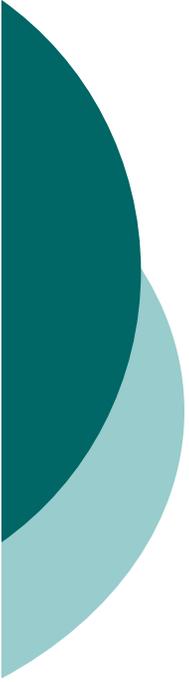# Predicting Relapse in Methamphetamine Dependent Individuals

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Stimulant Dependence

- **Stimulants**
  - **Cocaine**
  - **Methamphetamine**
  - **Amphetamine**
- **12 – 15% ever tried stimulants**
- **1-3% have stimulant dependence**
- **50% of sober stimulant dependent individuals relapse within a year.**

Relapse

- An important public health problem.

- Predicting relapse may help to deliver targeted interventions to those individuals at risk.

- Current methods to predict relapse have
  - Low specificity (many false positives)
  - Moderate sensitivity (frequent false negatives)
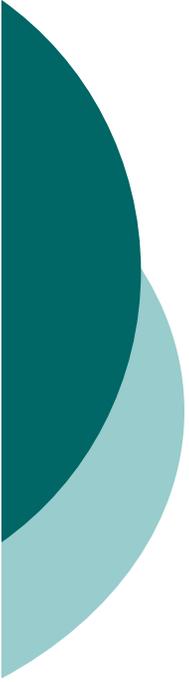
Decision Making and Relapse

- **Decision-making:**
  - Person has to select among several options.
  - Each option can be associated with positive or negative outcomes, which may be uncertain.

  - Key elements of decision situations:
    - Probability of an outcome associated with an option.
    - The positive or negative consequence.
    - The magnitude of the consequence

Study Goals

- **Neurobiology of decision-making dysfunctions in stimulant dependent subjects.**

- **Can functional magnetic resonance imaging be used as a tool to predict relapse?**

Subjects

VA DESERT PACIFIC
HEALTHCARE NETWORK

46 methamphetamine dependent subjects sober for a median of 25 days

6 lost to follow up

40 subjects followed up a median of 370 days

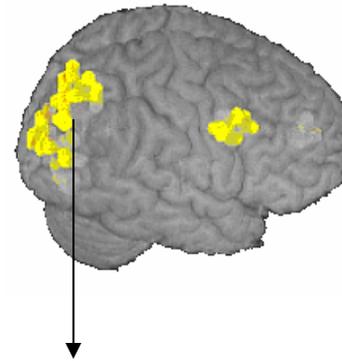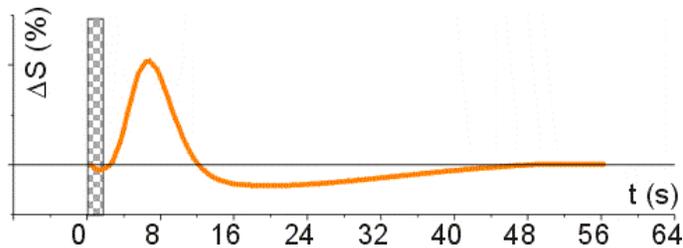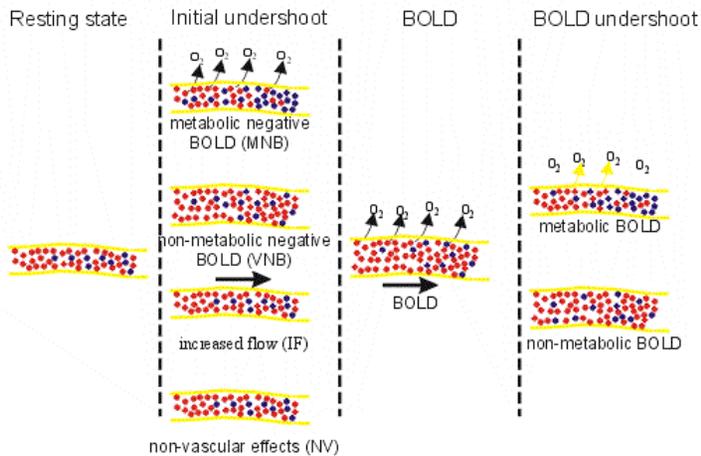NO RELAPSE:

22

RELAPSE:

18
279 days median sober time
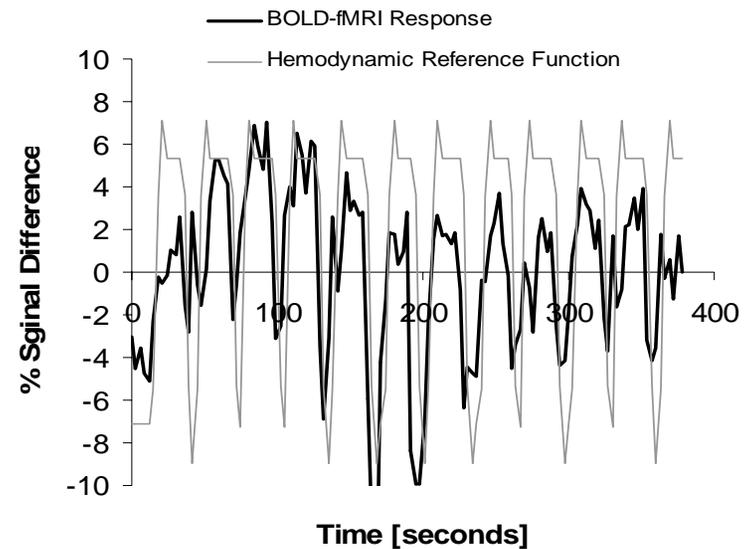
BOLD-fMRI

Hemoglobin is **diamagnetic** when <u>oxygenated</u> but **paramagnetic** when <u>deoxygenated</u>.

Physiology of tri-phasic response

Right parietal cortex voxel
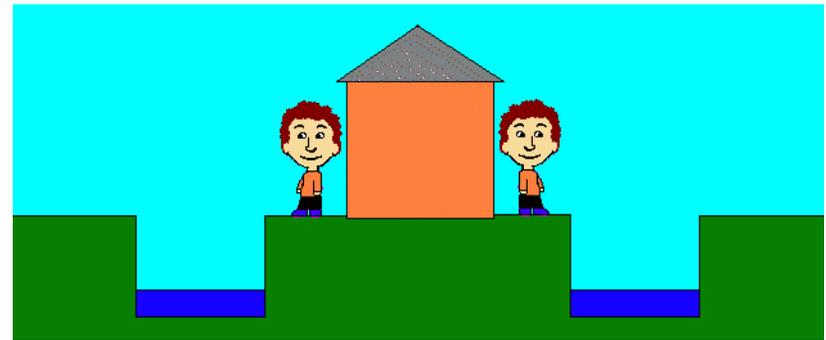
Assessment Protocol

Baseline Assessment:

Diagnostic: SCID
Symptom: BPRS / HDRS / YMRS
Neuropsychology: DKEFS
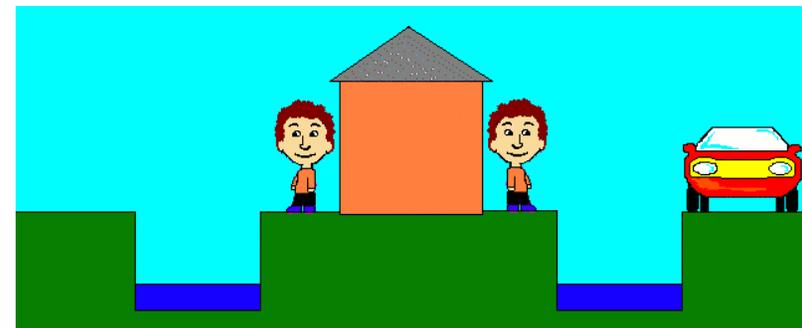Decision-making: Two-choice Prediction
task, Iowa Gambling Task

fMRI:

Block Design
Two-choice Prediction Task
versus
Two-choice Response Task

Two-Choice Prediction Task
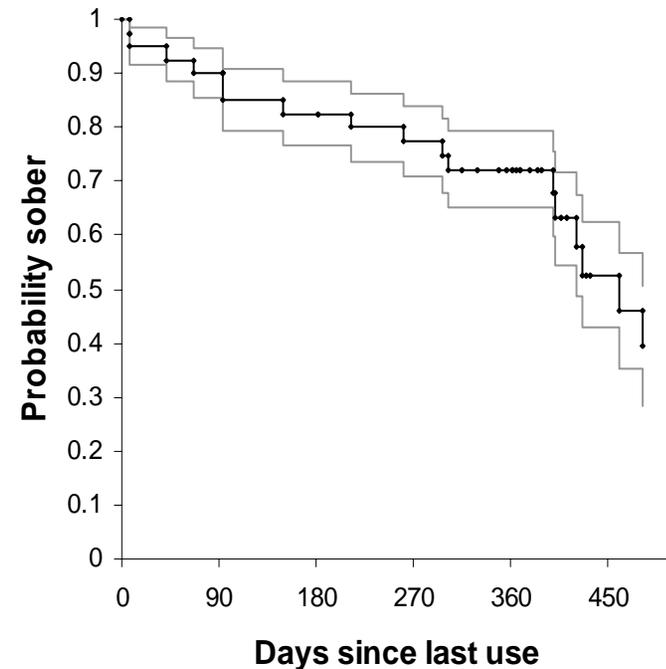

Two-Choice Response Task

Sobriety Survival Function

○ **Sobriety assessment:**

  ● Semi Structured Assessment for the Genetics of Alcoholism.

○ **Relapse:**

  ● any use of methamphetamine during any time after discharge.

Subjects' Socio-demographics

	Non-relapsers		Relapsers	
N	22		18	
Age (years)	40.3	8.8	41.9	9.0
Race/Ethnicity (n):				
Caucasian	15		12	
Other	7		6	
Marital Status (n)				
Married	1		2	
Divorced/Separated	17		10	
Never Married	4		6	
Education (years)	12.9	1.2	13.5	1.0

Subjects' Use Characteristics

	Non-relapsers		Relapsers	
Use Characteristics	Mean	SD	Mean	SD
Years of use	14.9	10.0	17.3	8.0
Sober days before imaging	27.4	8.3	27.8	11.0
Current Alcohol / Marijuana abuse (n)	5		7	
Follow up Characteristics				
Follow up duration [days]	437	165	440	304
Marijuana use during follow up (n)	1		2	
Cocaine use during follow up (n)	1		0	
Symptom Ratings				
HDRS 21	7.1	7.8	10.2	7.6
BPRS	27.3	7.9	30.4	6.8
YMRS	1.7	2.7	5.4	6.9

Behavioral Performance

Behavioral Measures	Non-relapsers		Relapsers	
	Mean	SD	Mean	SD
Response latency [msec]	808	361	794	794
Switching rate	0.50	0.12	0.49	0.10
Win-stay fraction	0.61	0.19	0.67	0.15
Lose-shift fraction	0.62	0.22	0.67	0.18

Nine brain areas differentiated relapsing and non-relapsing subjects:

- prefrontal, parietal and insular cortex.

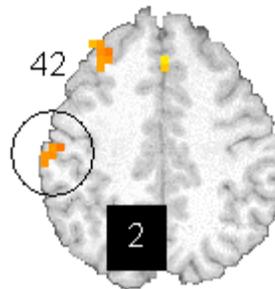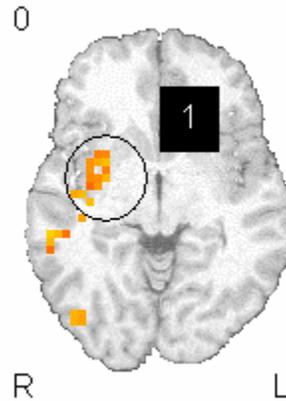○ **Non-relapsing individuals showed more activation than relapsing individuals**
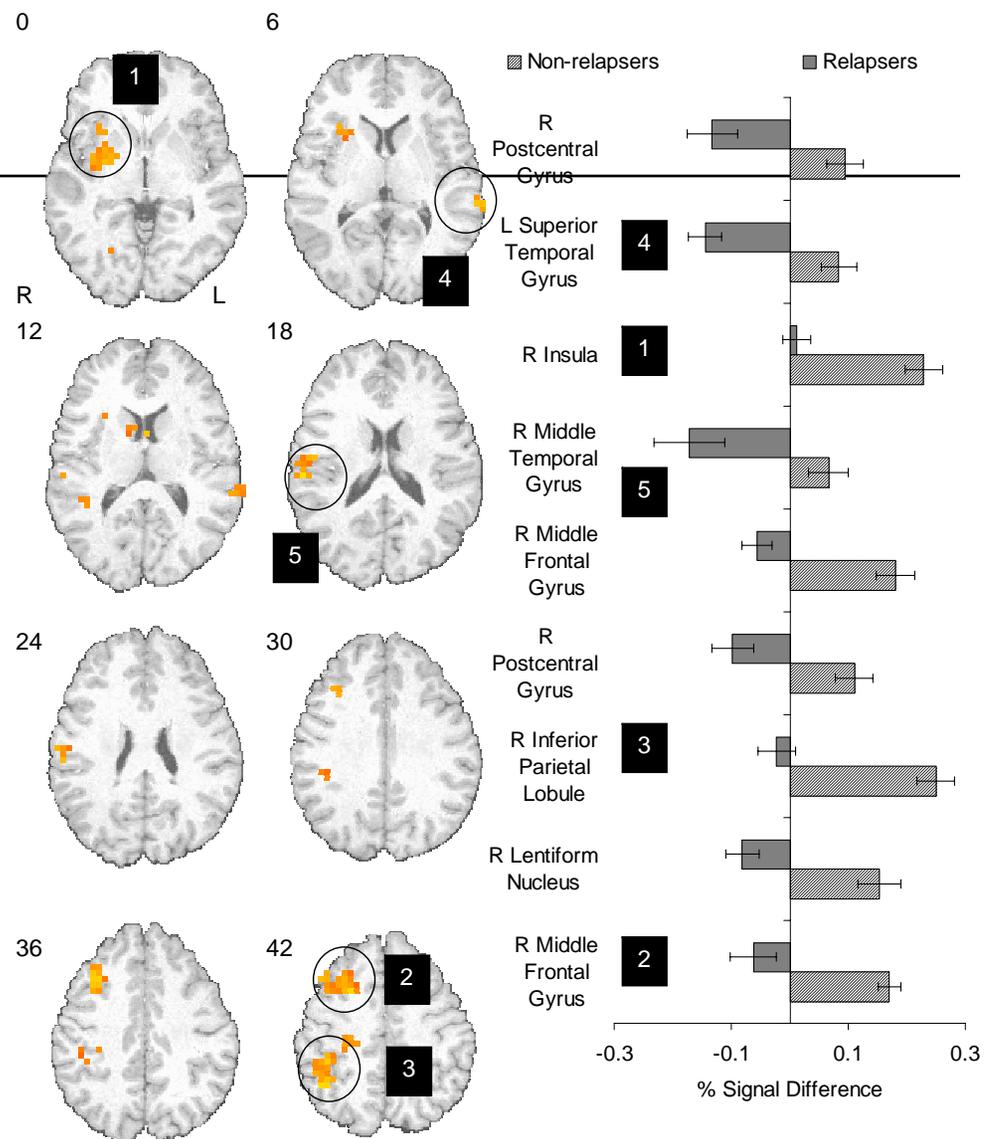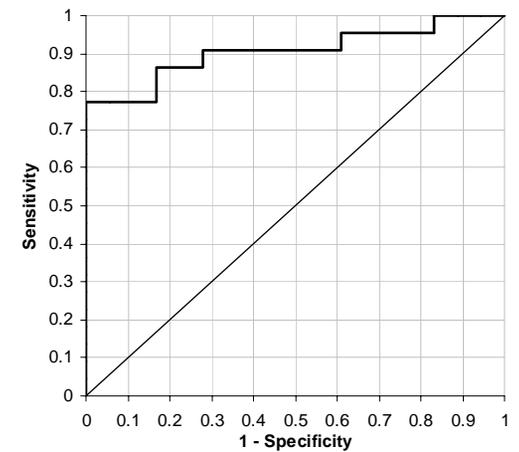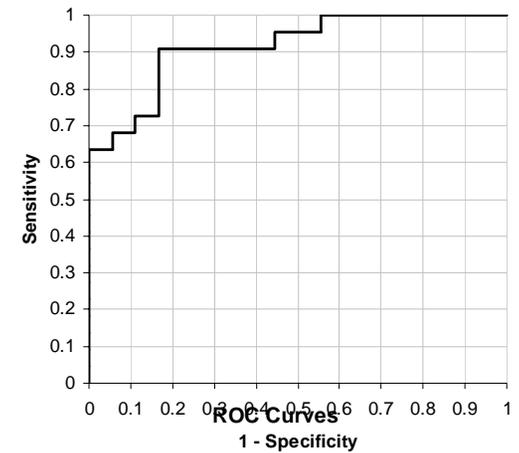
Prediction Accuracy

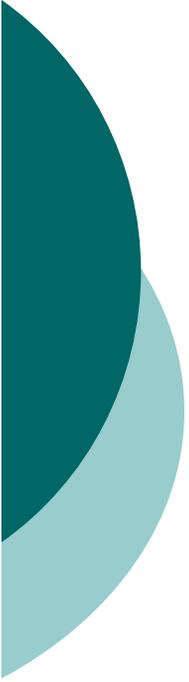|	Relapse	
	YES	*NO*
N (40 after a median of 370 days)	18	22
Correctly Predicted by Imaging	17	20
	Sensitivity 94.4%	Specificity 86.4%

Receiver Operator Curves

- With a specificity of at least 83.3%

- Sensitivity ranged from 54.5% to 90.9%.

Neural Systems Predicting Time to Relapse

○ **Activation in three different brain areas predicted increased time to relapse:**
- low activation in these areas at baseline was highly predictive of time to relapse (χ^2 = 23.9, df=3, p < .01)

| Area	Coefficient (SE)		Wald	p	Exp(B)	95% CI
R Middle Frontal Gyrus	-4.36	1.82	5.68	.017	.013	0.00 – 0.46
R Middle Temporal Gyrus	-3.38	1.66	4.10	.043	.034	0.001 – 0.89
R Posterior Cingulate	-5.960	2.22	7.18	.007	.003	0.000- 0.20
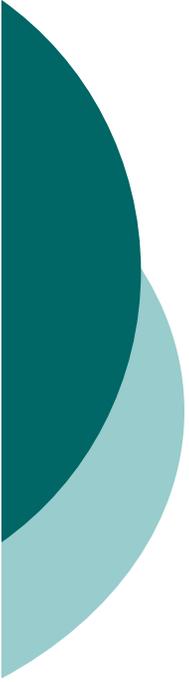
Summary & Conclusions

- **Functional Magnetic Resonance Imaging results predict relapse.**

- **Relapse = less activation in structures that are critical for decision-making**

- **Poor decision-making: "setting the stage" for relapse.**
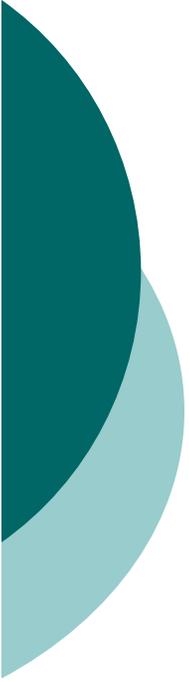
Candidate Processes

- **Insular cortex:**
  - Altered interoceptive processing during decision-making
  - Internal feeling states have less influence on predicting optimal behavior
- **Inferior parietal lobule:**
  - Poor assessment of the decision-making situation and subsequent reliance on habitual behavior.
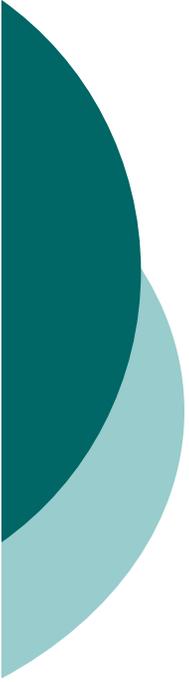
Take Home Message

- **Methamphetamine dependent subjects**
  - **Show brain patterns that can be used to predict whether and when relapse may occur.**
  - **Future studies:**
    - **What are the specific cognitive processes?**
    - **Do interventions have an impact on relapse?**
    - **Does this apply to other addictions?**