Neuroimagery et traitment des addiction

Colloque Toxicomanies Hépatites THS8
Les Rencontres de Biarritz
23-26 octobre 2007
Centre de Congrès Le Bellevue

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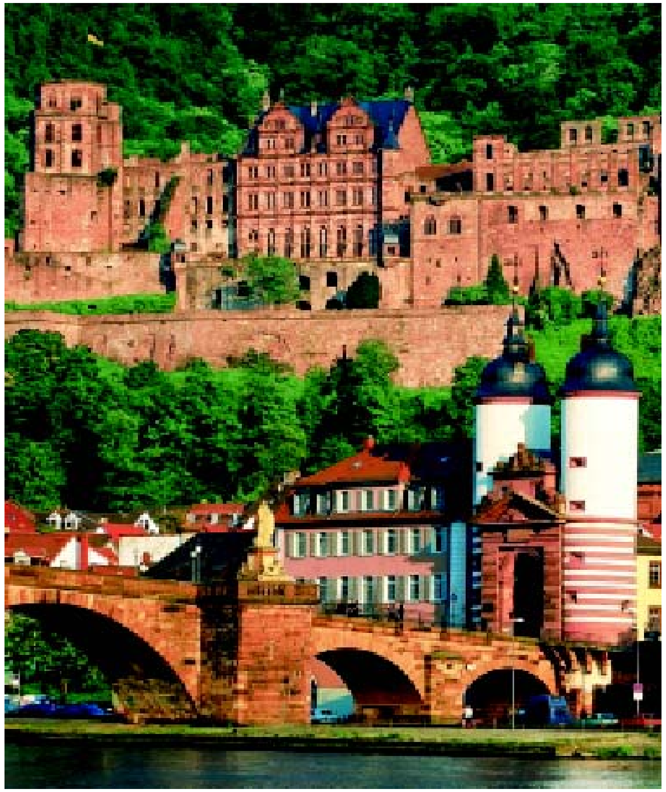
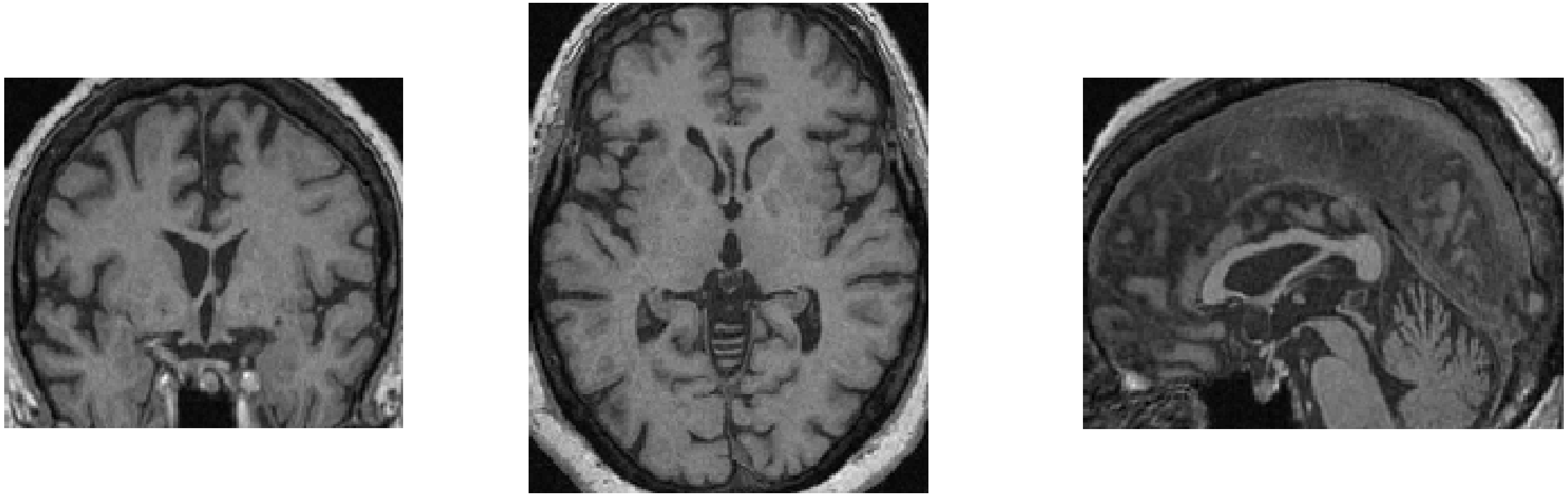
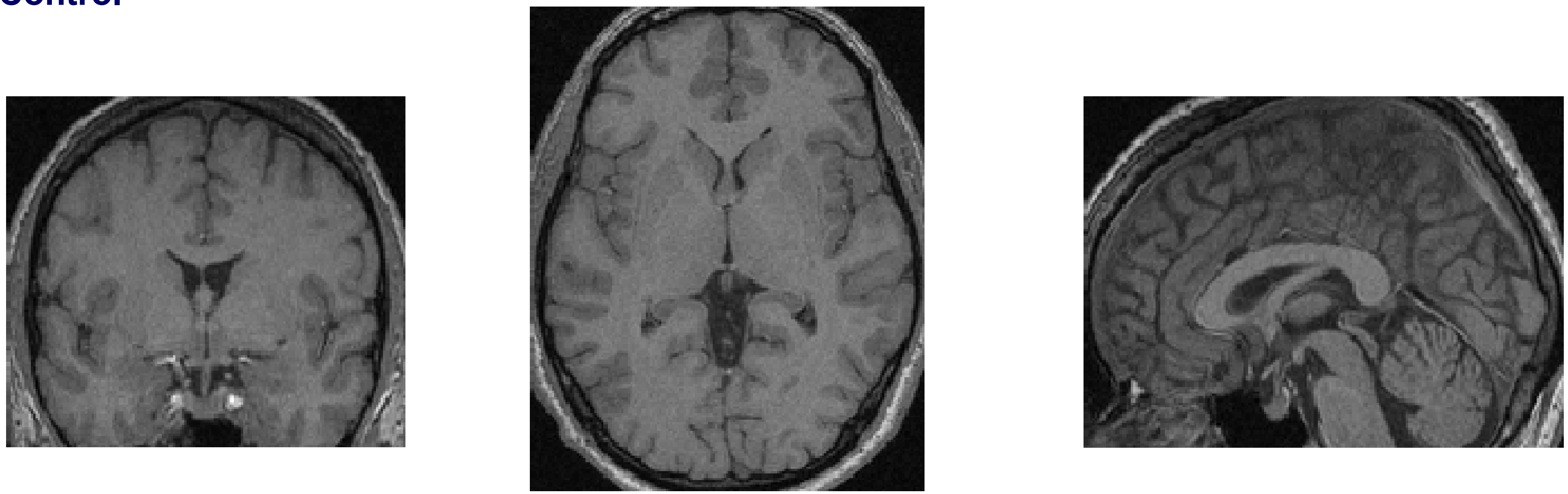
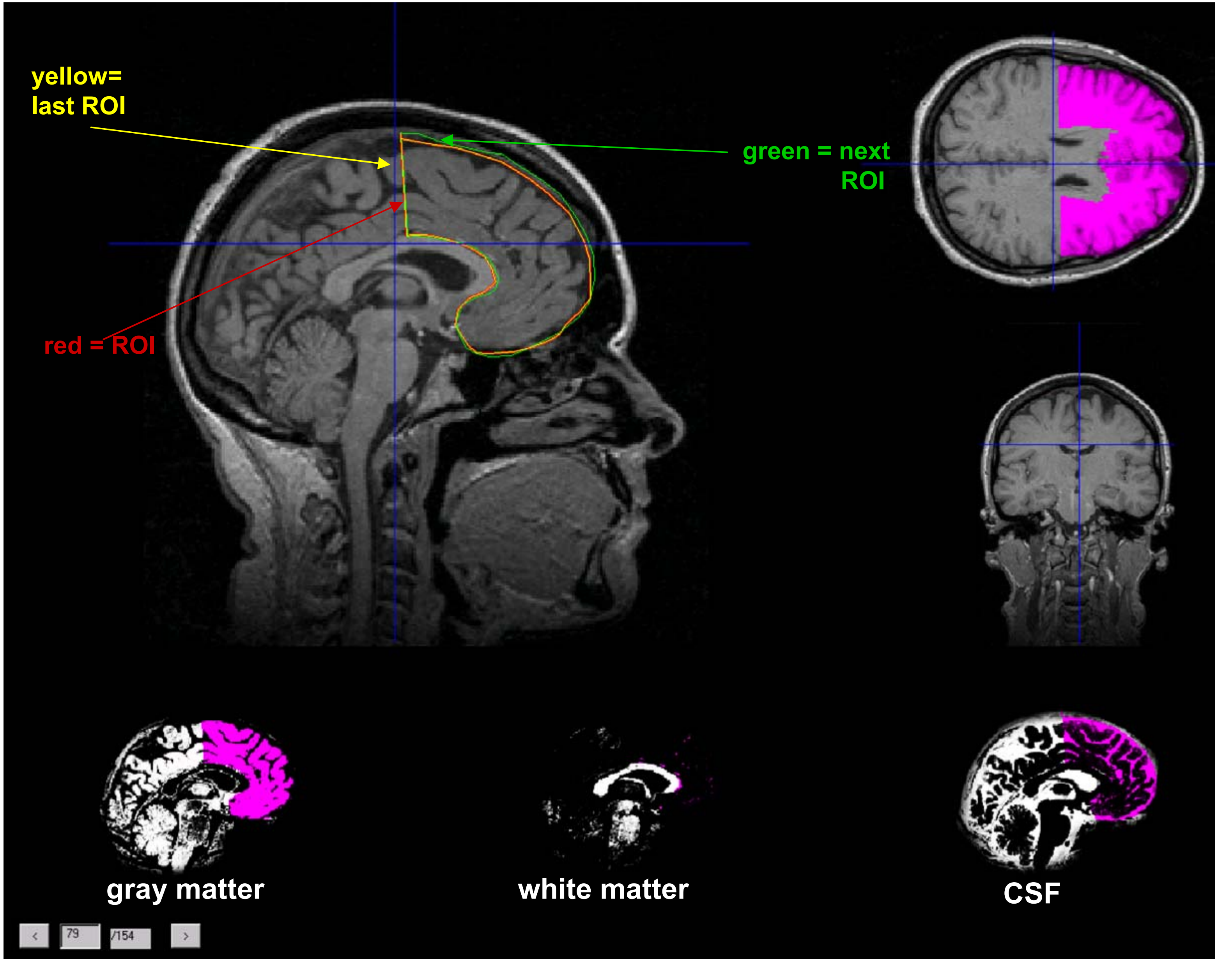


Patient

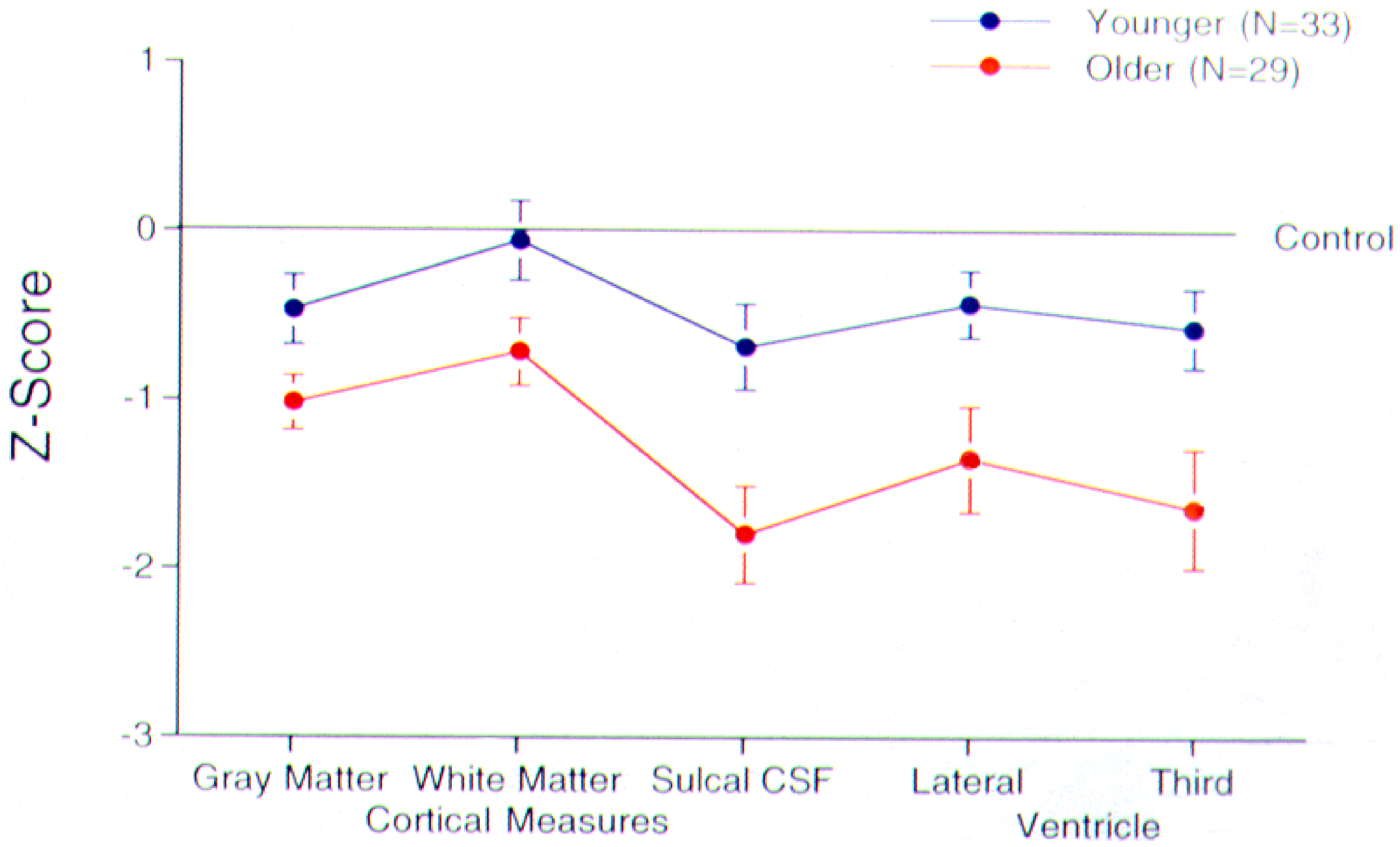


Control



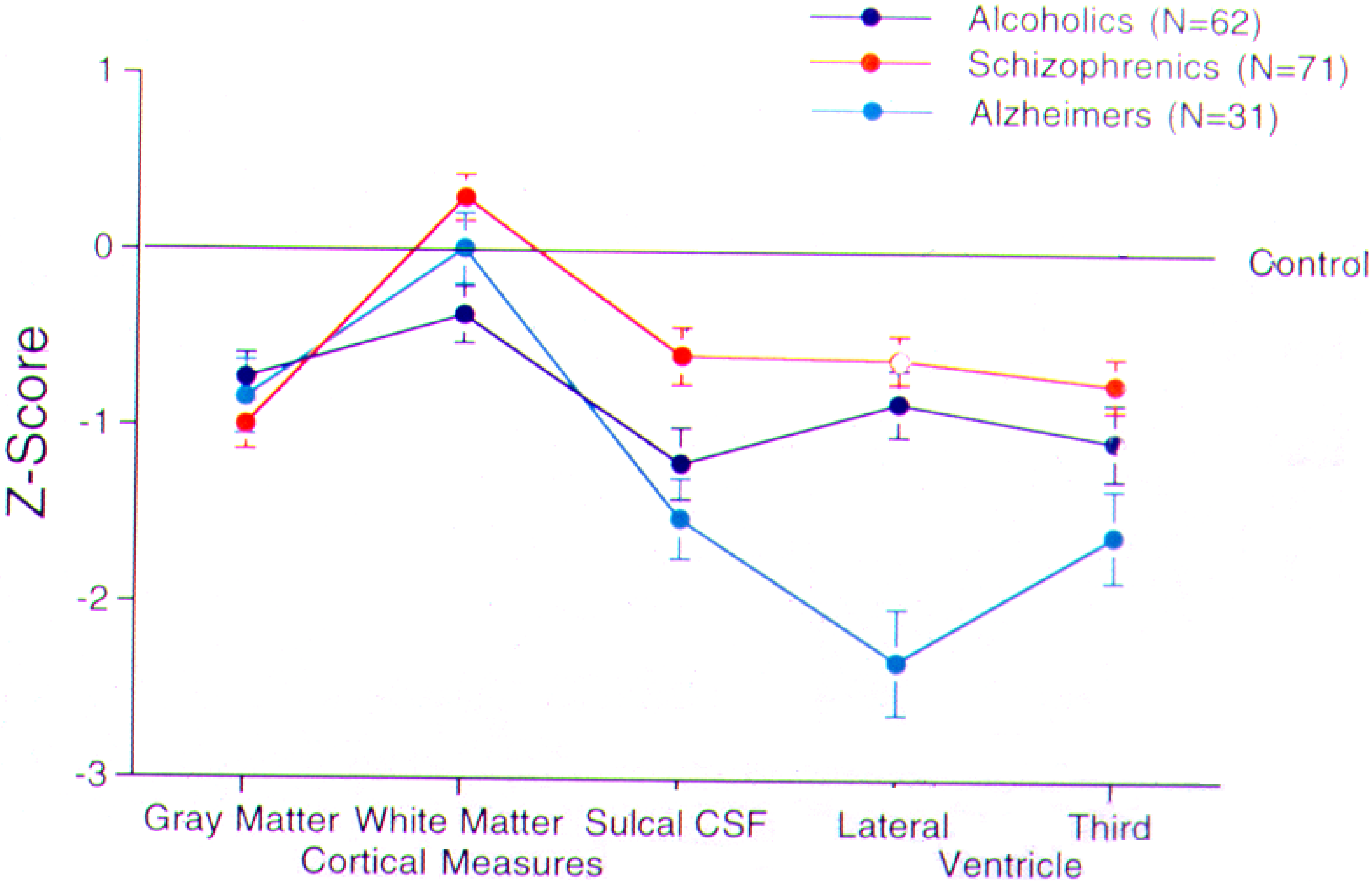

yellow=
last ROI
green = next
ROI
red = ROI
gray matter
white matter
CSF
79
/154

Age effects in alcoholism



Pfefferbaum et al. 1992

MR-Volumes



Pfefferbaum et al. 1992

0145-6008/05/2905-0896$03.00/0
ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH
Vol. 29, No. 5
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Neuroimaging of Gender Differences in Alcohol Dependence: Are Women More Vulnerable?

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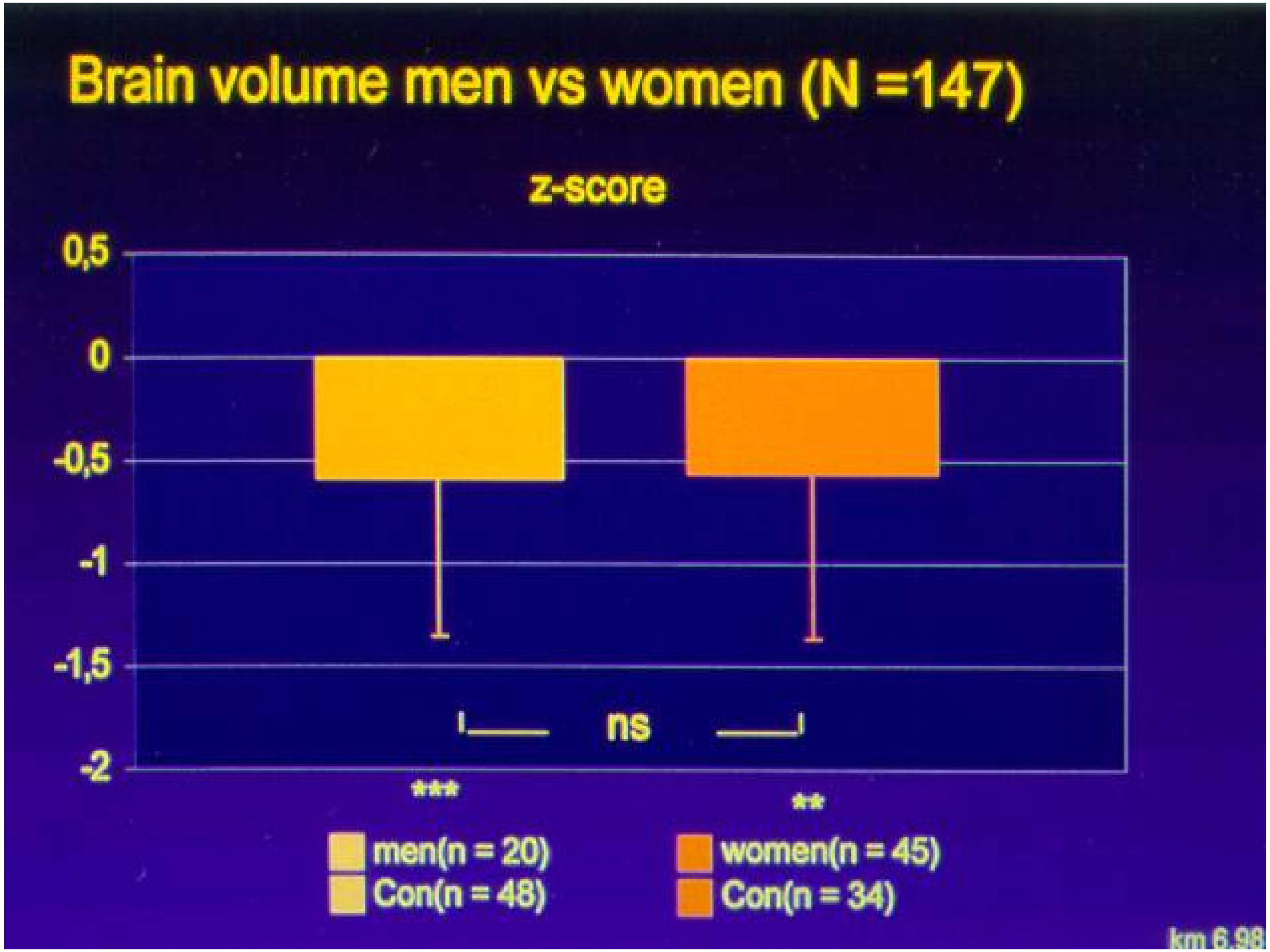
Background: Alcoholic brain damage has been demonstrated in numerous studies using neuropathology and brain imaging techniques. However, gender differences were addressed only in a few studies. Recent research has shown that development, course, and consequences of alcohol dependence may differ between female and male patients. Our investigation was built upon earlier research where we hypothesized that women develop alcoholic brain damage more readily than men do. To further compare the impact of alcohol dependence between men and women, we examined brain atrophy in female and male alcoholics by means of computed tomography (CT).

Methods: The study group consisted of a total of 158 subjects (76 women: 42 patients, 34 healthy controls; 82 age-matched men: 34 patients, 48 healthy controls). All patients had a DSM-IV and ICD-10 diagnosis of alcohol dependence. CT with digital volumetry was performed twice in patients (at the beginning and end of the 6-week inpatient treatment program) and once in controls.

Results: Patients of both genders had consumed alcohol very heavily. Although the average alcohol consumption in the year before the study was significantly lower in female alcoholics, this gender difference disappeared when controlled for weight. However, women had a significantly shorter duration of alcohol dependence. Despite this fact, both genders developed brain atrophy to a comparable extent. Brain atrophy was reversible in part after 6 weeks of treatment; it did not reach the level in the control groups.

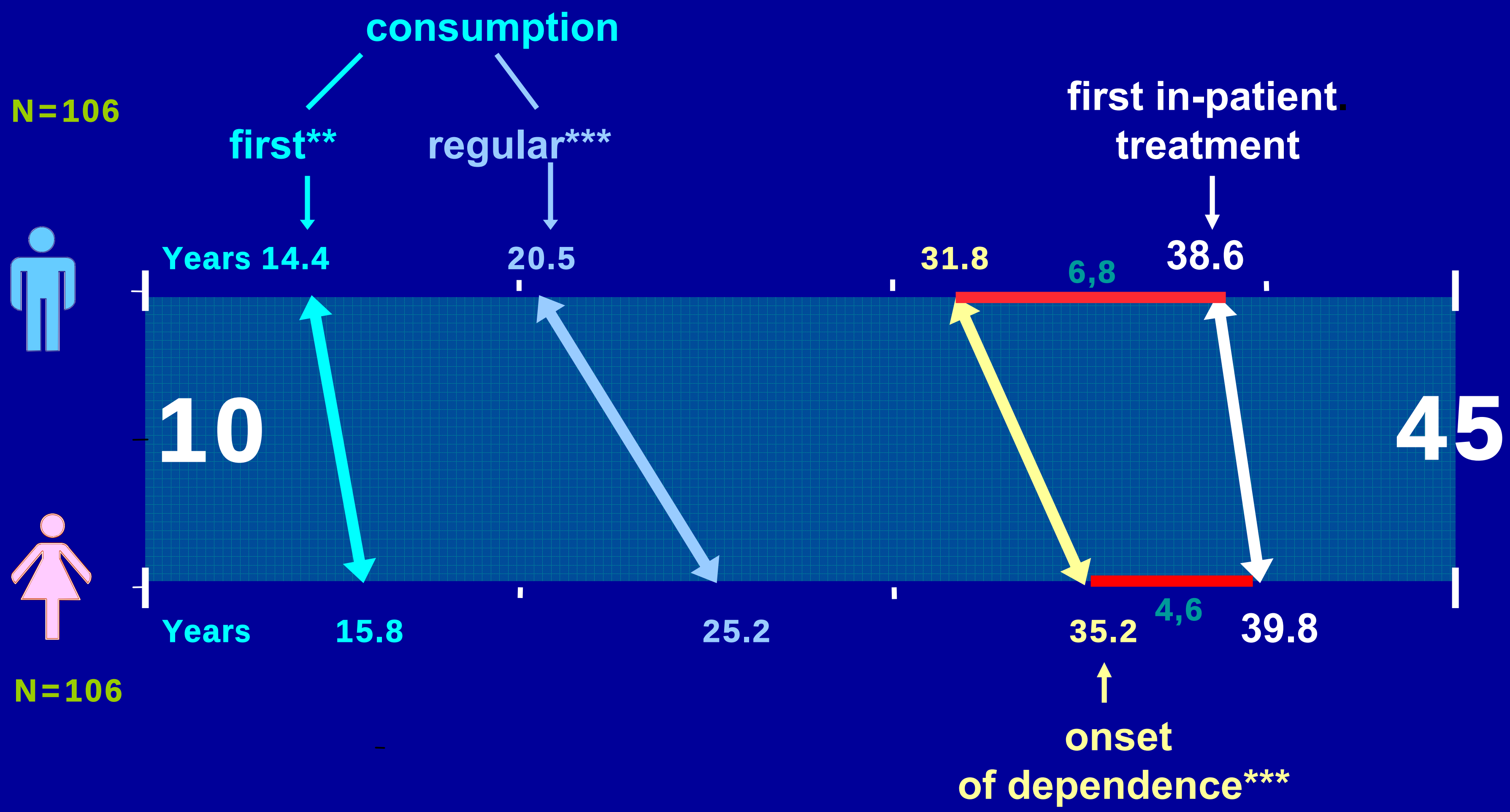
Conclusions: Gender-specific differences in the onset of alcohol dependence were confirmed. This is in line with the telescoping effect, where a later onset and a more rapid development of dependence in women were described. Under the assumption of a gradual development of consequential organ damage, brain atrophy seems to develop faster in women. As shown in other organs (i.e., heart, muscle, liver), this may confirm a higher vulnerability to alcohol among women.

Key Words: Alcohol Dependence, Brain Atrophy, Computed Tomography Scans, Gender Differences, Telescoping Effect.



Alcoholism: Clin & Exp Research 2005

Developmental Course of alcohol dependence in women and men

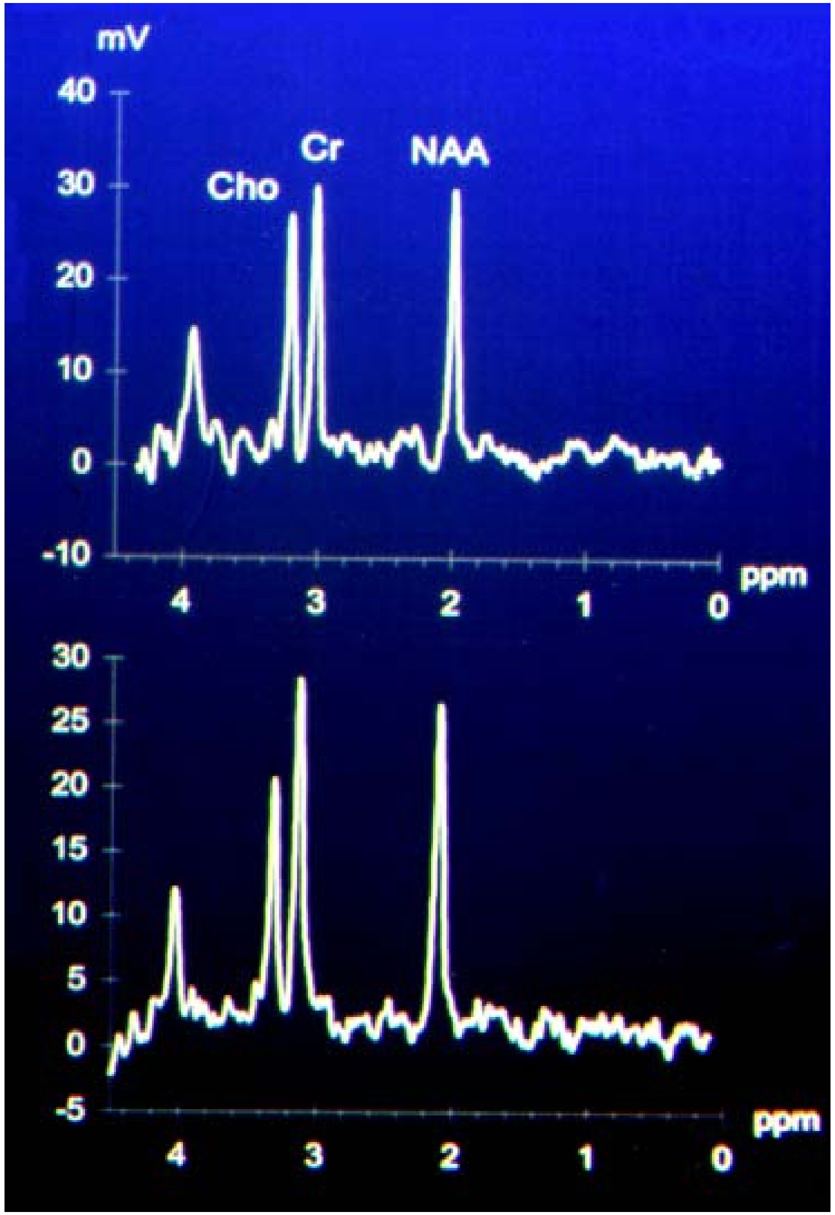


Alcoholism: Clin & Exp Res 2005

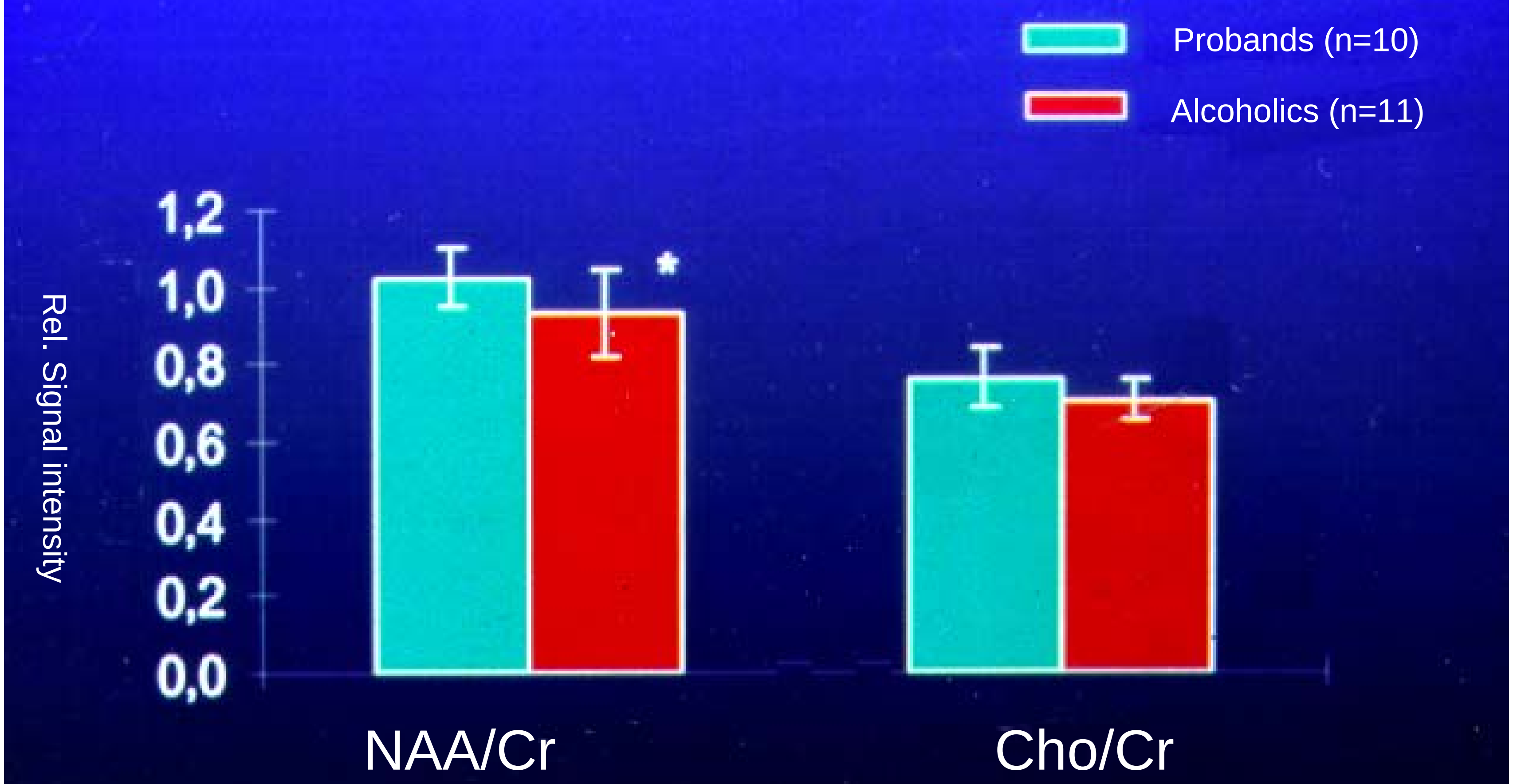
Results: spectroscopy alcohol dependence (TE 135ms)

Control

Alcohol dependence



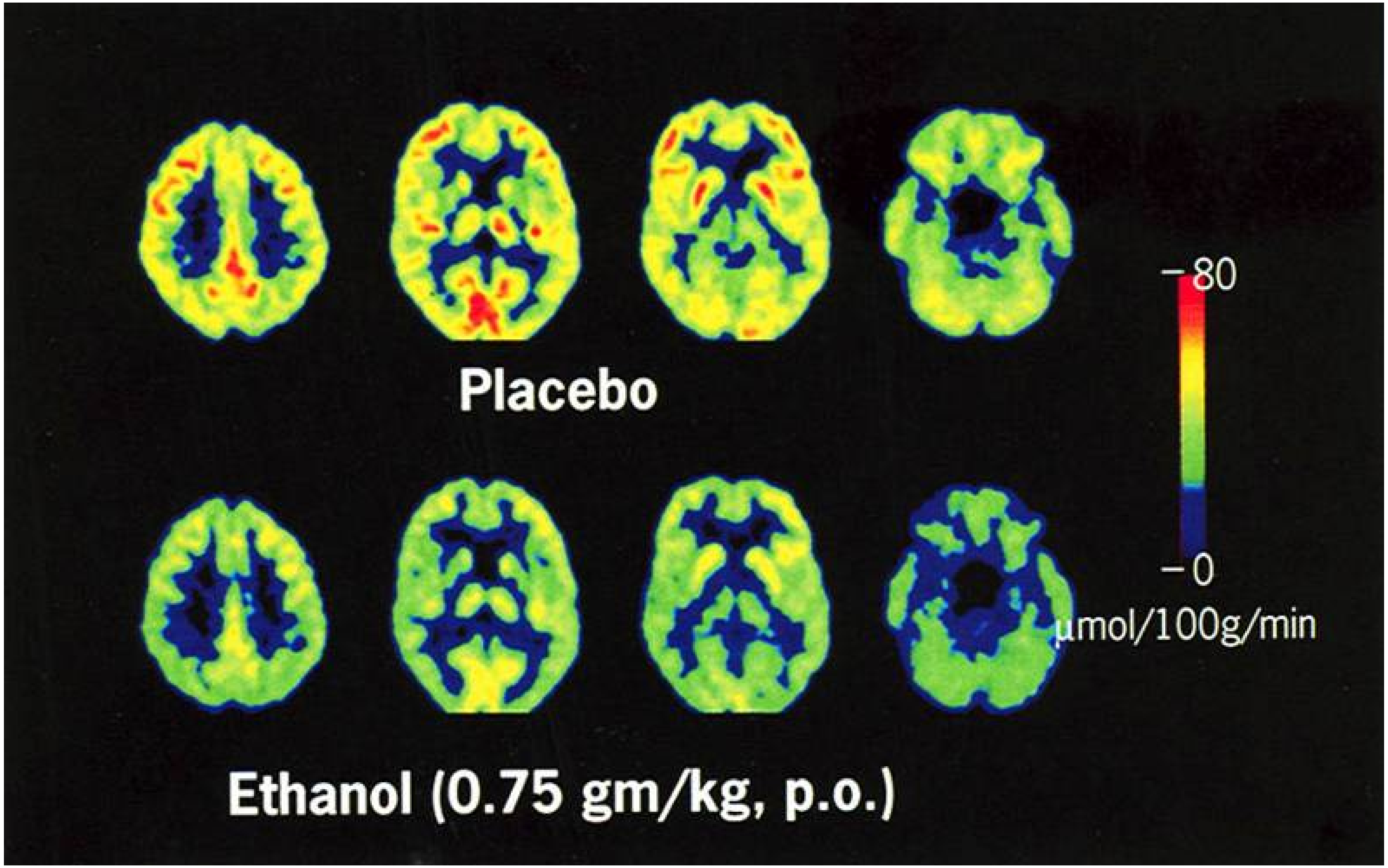
H-Spectroscopy cerebellum (TE 135ms)



*significant (p<0,05)

Alcoholism: Clin & Exp Res 1999

Fluorodeoxyglucose (FDG)-PET images of normal subject after placebo (diet soda) and ethanol (0.75 g/kg)



Wang et al., 2000

DA D_2 receptors in alcoholics

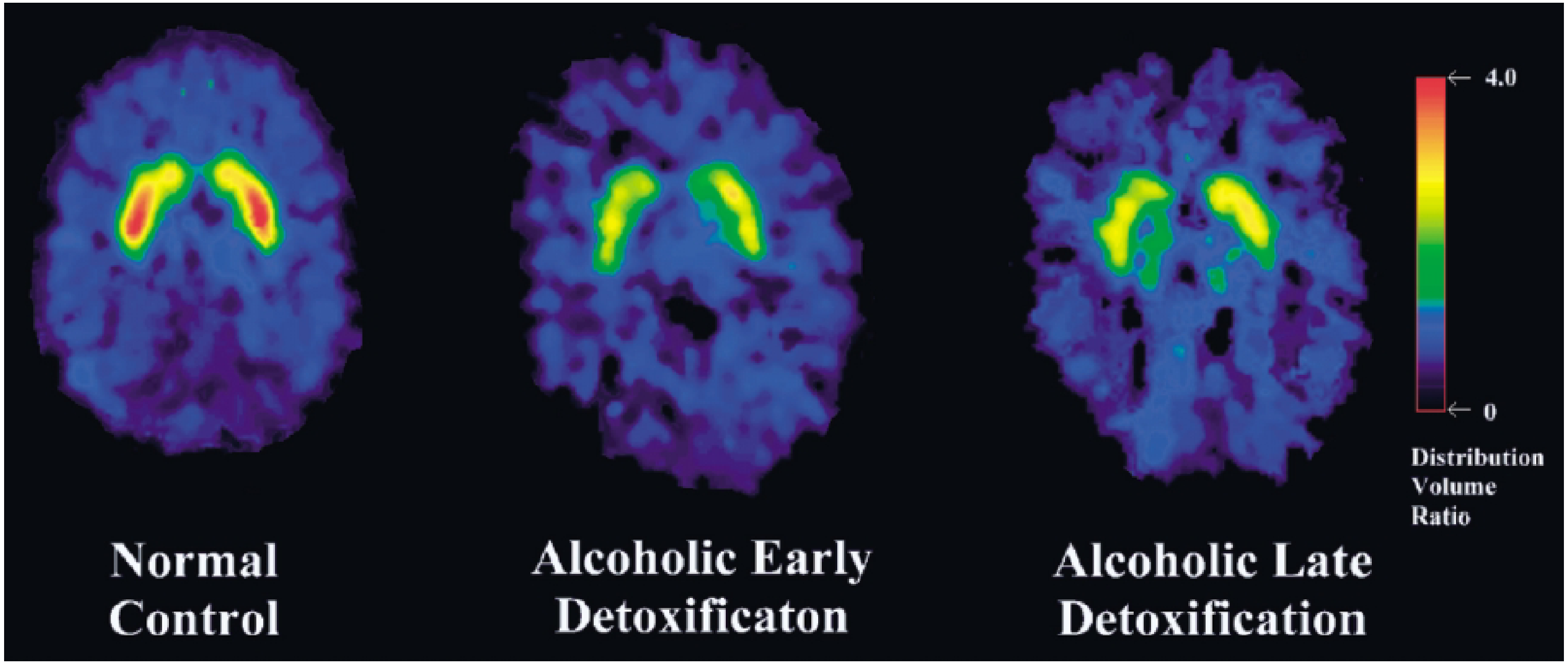


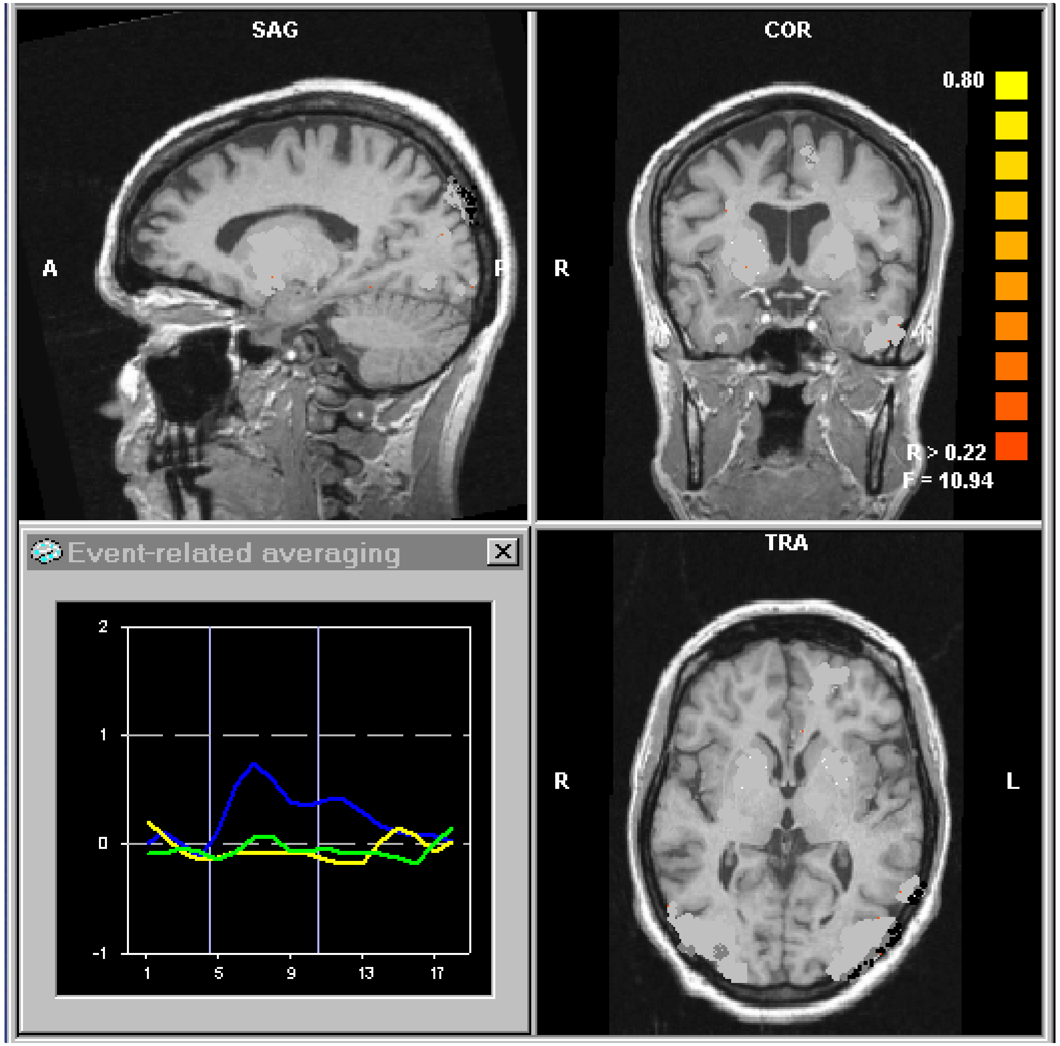
Fig. 1. DV ratio images for [^{11}C]raclopride in a normal control and in an alcoholic tested during early and late detoxification at the level of the striatum. These images were obtained with a CTI PET scanner.

Volkow et al. Psychiatry Res 2002

Alcoholic drinks

Cue reactivity

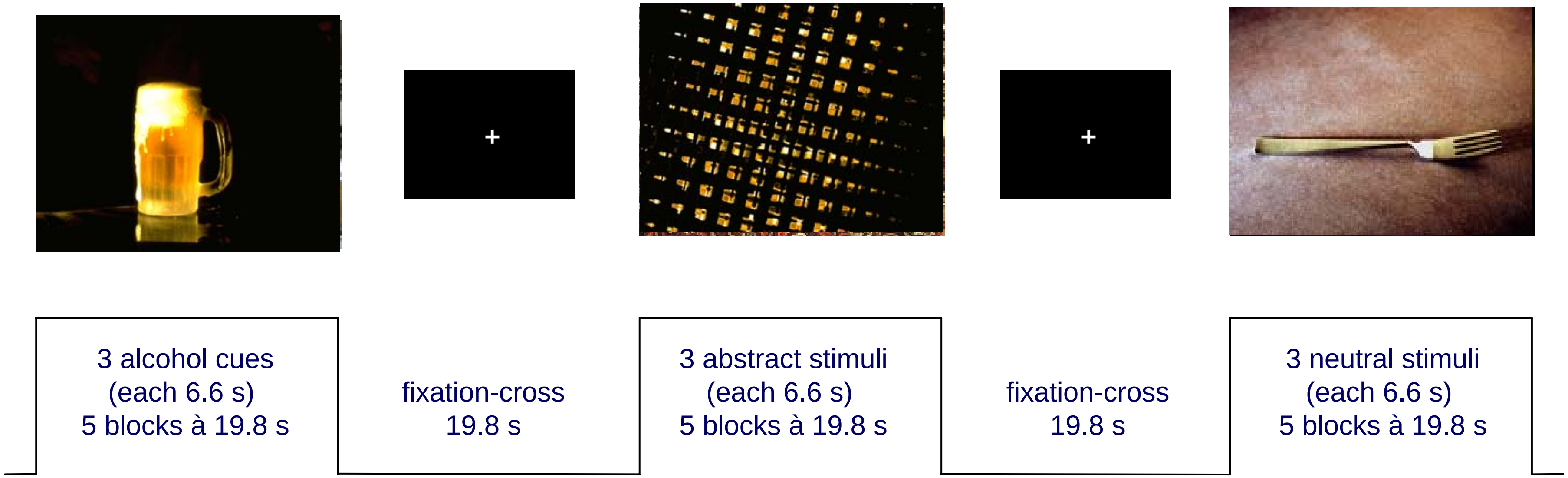
- Autonomic, cognitive & behavioral responses to drug-related stimuli
- Pairing of drug effects and withdrawal effects with environmental stimuli during development of dependence (classical conditioning)
- Cues control drug seeking and drug taking behavior
- Relevant for maintenance of drug dependence



SAG
COR
TRA
A
P
R
R
L
0.80
R > 0.22
F = 10.94
Event-related averaging
2
1
0
-1
1
5
9
13
17

Methods: fMRI

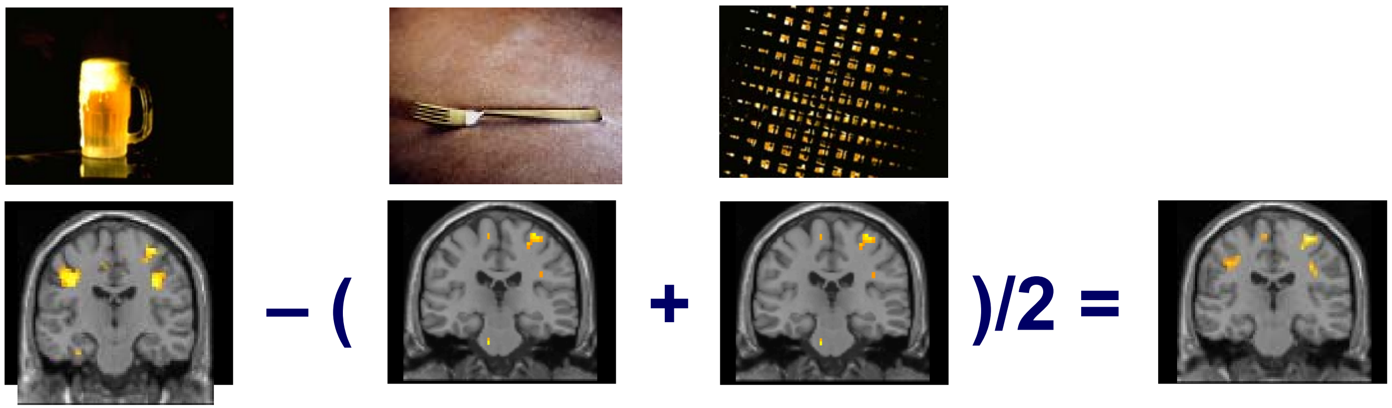
- 1.5 Tesla MR-scanner (Siemens Vision)
- presentation of stimuli in a block design (~11min)



Analysis of fMRI data

- Analyses with SPM
- Preprocessing (realignment, normalization)
- Computation of individual contrast images:

cues – control stimuli



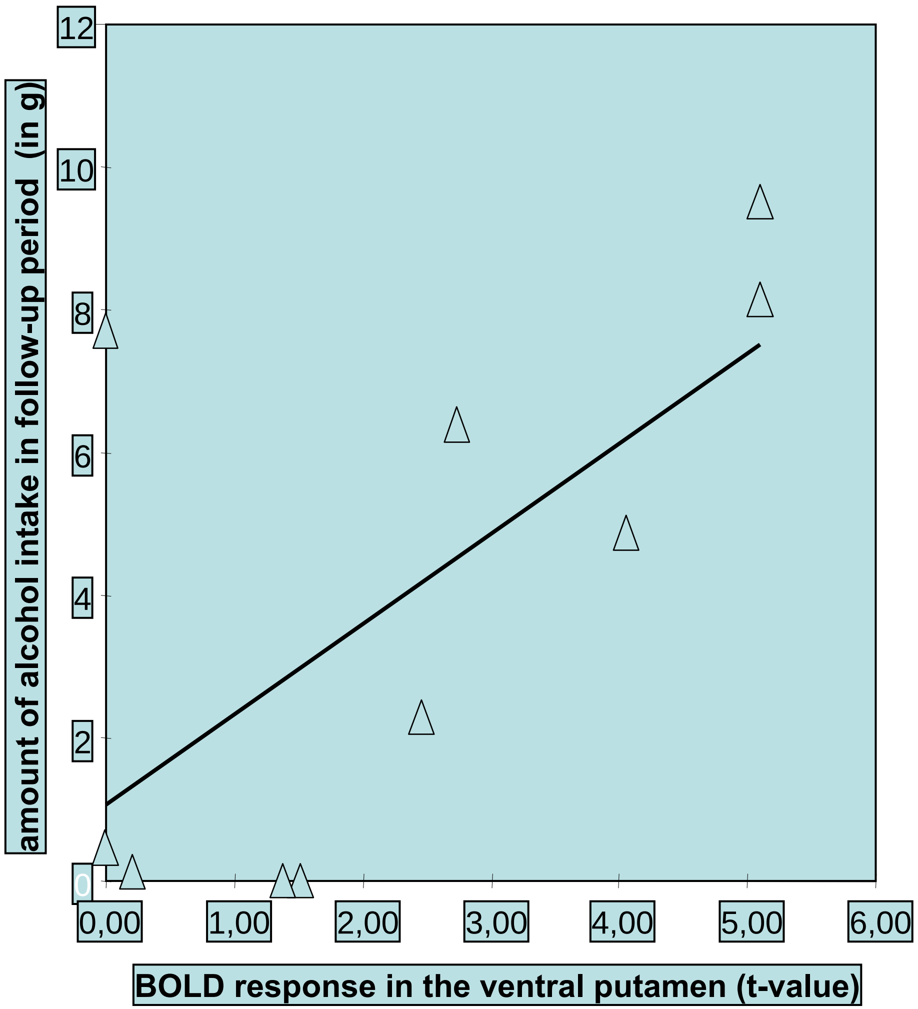
- Correlation of the BOLD response with different variables

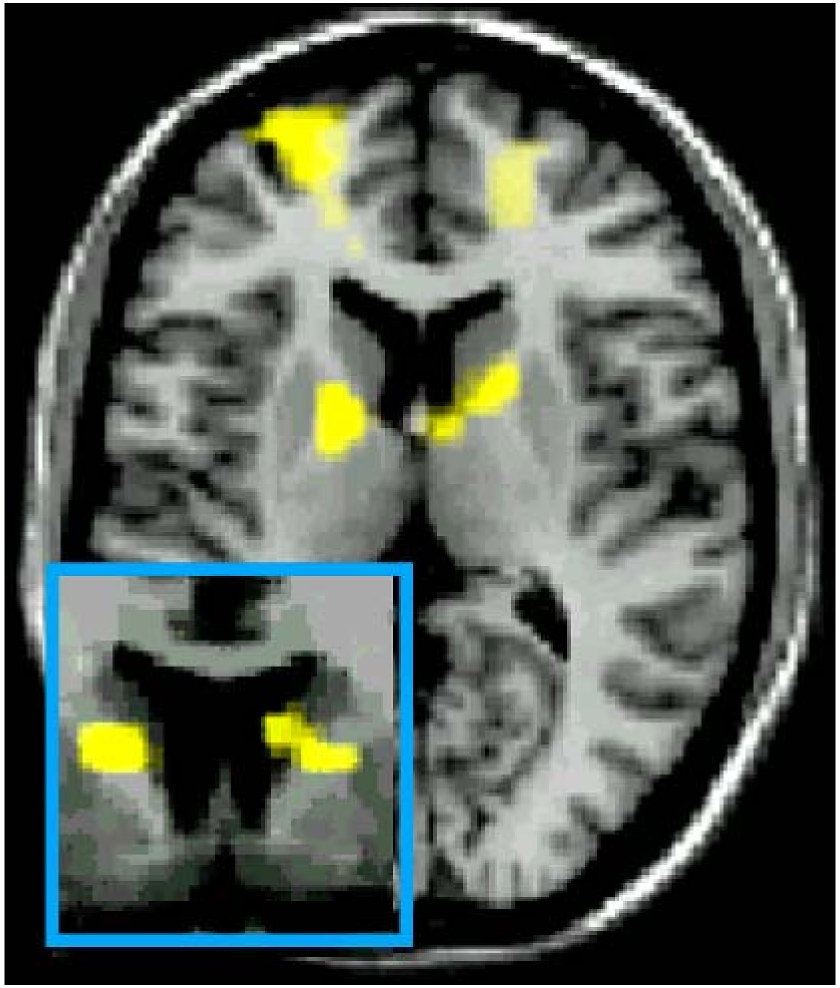
Reactivity to alcohol cues: fMRI studies

- Cue-elicited brain activity consistently found in the
  - striatum
  - amygdala
  - anterior cingulate
  - prefrontal cortex
  - insula

(Braus *et al* 2001; George *et al* 2001; Schneider *et al* 2001; Wrase *et al* 2002; Tapert *et al* 2003; Grüsser *et al* 2004; Myrick *et al* 2004; Tapert *et al* 2004)

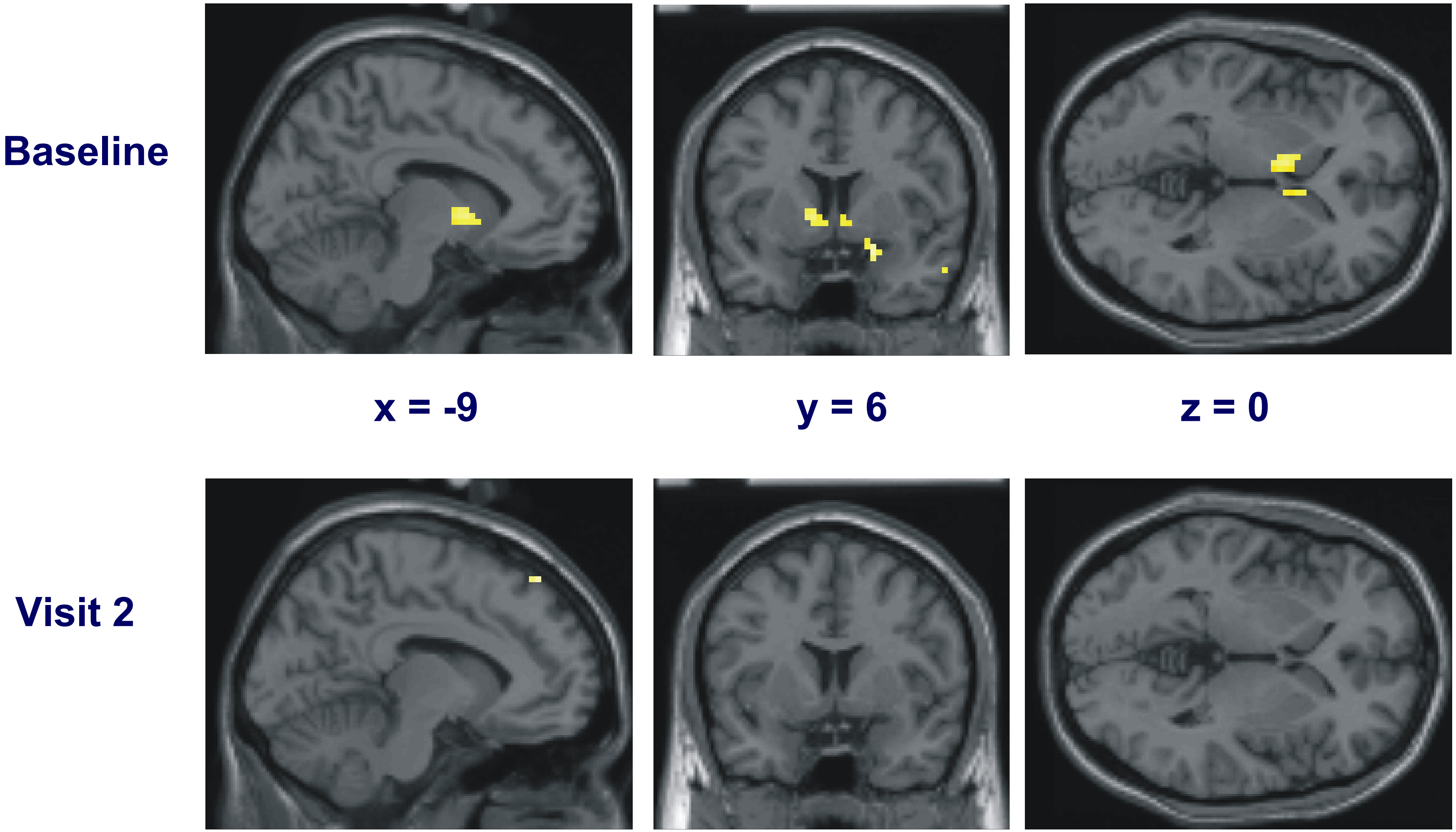
Activation and Course





Psychopharmacology 2003

Single Patient
alcohol > neutral
# p<.001, k>=10

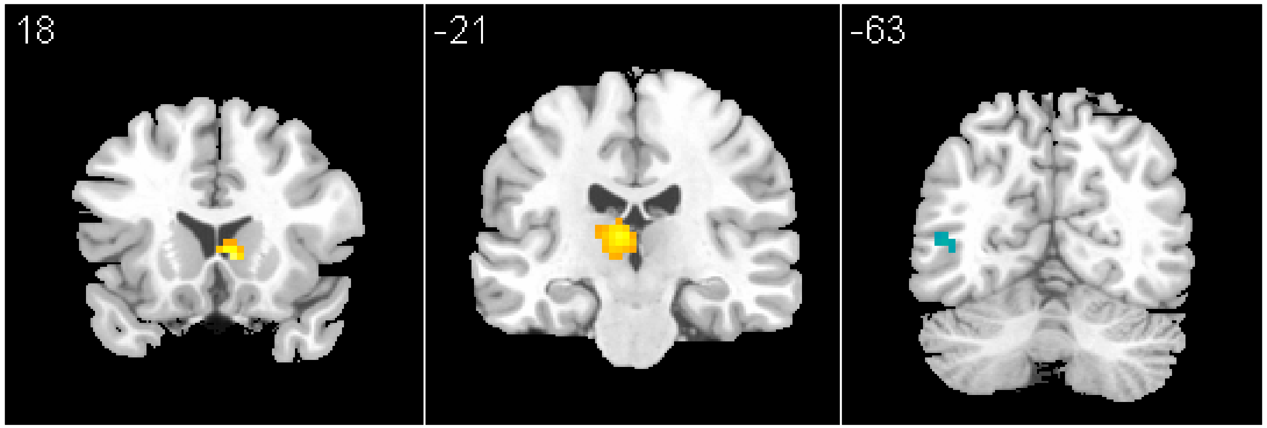


Changes During Treatment

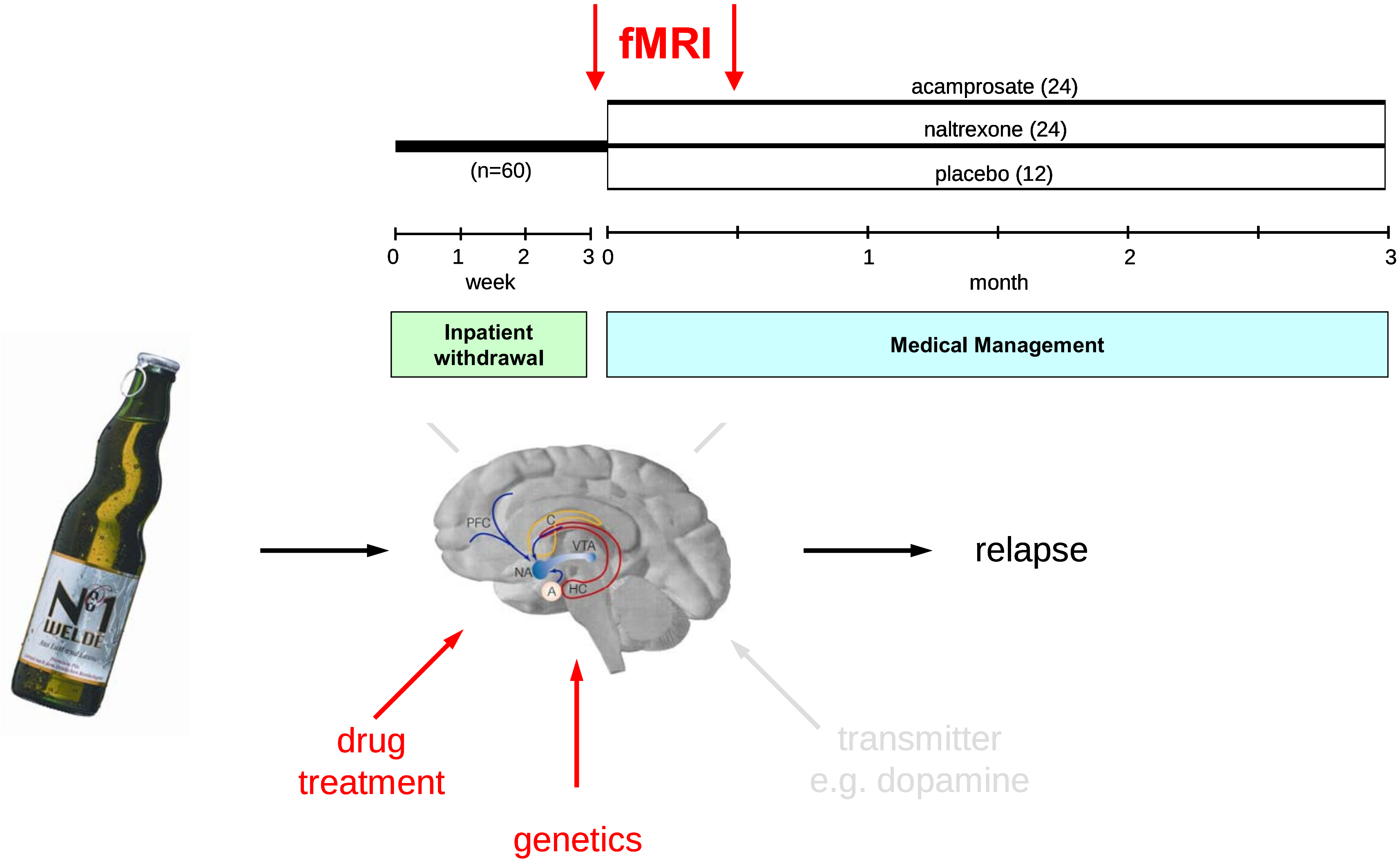
Average of 32 patients, changes over time

Baseline vs. visit 2

$p \leq 0.005$; $K_E \geq 10$

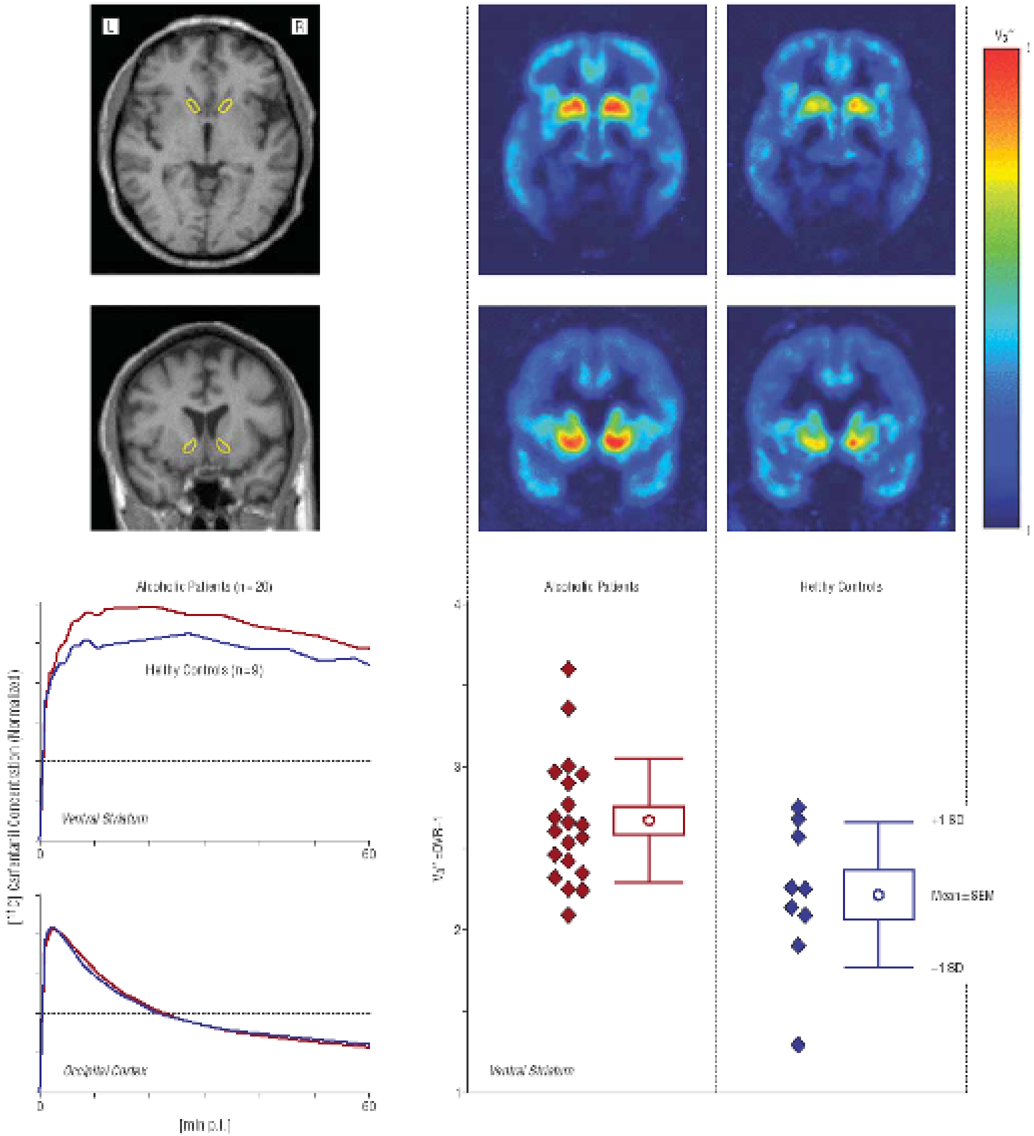


Next steps / study design: project predict



Mann et al.; ACER (in press)

Central μ-opiate receptor availability (V_3”).

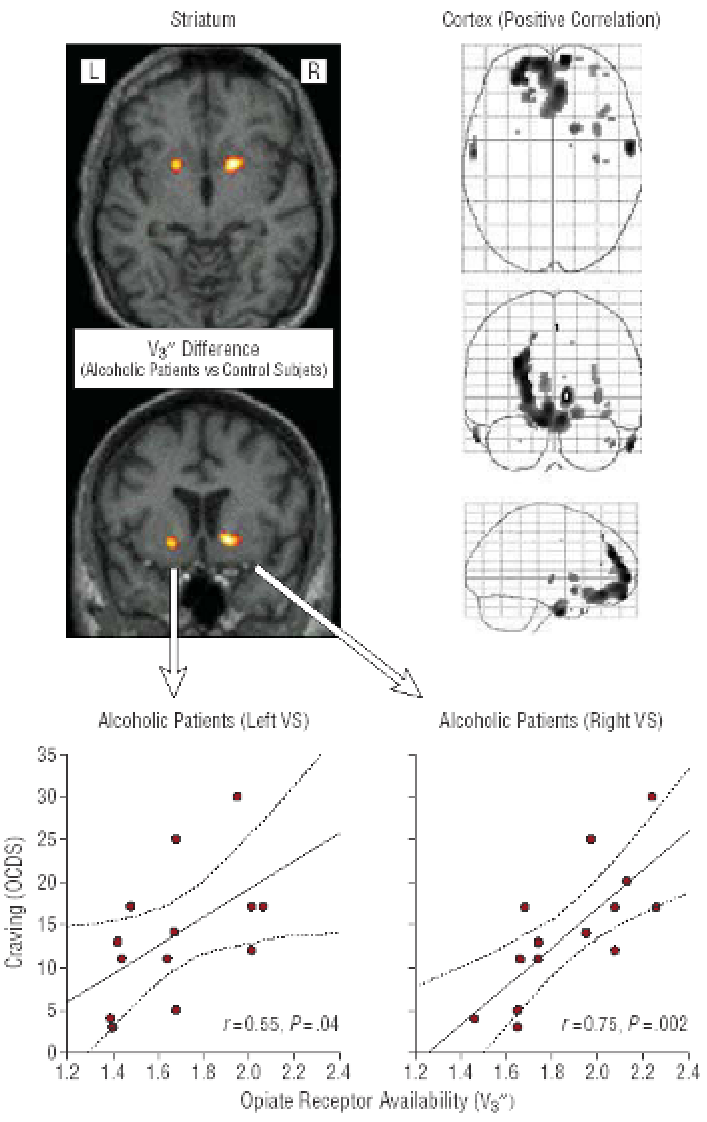


ROIs for the ventral striatum, including the nucleus accumbens

ROI analysis: interindividually averages time activity curves, normalized to occipital area under curve

Archives General Psychiatry 2005

Correlation between V_3“ and alcohol craving



Left, absolute group difference in V3“ between alcoholic patients and control subjects (top).

Right, SPM analysis of correlation between V_3“ and OCDS (voxel-level threshold: *P*<.001, *t*>3.93). The large cluster in the left frontal cortex survived correction for the entire volume (corrected *P*<.001).

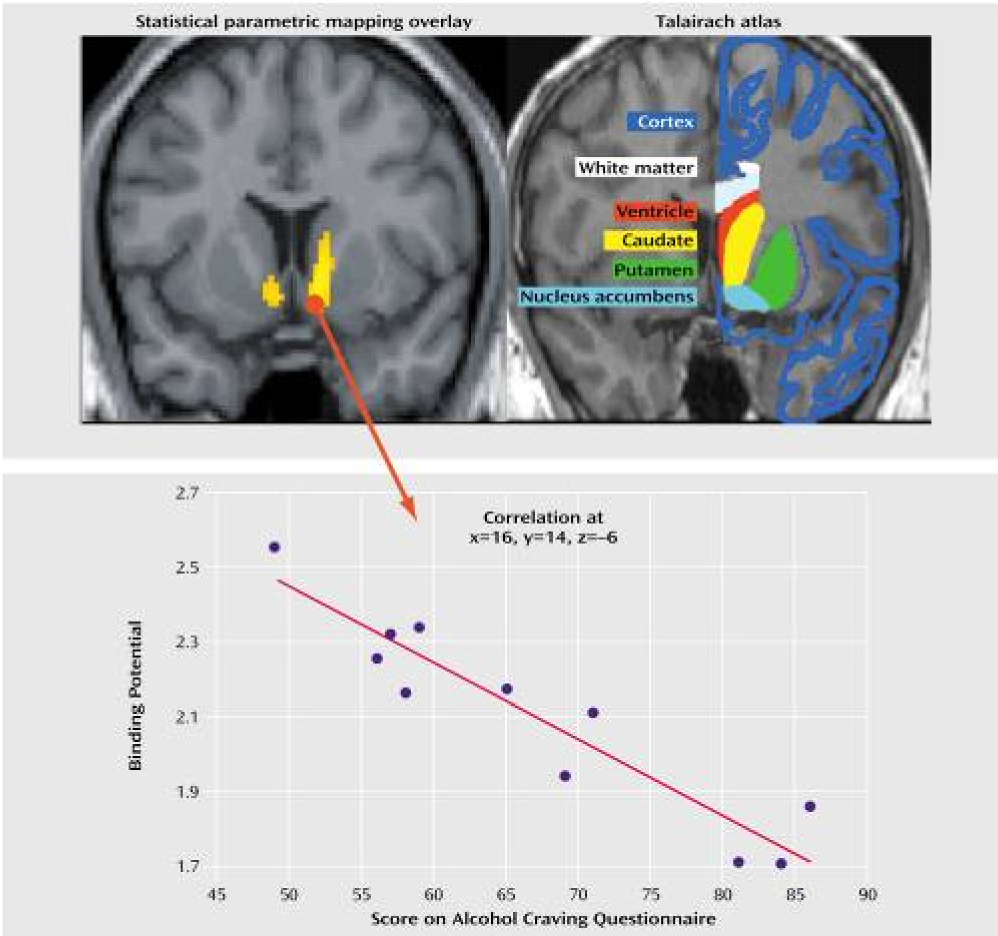
Arch Gen Psychiatry 2005

DRD2 availability & cue reactivity

- 11 males
- Age: 45 ± 7 years
- Alcohol dependent (DSM-IV)
- Abstinent for at least 2 weeks
- Free of any medications for at least 1 week
- [^{18}F]-DMFP PET, fMRI, ACQ

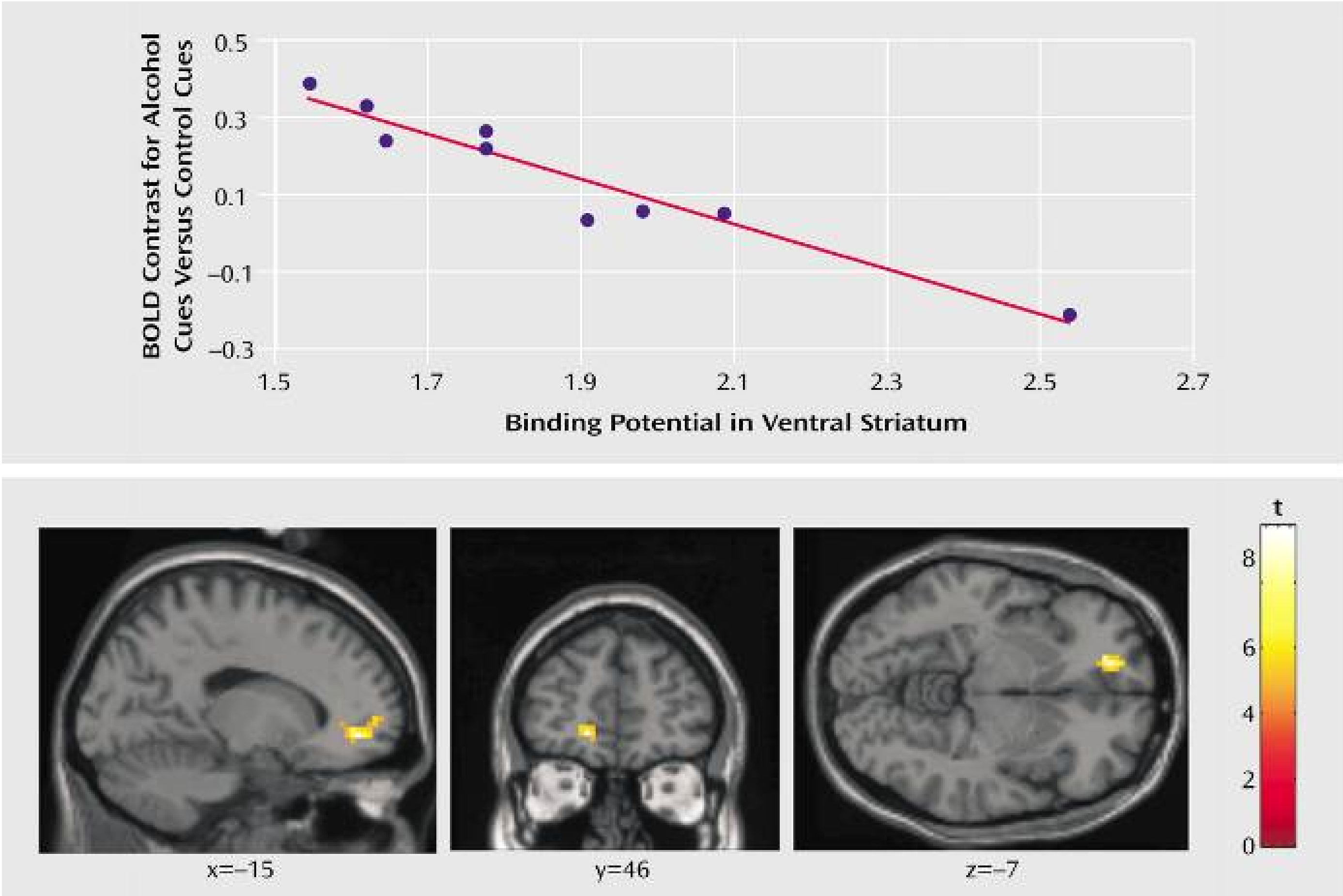
- 13 Control subjects (matched for age and gender)

DRD2 availability & craving



Heinz et al Am J Psychiatry 2004

DRD2 availability & neuronal cue reactivity



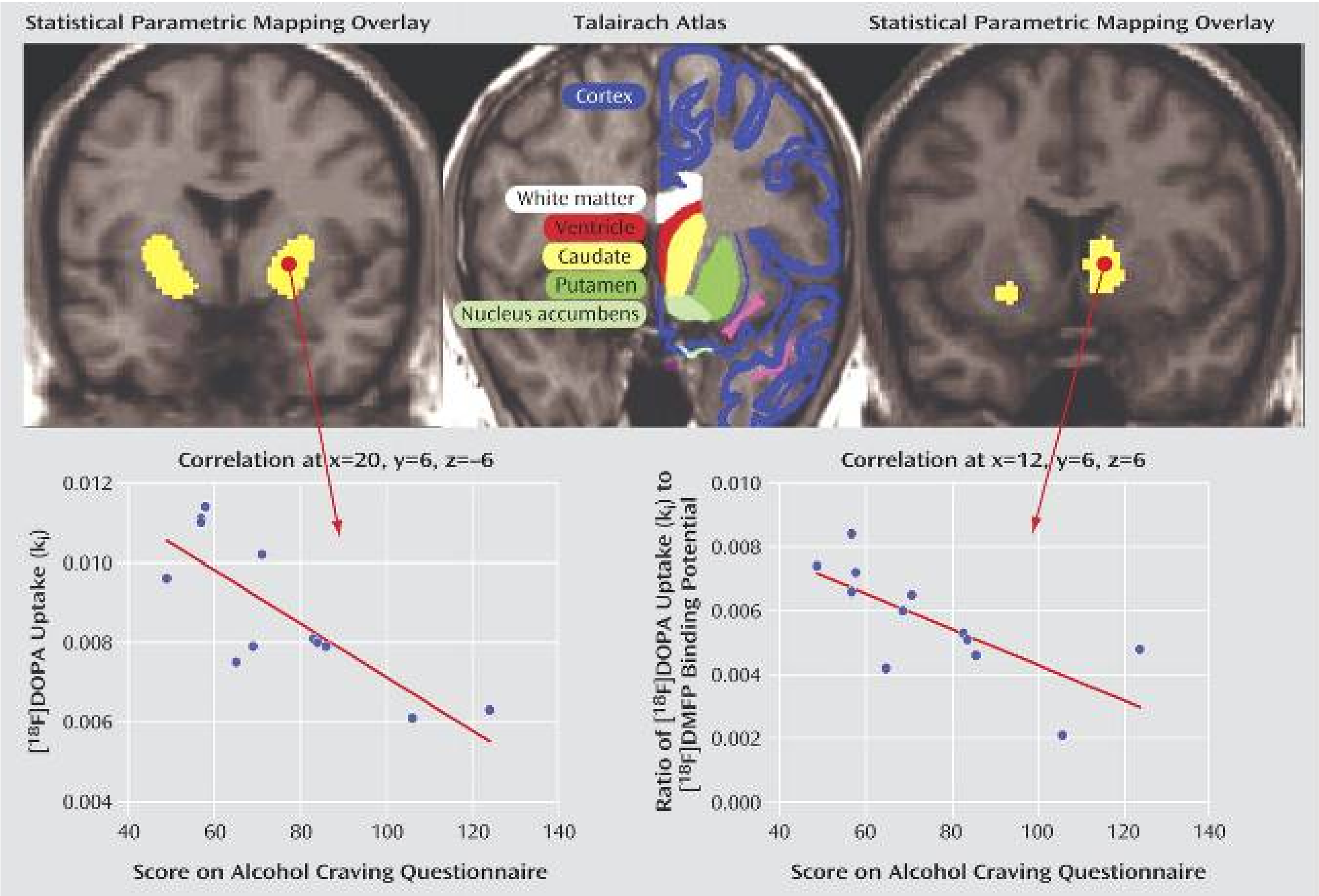
Heinz et al Am J Psychiatry 2004

DA synthesis capacity & cue reactivity

- 12 males
- Age: 43 ± 8 years
- Alcohol dependent (DSM-IV)
- Abstinent for at least 2 weeks
- Free of any medications for at least 1 week
- [^{18}F]-DOPA PET, fMRI, ACQ

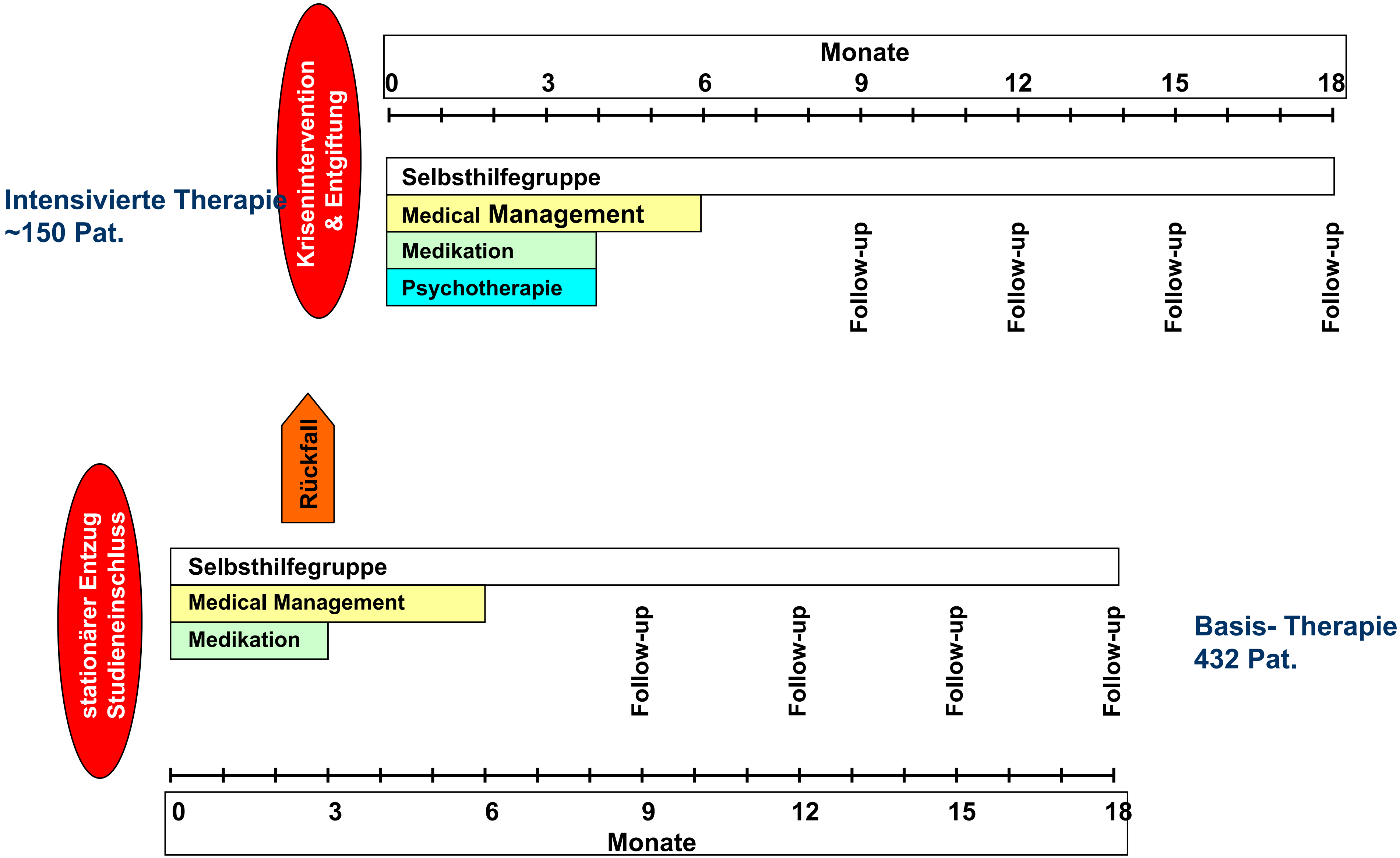
- 13 Control subjects (matched for age and gender)

DA synthesis capacity & craving



Heinz et al Am J Psychiatry 2005

Therapieschema Project Predict



Summary / Discussion

- Neuronal cue reactivity associated with treatment response
  - ⇨ Replication (larger sample, other drugs)
  - ⇨ Identification of patients at high risk
  - ⇨ Effects of treatment (drugs, psychotherapy)

Project Predict Research Group

Steering Committee

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Freiburg:	Michael Berner Riggo Brueck Martin Härter
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Preclinical Studies

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Health Economy

PI:	Hans Salize
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