroups, predicting future vulnerability / outcome, and thus...providing treatment targets?**

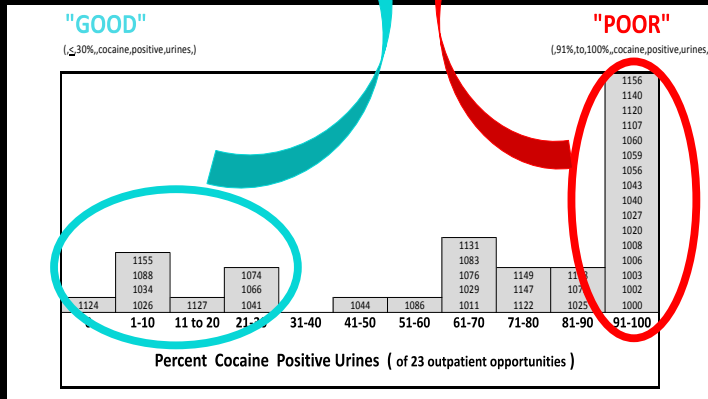
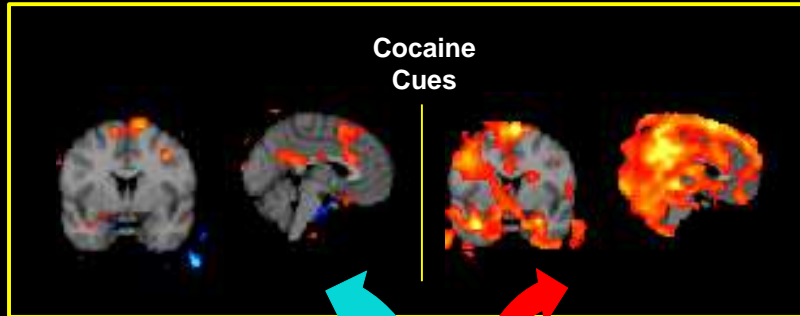


Cocaine patients with future **POOR** drug use outcomes have a heightened brain response to **6 second Cocaine (v. Neutral) VIDEO clips** – in our Craving Inhibition task.

OUTCOME Phenotype

“GOOD”

“POOR”



Top Figure. Dramatic brain response to 6 second cocaine (v. neutral) video clips for cocaine patients with POOR (n=12) v. GOOD (n=9) outcomes. SPM8 Images (t maps) thresholded at $2 < T < 5$ for display on MNI template.

[Images above based on first half of the 6-second task, to minimize impact of carryover on the neutral referent. Data available for n=9 from “GOOD” ; n=12 from the “POOR” subgroup].

Bottom Figure. Histogram of two phenotypic extremes chosen to examine the brain response to 6 sec cocaine videos: “GOOD”, $\leq 30\%$ cocaine positive/missing urines during 12 outpatient weeks, and “POOR” ($>90\%$ cocaine positive or missing urines during the 12 outpatient weeks).

Does the brain response to 6 sec cocaine reward cues have a **“PROGNOSTIC”** role ?

Yes –

We **can** link the brain response to (visible) cocaine cues to **relapse**.

Individuals who will proceed to **“POOR”** urine outcomes ($>90\%$ cocaine-positive or missing) have a heightened brain response to cocaine cues...whereas those proceeding to **“GOOD”** outcome have a low response.

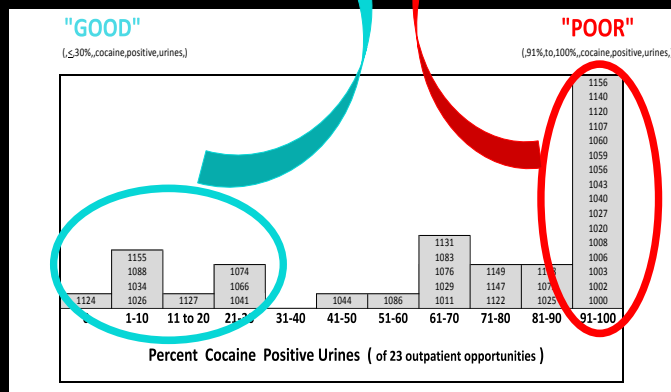
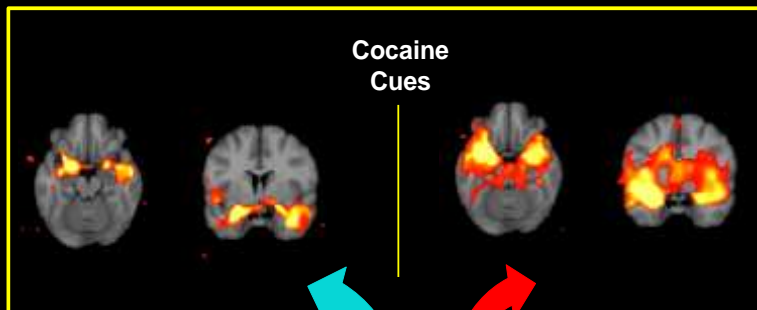
33 msec “Unseen” Cocaine Cues

Cocaine patients with future **POOR** drug use outcomes have a heightened pre-treatment intra-limbic (R amygdala) connectivity during 33 msec “unseen” cocaine cues

OUTCOME Phenotype

“GOOD”

“POOR”



Top Figure. Brain connectivity response in motivational circuitry to “unseen” cues for cocaine patients with POOR (n=12) v. GOOD (n=9) outcomes. SPM8 Images (t maps) thresholded at 5, range +10 to -10 for display on MNI template.

Bottom Figure. Histogram of drug use outcomes following discharge from the inpatient stay. Two phenotypic extremes were chosen for examination of the brain response to 33 msec cocaine cues: “GOOD”, $\leq 30\%$ cocaine positive or missing urines during the 12 outpatient weeks, and “POOR” ($>90\%$ cocaine positive or missing urines during the 12 outpatient weeks).

Does the brain response to 33 msec cocaine reward cues have a **“PROGNOSTIC”** role ?

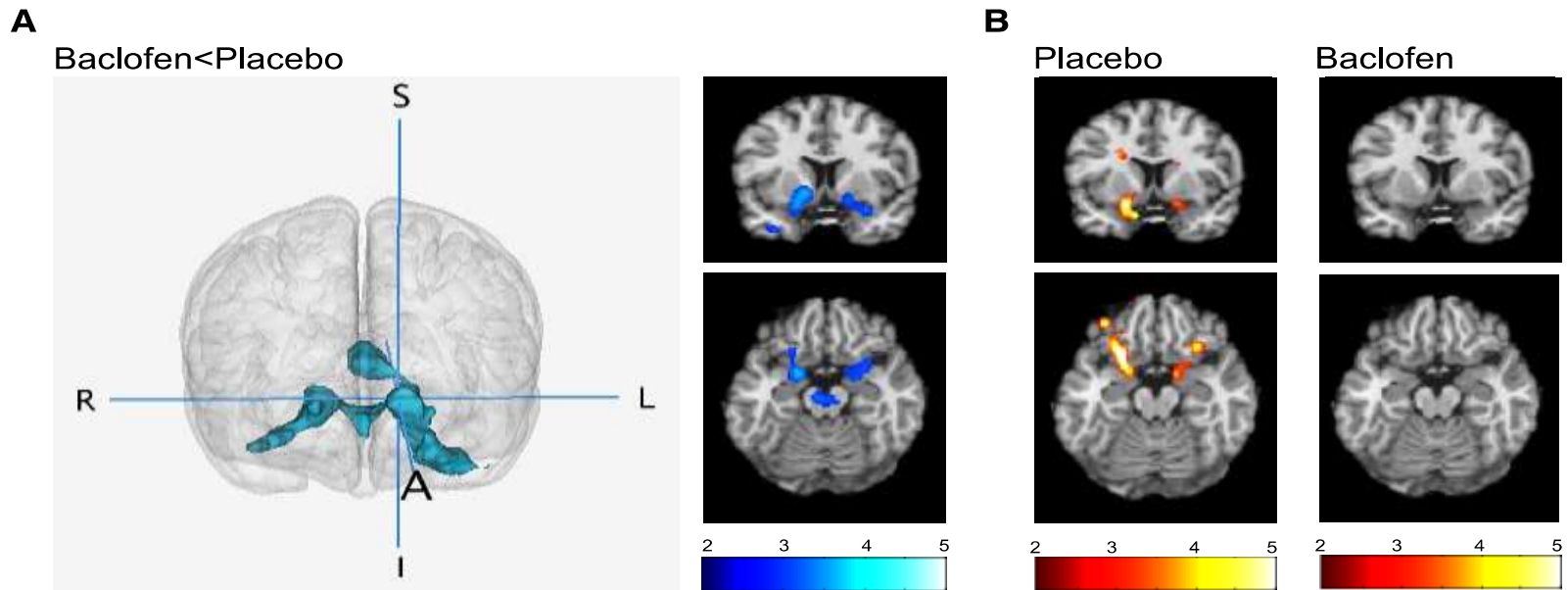
Yes –

We can link the brain response to 33 msec “UNSEEN” cocaine cues to relapse.

Individuals who will proceed to “POOR” urine outcomes ($>90\%$ cocaine-positive or missing) have a heightened intra-limbic (amyg conx.) to 33msec cocaine cues...whereas those proceeding to “GOOD” outcome...do not.

Does the brain response to **cocaine reward cues** have a **[[[“PROGNOSTIC” role ?]]]** in screening candidate medications, and predicting treatment response?

The GABA B agonist baclofen blunts limbic activation to 33 msec cocaine cues



(A) Baclofen-as compared to placebo-treated cocaine patients (B) show blunted activation in a large inter-connected cluster spanning v. striatum, v.pallidum, amygdala, midbrain and OFC. *Our “unseen” cue probe is sensitive to a DA-modulating medication.* **Young et al. *Journal of Neuroscience*, 2014.**

Does the brain response to **FOOD and SEXUAL** reward cues have a
[[[“PROGNOSTIC” role ?]]]

Yes – Burger and Stice, NI, 2014. → caudate inc. (**food cues** -- anticipation) and pallidum decrease (to food receipt) predicted weight gain in healthy young women at 12 mo.

Yes – Demos and Heatherton, JN 2012 → Nacc inc. to **food** or **sexual** cues predicted future BMI, and sexual activity (at 6 months).

Stay tuned ! – Childress and Lowe → using fMRI-**food** cues to predict weight gain in eating disorders (from bulimia to anorexia) – just underway....

Stay tuned !– Childress & Teitelman -- > using fMRI-**sexual** cues to predict unprotected sex (HIV sexual risk) in young urban women at risk for HIV (n=56).



ADDICTION



Q 1: Can fMRI distinguish cue responses related to.... **"reward"** vs. **"addiction"** ?

"DIAGNOSTIC" role ? **]]** NOT yet

[[[

Q 2: Can fMRI (still) be powerful in parsing **phenotypic subgroups**, **predicting future vulnerability / outcome**, and thus...**providing treatment targets – screening candidate medications?**



[[["PROGNOSTIC" role ?]]] YES



Acknowledgements

NIDA U54 (New Cocaine Cooperative Medication Development Ctr.)

NIDA P50 Cocaine Medication Development Center

NIDA P60 DA 005186 (Improving Treatment of Drug Abuse)

NIDA RO1 DA 10241 (Coc Cue + Inhibition)

NIDA RO1 DA 12162 (Coc Cue + Baclo)

NIDA RO1 DA 15149 (Coc Cue – ASL fMRI)

NIDA KO1 (Nic Cue, Franklin)

NIDA K23 (Opiate Cue, Langleben)

NIDA CSP #1021 (Baclofen Multi-site Clinical Trial)

NIDA R01 DA025906 (“Unseen” Coc Cue Extinction)

NIDA R21/R33 DA026114 (Coc Cue + Real-time fMRI)

NIDA T32 Translational Addiction Research (Childress/Pierce)

NIDA RO1 Pharmacoresponsive endophenotypes (Franklin)

NIDA RO3 Affect Dysregulation as a vulnerability (Suh)

DANA Foundation (SPECT imaging of DAT in nicotine dep: Franklin)

ALEXANDER Foundation -- novel fMRI

CURE Addiction Center of Excellence (Childress)

VA Medical Research Division / MIRECC



Ned the Neuron visits
The Art of Neuroscience
at SfN



H Kathleen Childress Designs from the "Synapse Series"