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# **Differential Brain Activity in Alcoholics and Social Drinkers to Alcohol Cues: Relationship to Craving**

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# Background

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- Functional imaging techniques have been increasingly used to evaluate craving
- Techniques include SPECT, PET, fMRI
- Considerable data with cocaine
- Few studies with alcohol

# Standard Methodology

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- Subject is given a cue
  - Pictures or video
  - Handling paraphernalia
  - Imagery
  - Odor
  - Sip or infusion
- Craving rated
- Images obtained

# Imaging and Craving for Alcohol

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|                 | Technique | Cue              | Findings   |
|-----------------|-----------|------------------|--|
| Modell, 1995    | SPECT     | taste            | R Caudate  |
| George, 2001    | fMRI      | taste/<br>visual | L DLPC, Anterior<br>thalamus                       |
| Schneider, 2001 | fMRI      | odor             | R Amg/hippo area, Sup<br>Temp gyrus, cerebellum    |
| Braus, 2001     | fMRI      | visual           | Ventral putamen, basal<br>ganglia                  |
| Wrase, 2002     | fMRI      | visual           | Ventral striatum, Ant Cing,<br>Orbitofrontal gyrus |
| Hommer, 1997    | PET       | mCPP             | Blunted OFC and PFC,<br>↑cerebellum and post cing  |

# Methods

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- While in a Philips 1.5 T MRI scanner, 10 non-treatment seeking alcoholics and 10 age and gender matched social drinking controls were given a sip of their favorite alcoholic beverage
- Subjects were then shown a 13 minute randomized presentation of visual cues (alcohol, non-alcohol beverage, and two control conditions) while changes in regional brain activity were measured in 15 transverse T2\*- weighted BOLD slices
- After each block of cues, subjects were asked to rate their current urge to drink alcohol
- Post scanning, fMRI data and subjective craving results were compared between the alcohol and control groups

# Stimulus Presentation

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# 1.5T Control Room

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# Examples of the various visual cues from Normative Appetitive Picture System (NAPS)

**Alcohol (A)**



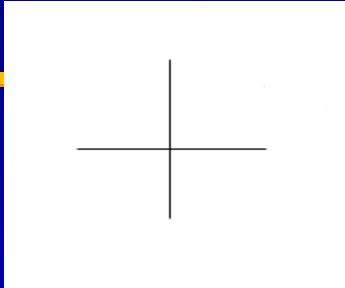
**Beverage (B)**



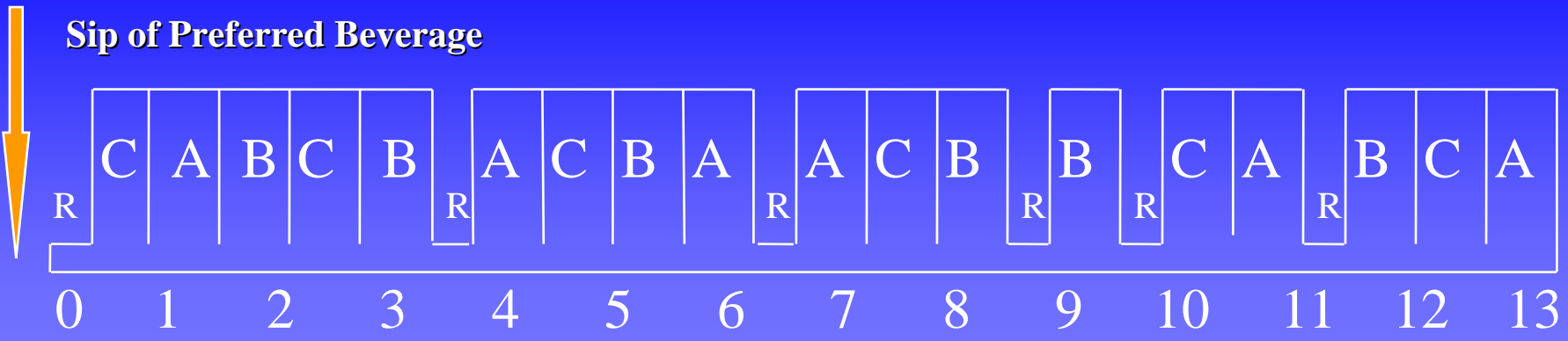
**Visual Control (C)**



**Rest (R)**



## Time Course of the Presentation of Stimuli During fMRI



\*Craving rated after each block

**Comparisons:** Alcohol - Beverage  
 Alcohol - Vis Ctrl  
 Vis Ctrl - Rest

Beverage - Vis Ctrl  
 Beverage - Rest



# Demographics

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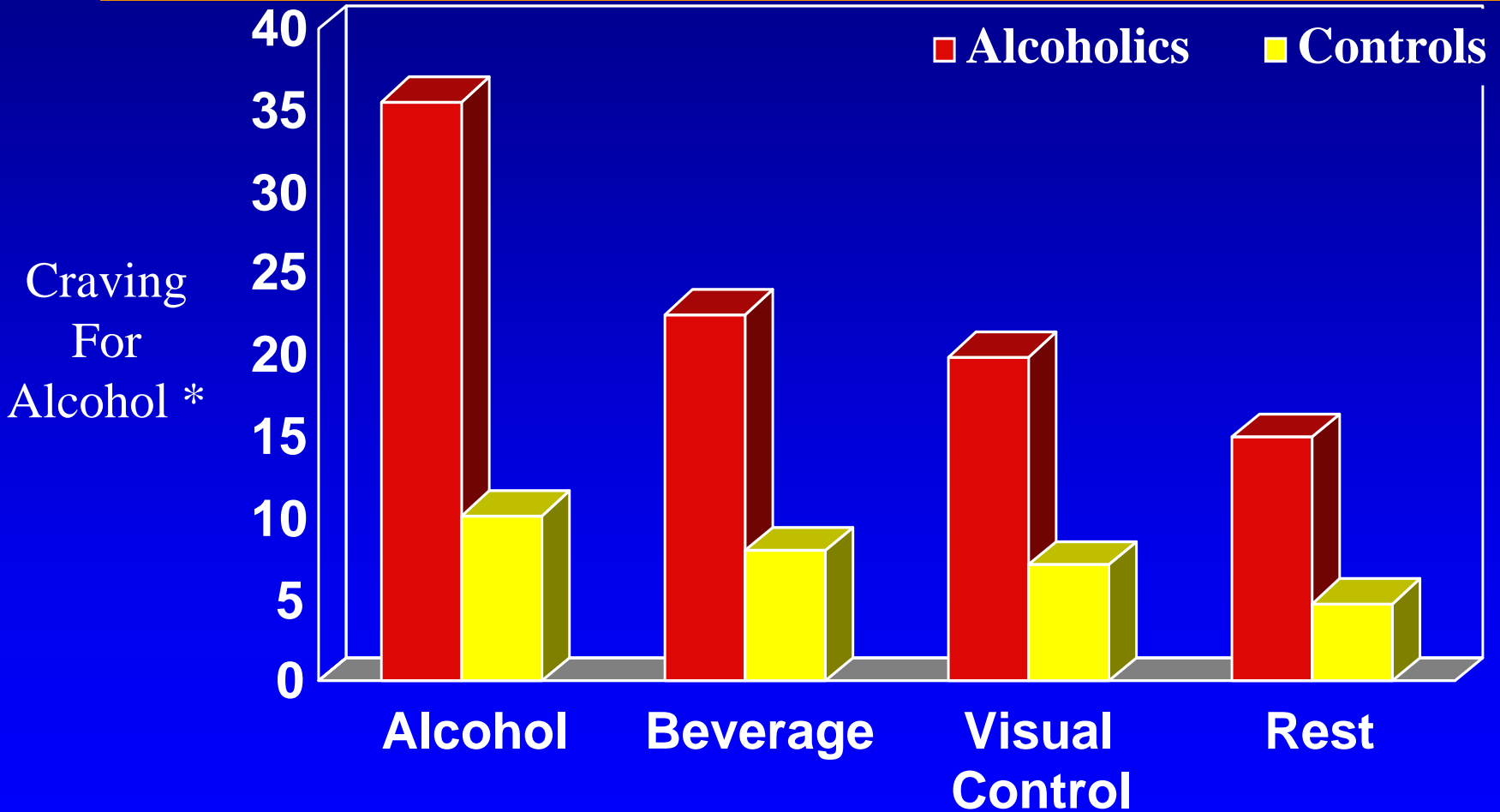
|                    | Alcoholics<br>(n=10) | Social Drinking<br>Controls (n=10) | Statistics     |
|--------------------|----------------------|------------------------------------|----------------|
| Age                | 33.60±11.51          | 33.10±10.44                        | Nonsignificant |
| Education          | 15.15±1.73           | 16.30±1.57                         | Nonsignificant |
| Gender (% Male)    | 80%                  | 80%                                | Nonsignificant |
| Race (% Caucasian) | 70%                  | 100%                               | Nonsignificant |

# Alcohol Use Parameters

|                         | Alcoholics<br>(n=10) | Social Drinking<br>Controls (n=10) | Statistics              |
|-------------------------|----------------------|------------------------------------|-------------------------|
| Drinks In Past<br>Month | 164.39 ± 99.54       | 11.93 ± 10.34                      | t = 4.82, df=18, p<0.01 |
| Drinks/Drinking<br>Day  | 8.17 ± 4.14          | 2.18 ± 1.34                        | t = 4.35, df=18, p<0.01 |
| Amount of<br>Craving    | 42.60 ± 22.17        | 8.30 ± 12.02                       | t = 4.30, df=18, p<0.01 |
| Frequency of<br>Craving | 35.90 ± 23.79        | 8.30 ± 12.02                       | t = 3.28, df=18, p<0.01 |
| OCDS *                  | 9.80 ± 4.78          | 2.6 ± 1.84                         | t = 4.77, df=18, p<0.01 |

\* Obsessive Compulsive Drinking Scale

# Within MRI Craving Ratings by Stimulus Condition



Between Subject Effects -  $F=10.712$ ,  $df=1$ ,  $p=.004$

\* Craving was rated on an analog rating scale (Range = 0 - 100)

# Image Data Analysis

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- Data were motion detected and corrected to  $<1\text{mm}$  using MEDx 3.3
- Data were then temporally filtered, spatially normalized into Talairach space, and spatially smoothed
- Individual z maps were generated using a delayed boxcar model, temporal smoothing, and an uncorrected F threshold of 0.999
- A cluster analysis was performed using SPM96 in MEDx3.3 on the group data (1-tailed z-map threshold of  $p<.05$  and spatial extent threshold of  $p<.05$ )
- A priori the alcohol minus beverage brain activity was considered the most salient contrast.

# Alcohol - Beverage Condition

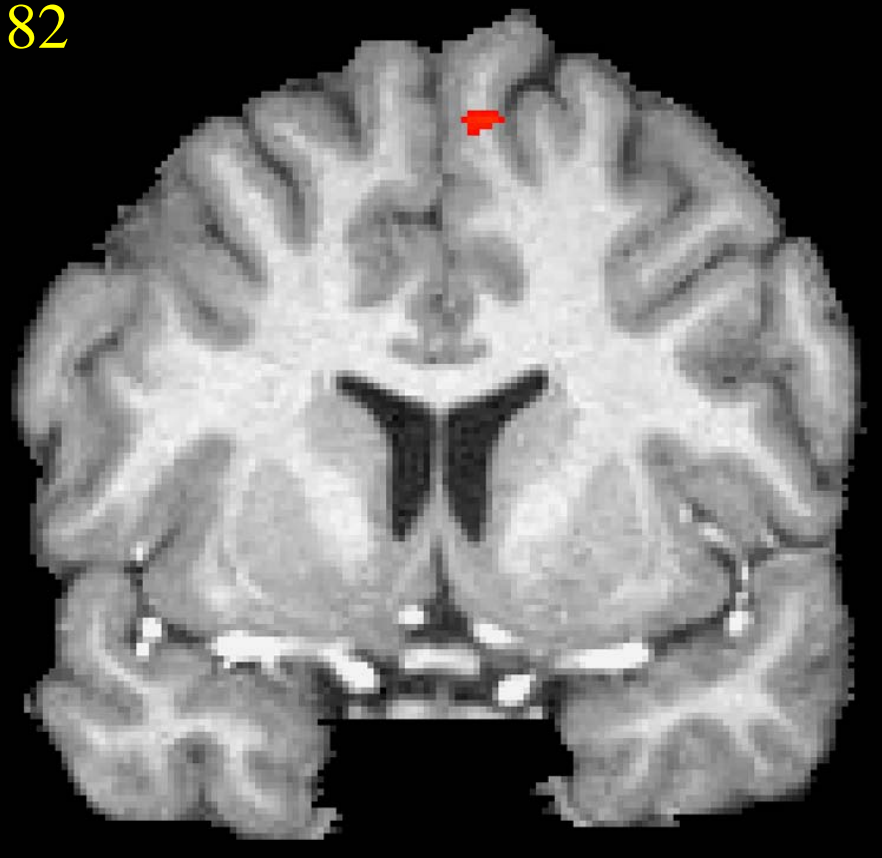
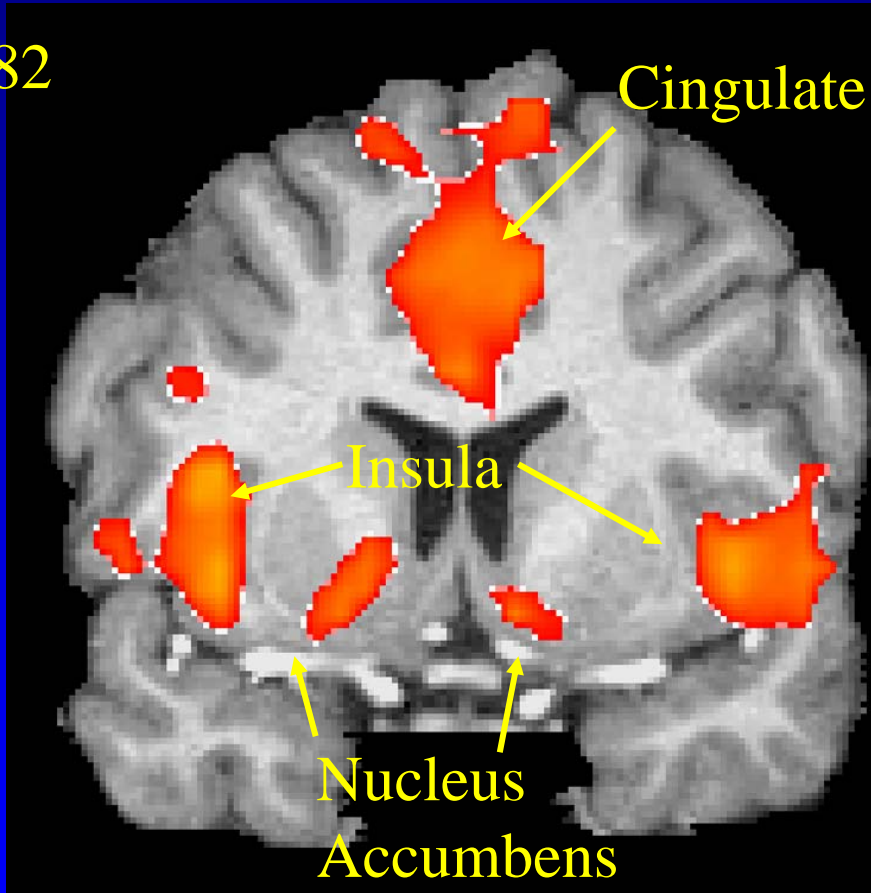
82

Cingulate

82

Insula

Nucleus  
Accumbens



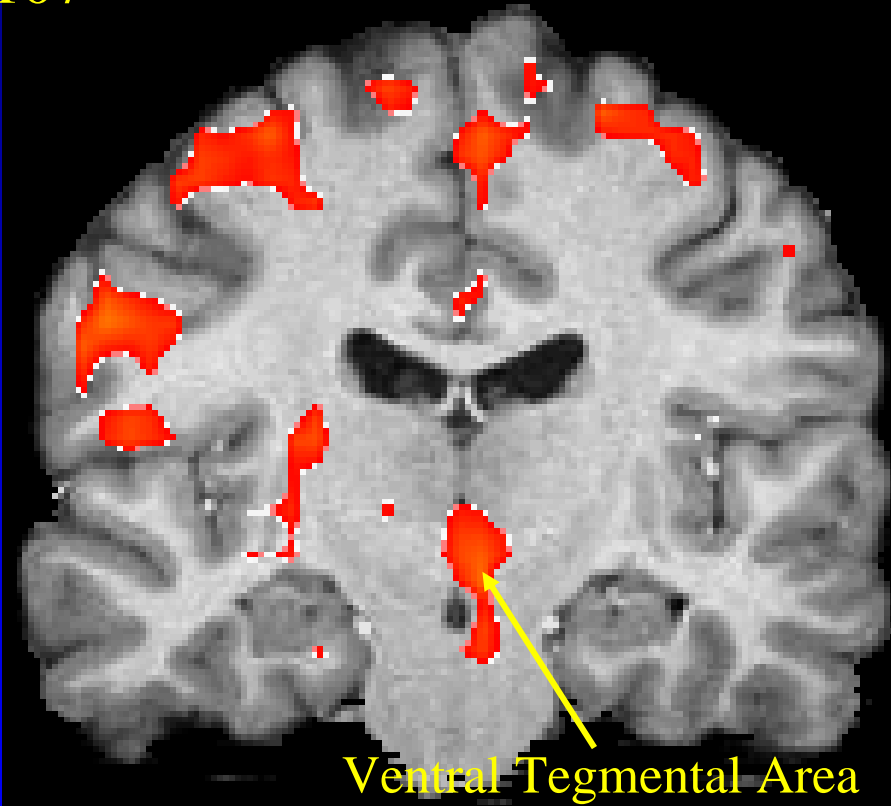
Alcoholics (n=10)

Controls (n=10)

Z=1.645 Ex .05

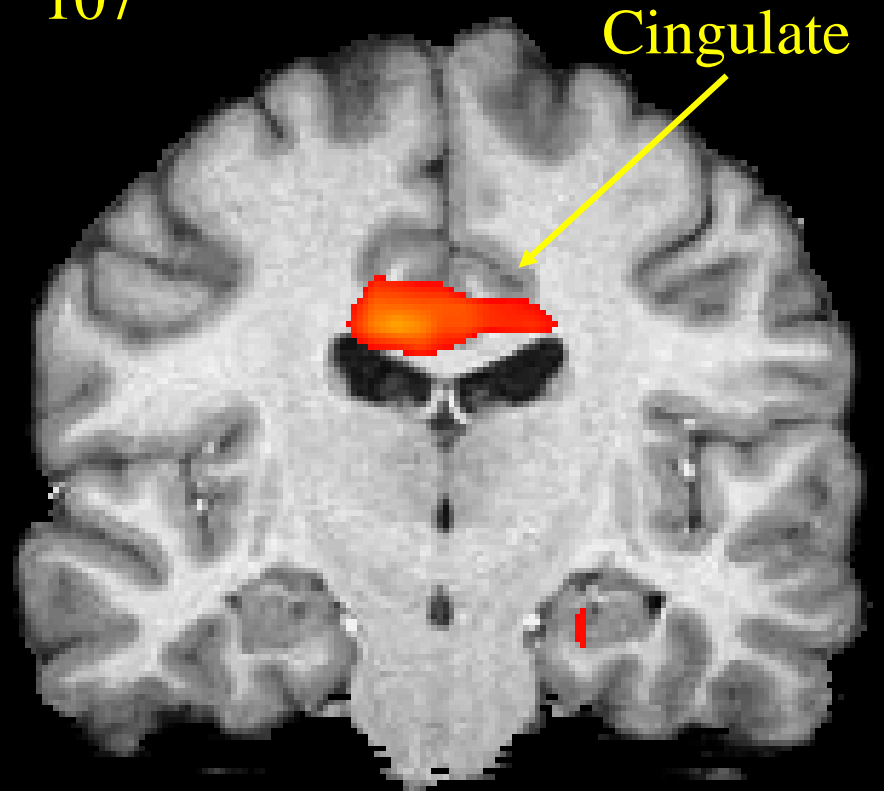
# Alcohol - Beverage Condition

107



Alcoholics (n=10)

107

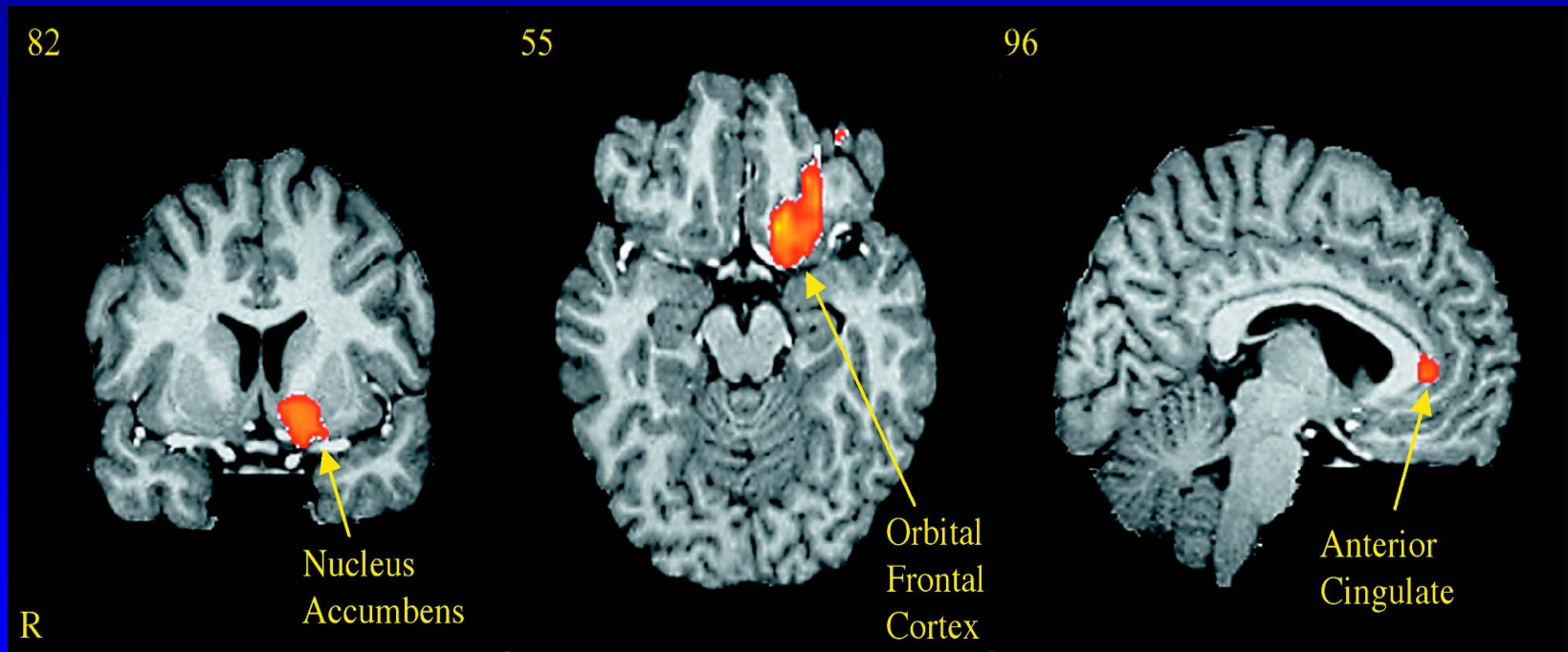


Controls (n=10)

Z=1.645 Ex .05

# Correlation of Image Data with Real Time Craving Ratings

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# Other Study Findings...

|                 | INSULA | CINGULATE | NAC | OFC |
|-----------------|--------|-----------|-----|-----|
| <b>COCAINE</b>  |        |           |     |     |
| Grant, 1996     |        | X         |     | X   |
| Breiter, 1997   | X      |           | X   |     |
| Mass, 1998      |        | X         |     |     |
| Childress, 1999 |        | X         |     |     |
| Wang, 1999      | X      |           |     | X   |
| Garavan, 2000   |        | X         |     |     |
| Kilts, 2001     |        | X         | X   |     |
| Wexler, 2001    | X      |           |     |     |
| <b>HEROIN</b>   |        |           |     |     |
| Sell, 2000      | X      |           |     | X   |
| <b>NICOTINE</b> |        |           |     |     |
| Brody, 2002     | X      | X         |     | X   |



# Limitations

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- Small sample size
- Exclusion of subjects due to head movement
- Unable to find between group differences in brain activity

# Conclusions

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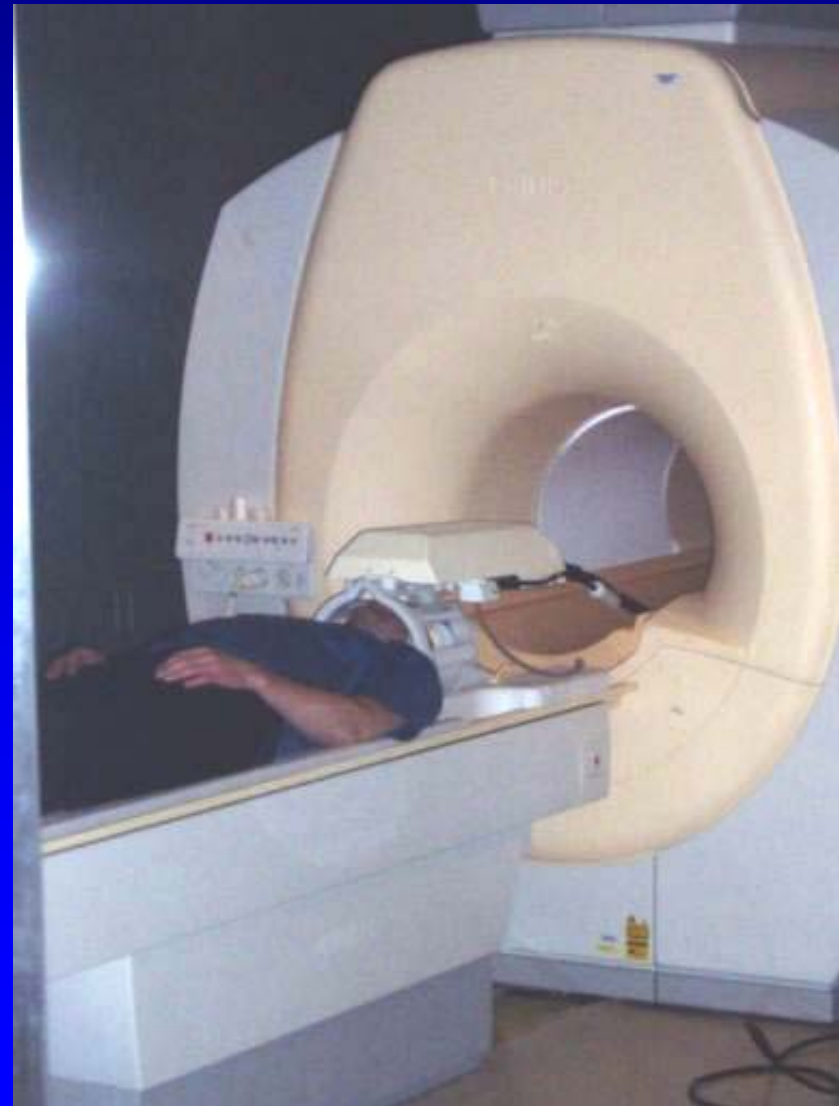
- Alcoholics, when exposed to alcohol cues, have increased brain activity in areas that have been reported to subserve craving for other substances of abuse.
- Furthermore, this study adds to a growing literature supporting the notion that craving for alcohol can be accomplished in the MRI environment

# Future Directions

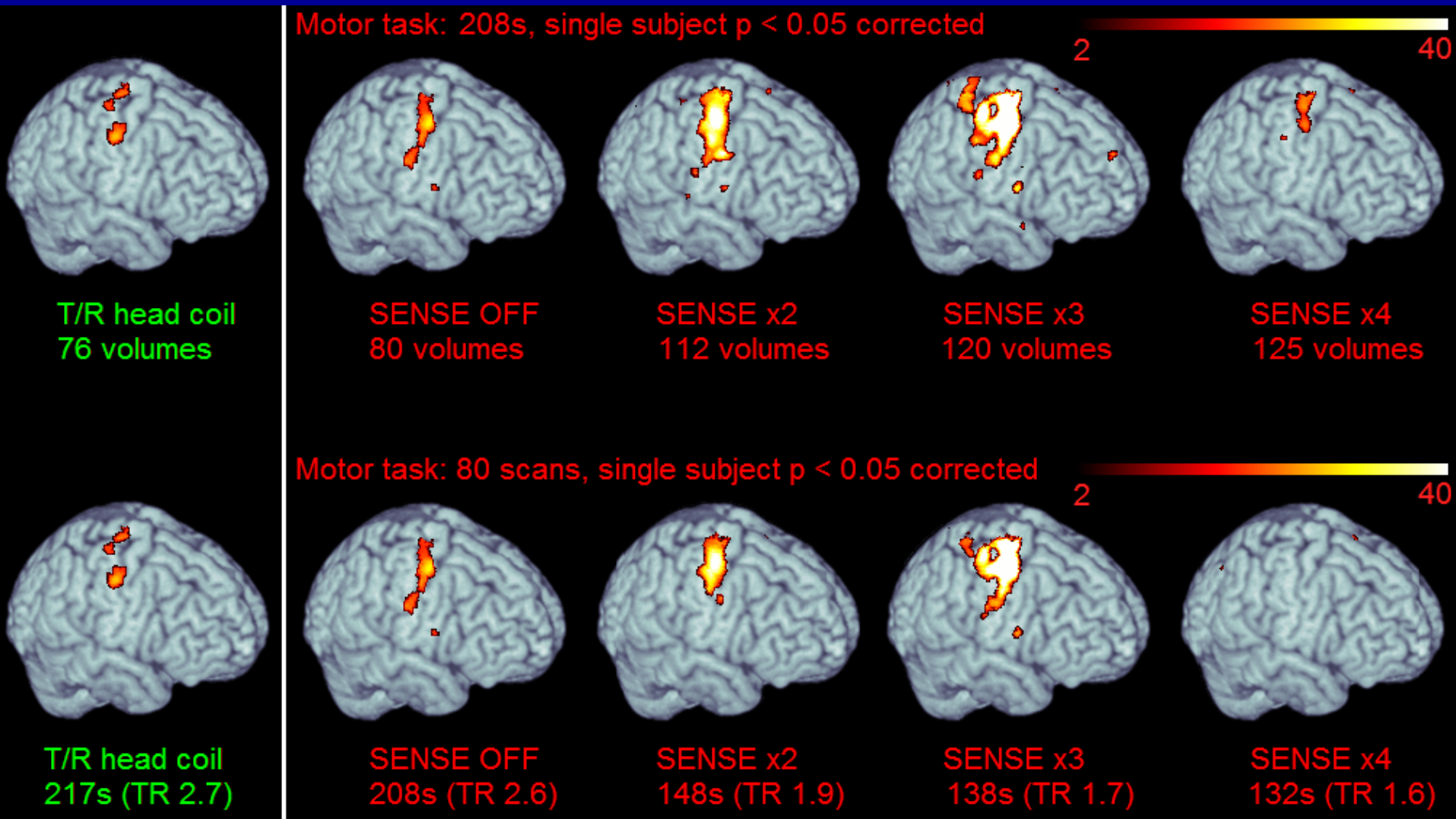
## Philips 3T: Big Maggie

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- **Potential** benefits of multichannel acquisition (SENSE)
  - Reduce spatial distortion
  - Faster image acquisition
  - Better Signal-to-noise

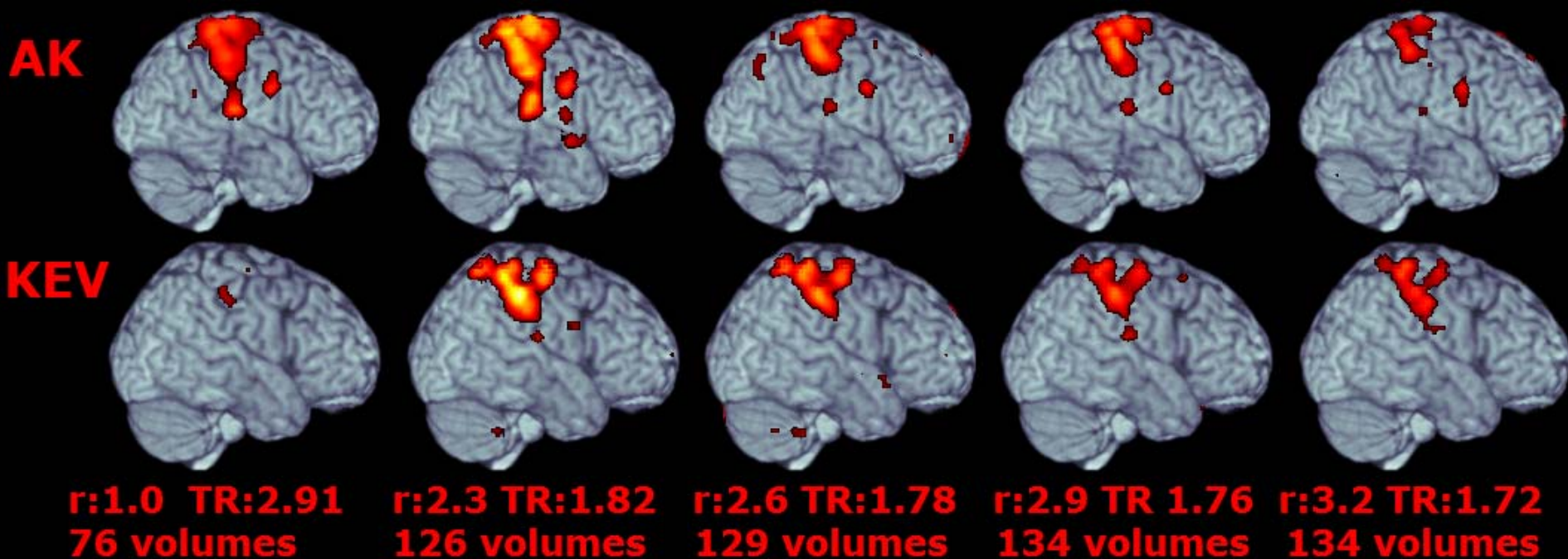


# Old T/R headcoil vs SENSE headcoil



# SENSE: best signal in 240 seconds

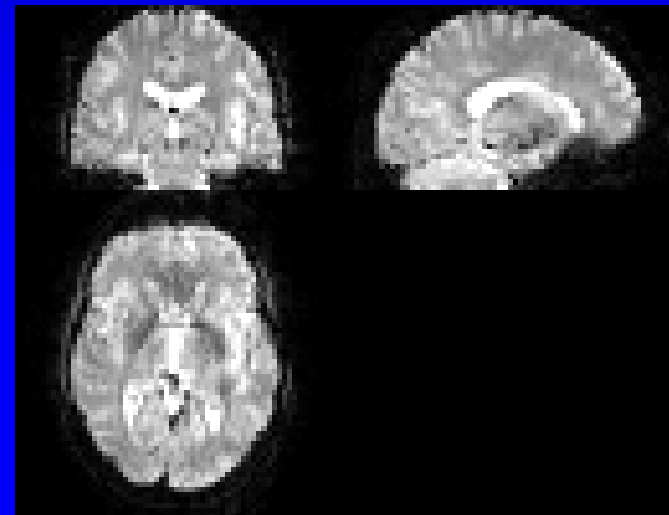
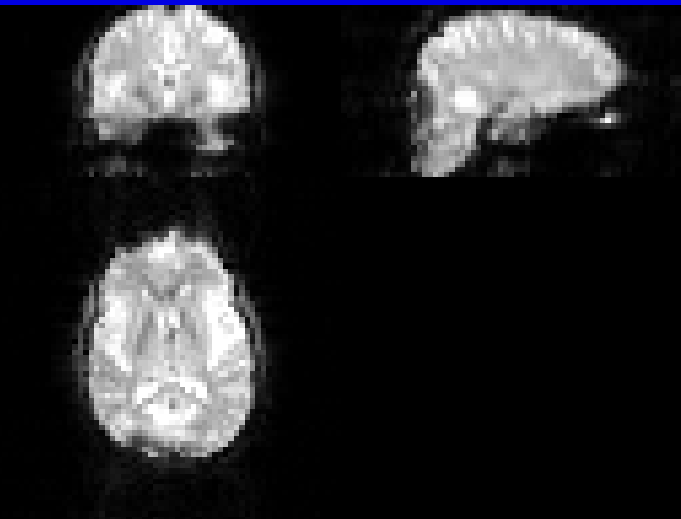
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# Improvements

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- Left: April 2003 (TR = 4s)
- Right: November 2003 (x2.3, TR = 1.8s)





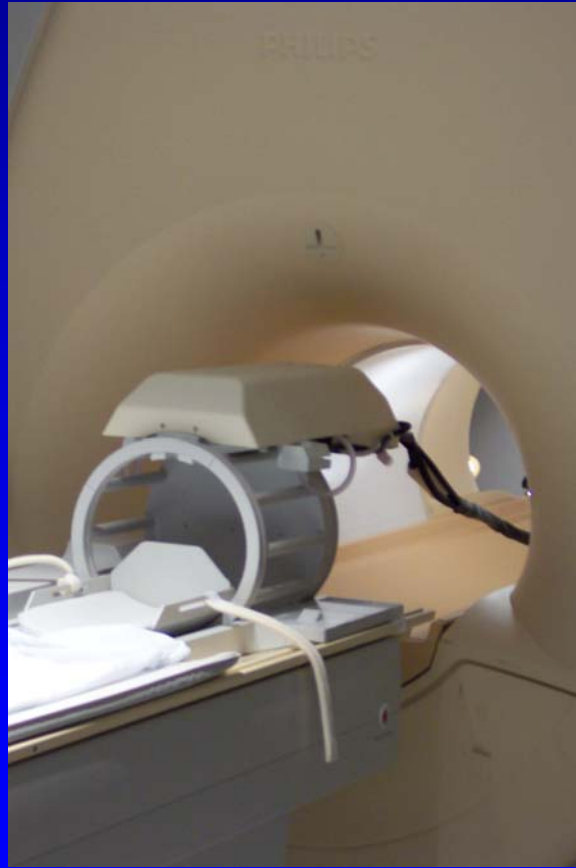
# 3T Control Room

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# New Stimulus Presentation Hardware

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# Acknowledgements

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