



Charité



## Major psychoses and substance abuse: evidence for common limbic alterations

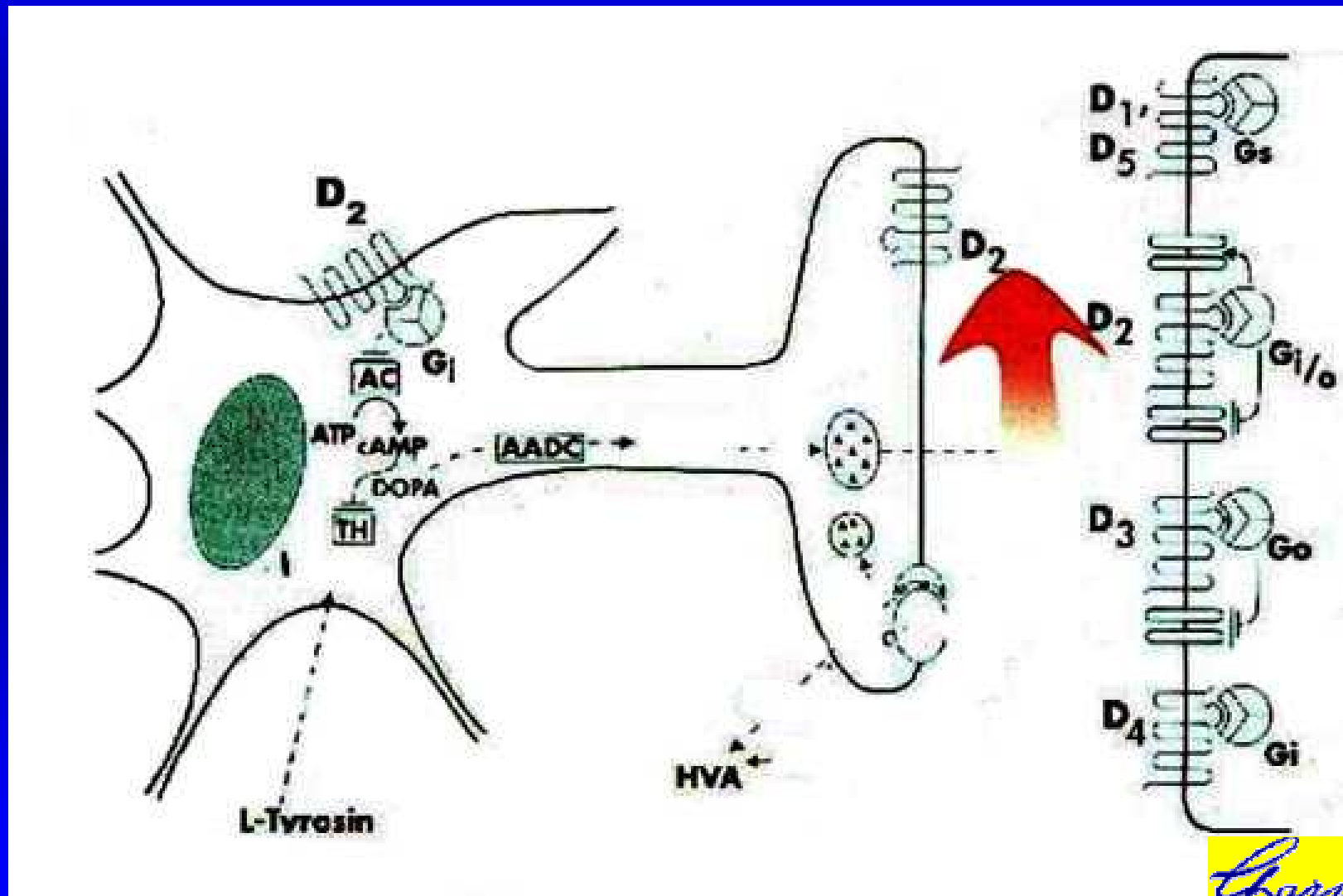
Andreas Heinz

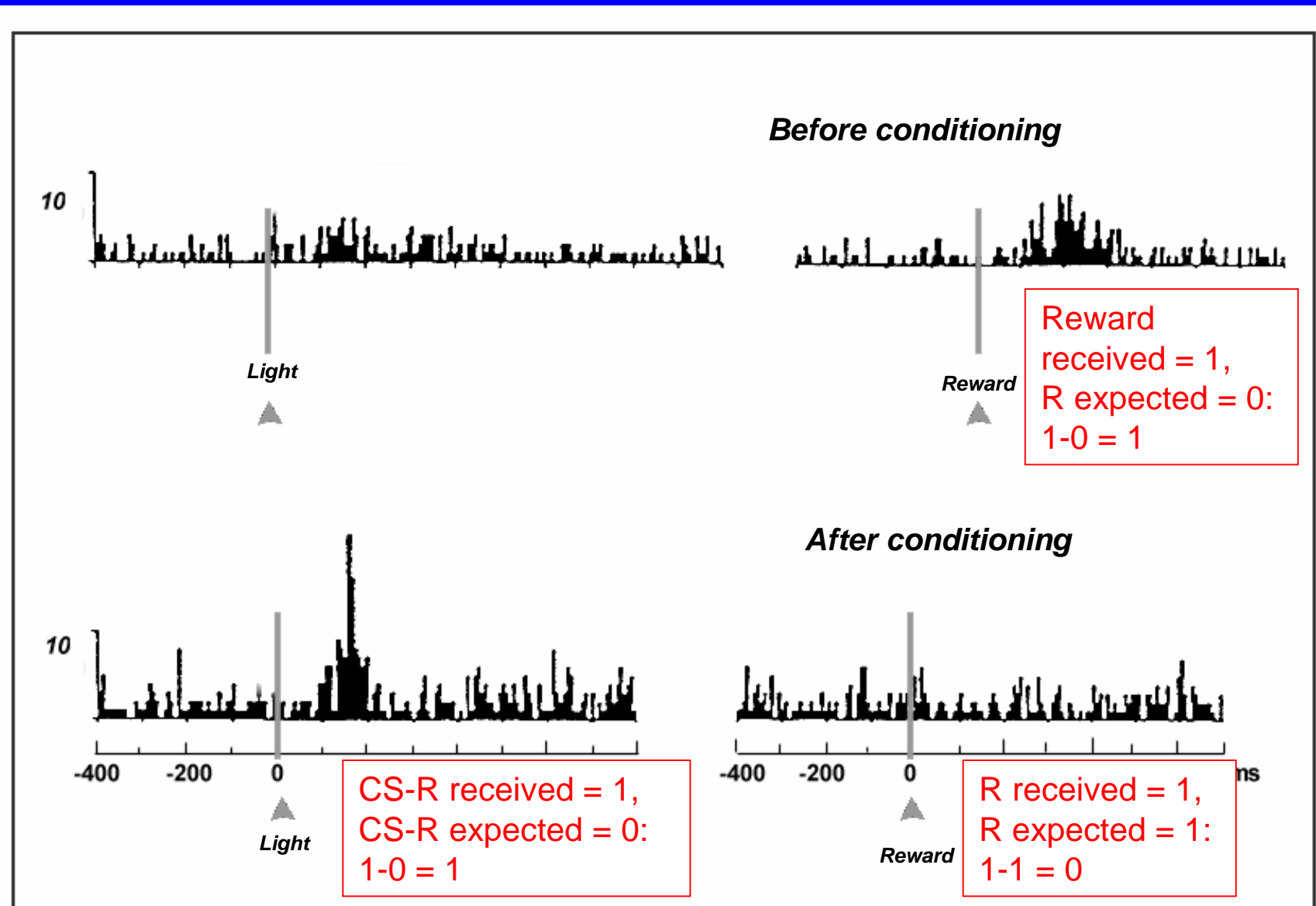
Department of Psychiatry und Psychotherapy

Charité – University Medical Center Berlin

Campus Charité Mitte & St. Hedwig Kliniken

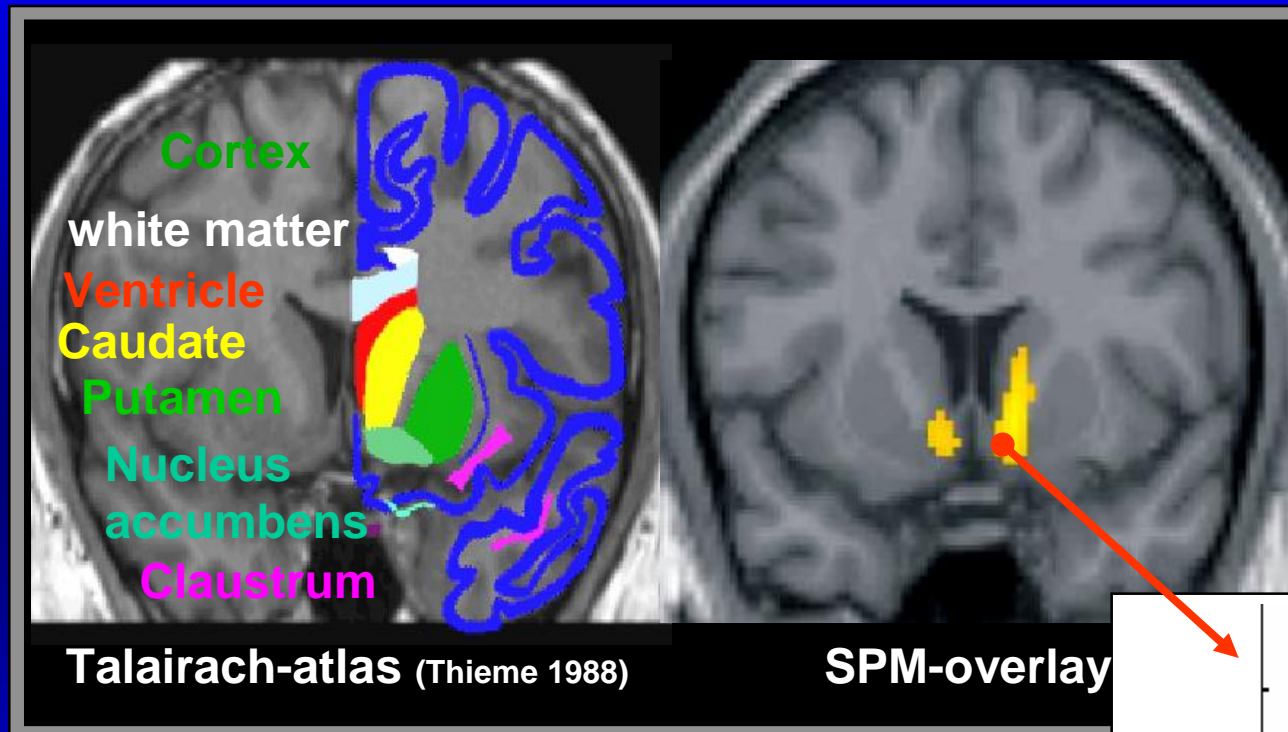
# Acute alcohol effects



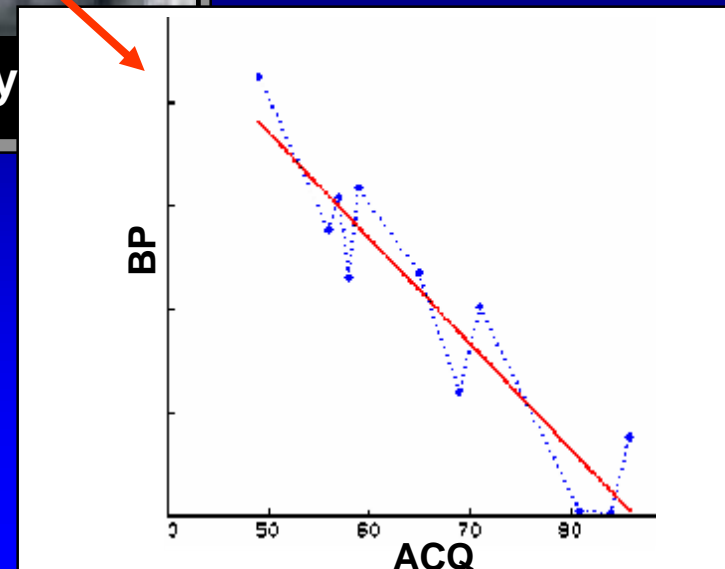


Schultz et al., 1993

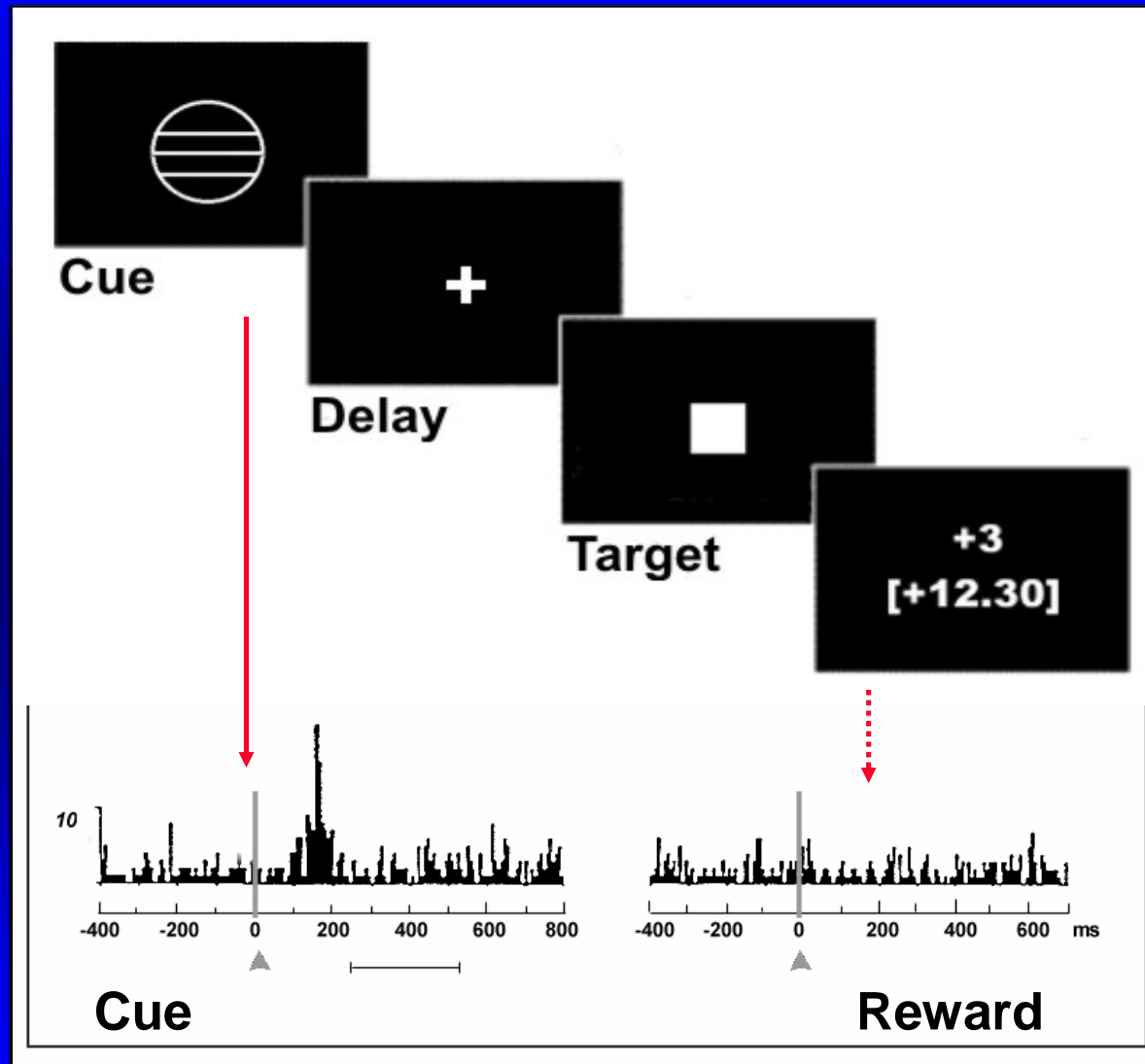
# Dopamine D2-receptor availability and craving in detoxified alcohol-dependent patients



Correlation with acute craving



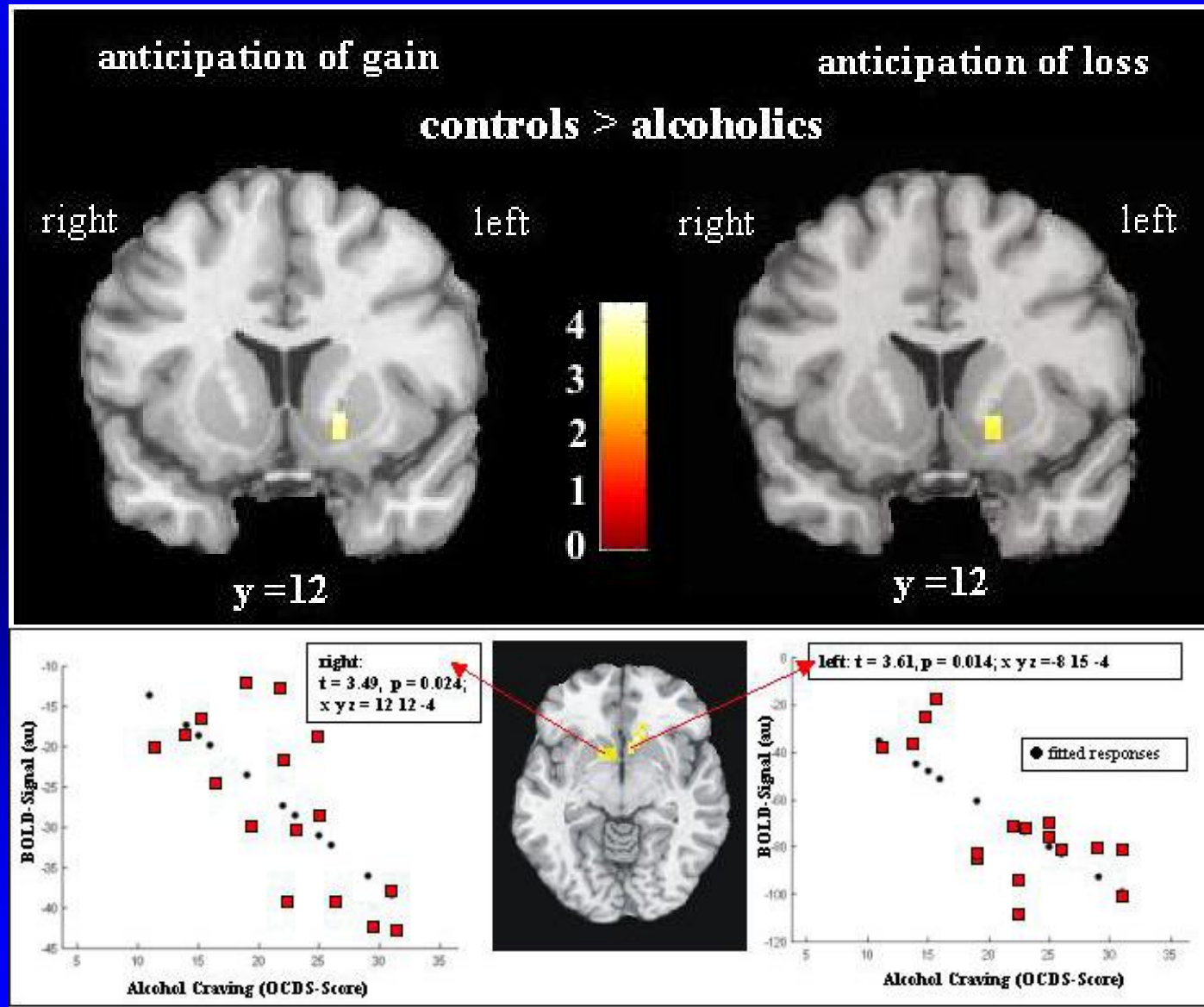
# Reward-anticipatory versus rewarding stimuli



Knutson et al., J Neurosci 2001

Schultz et al., Science 1996

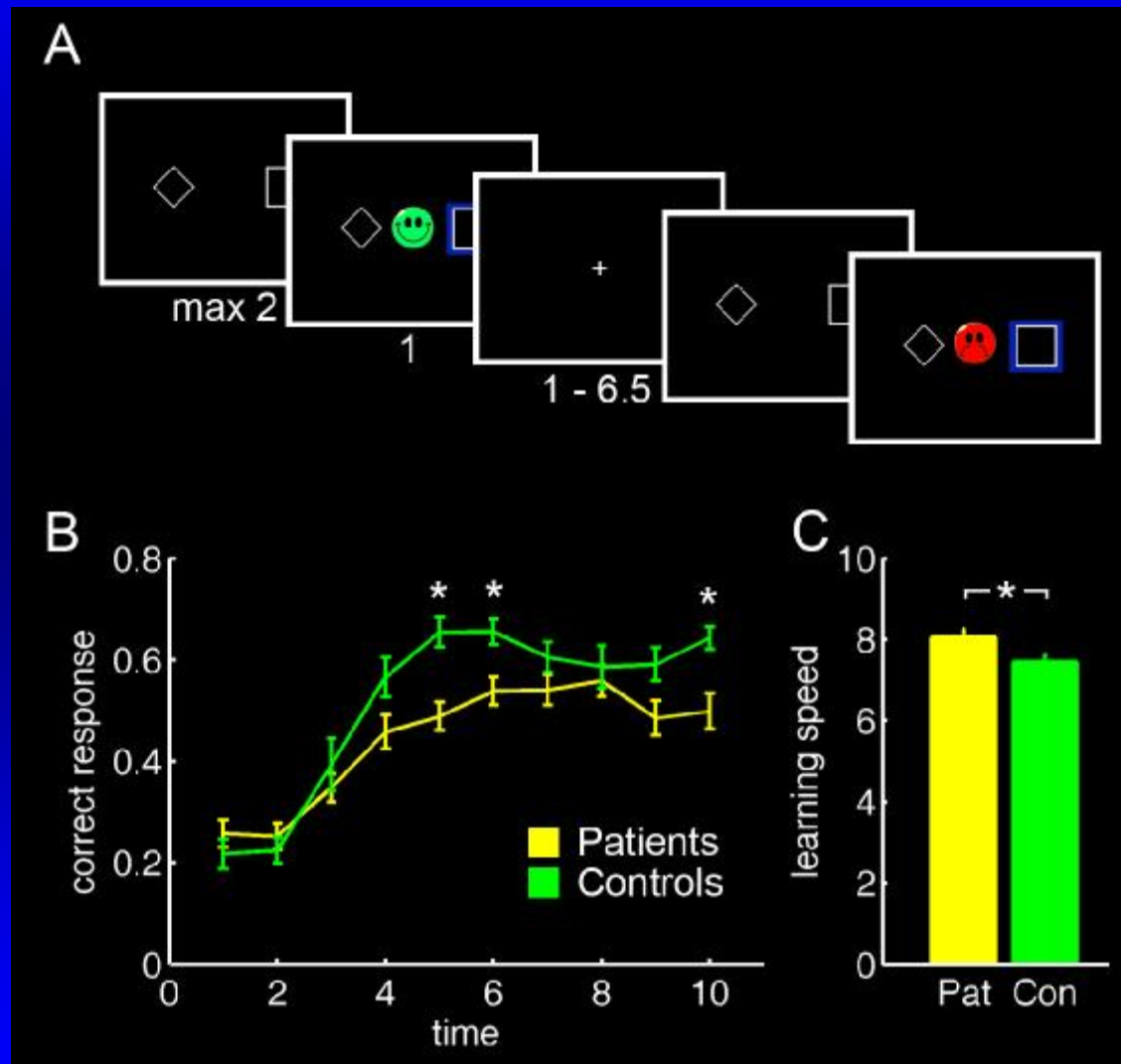
# Lack of activation of the ventral striatum in alcohol-dependent patients vs. Controls during reward anticipation



Wrase et al.  
Neuroimage  
2007

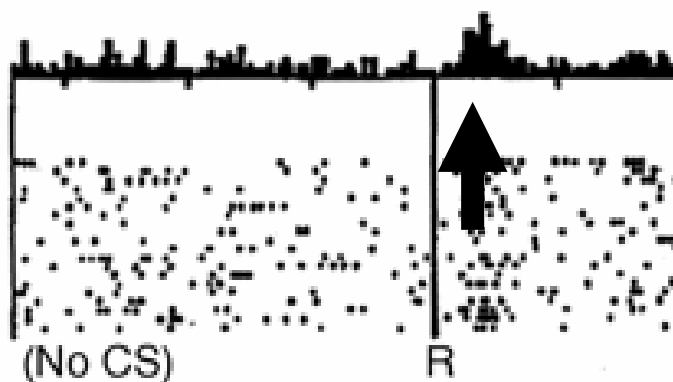
Charité

# Reduced reward-associated learning in alcohol-dependent patients



# Do dopamine neurons report an error in the prediction of reward?

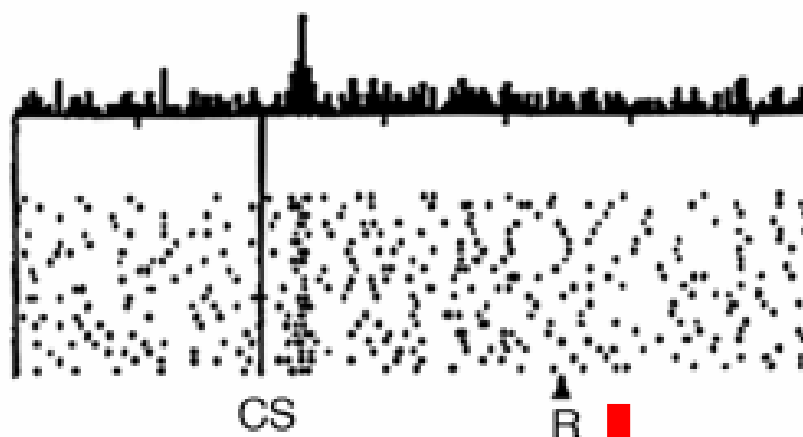
No prediction  
Reward occurs



Schultz et al.,  
Science 1997

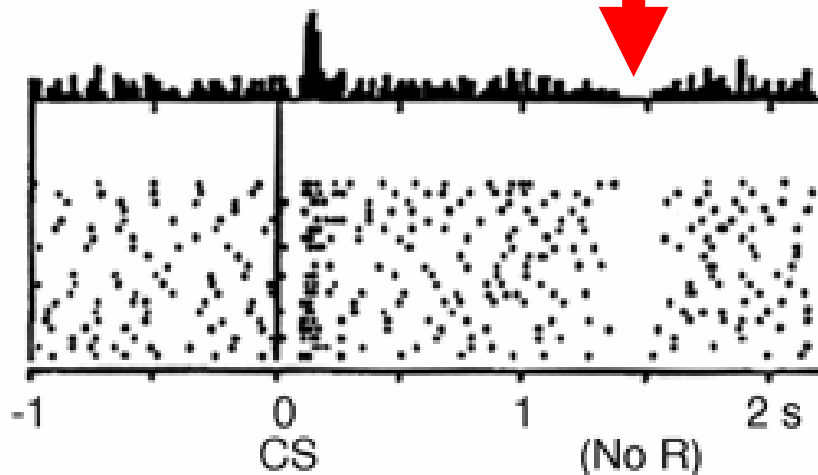
R received = 1,  
R expected = 0:  
 $1 - 0 = 1$

Reward predicted  
Reward occurs



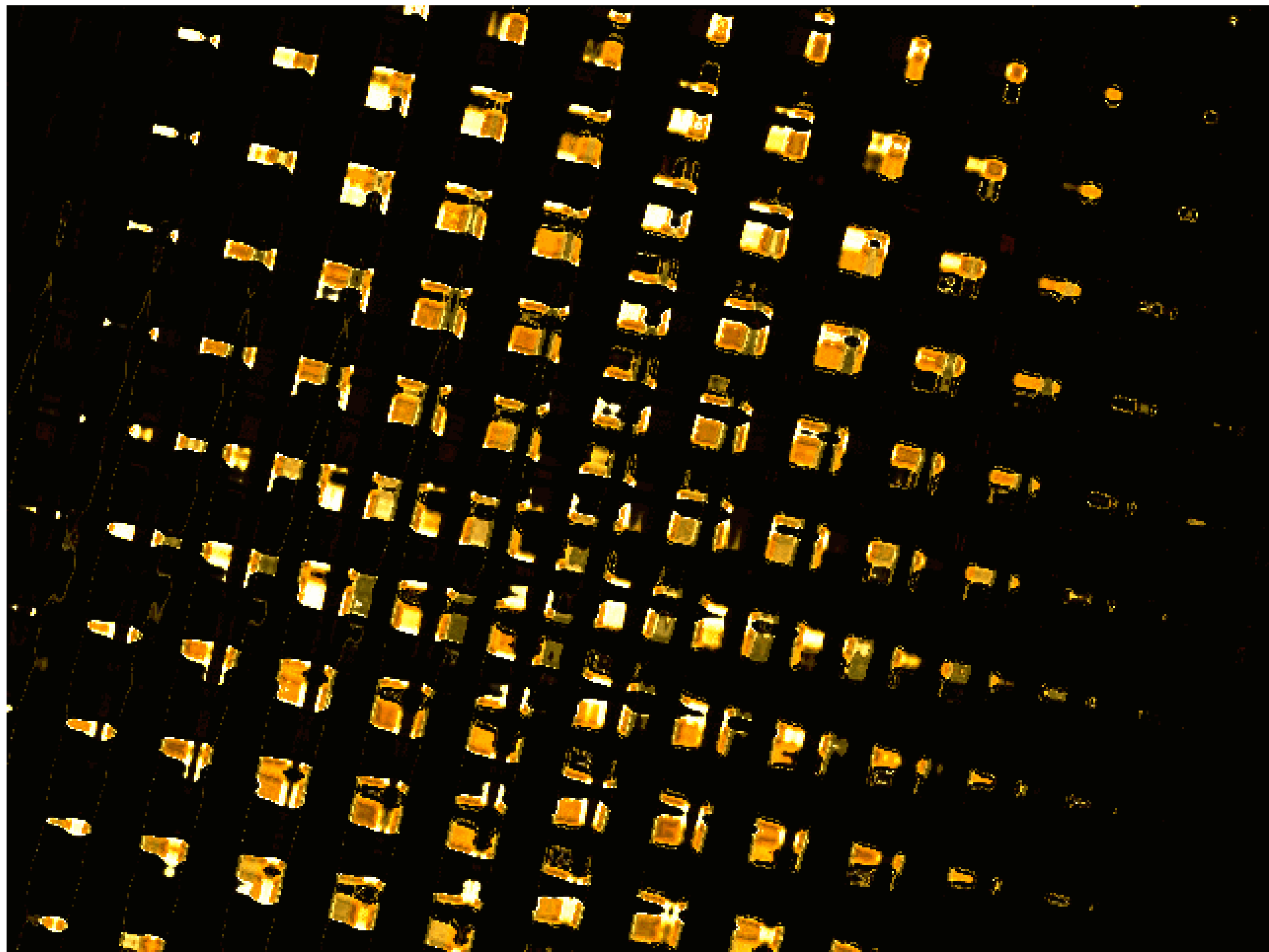
R received = 1,  
R expected = 1:  
 $1 - 1 = 0$

Reward predicted  
No reward occurs

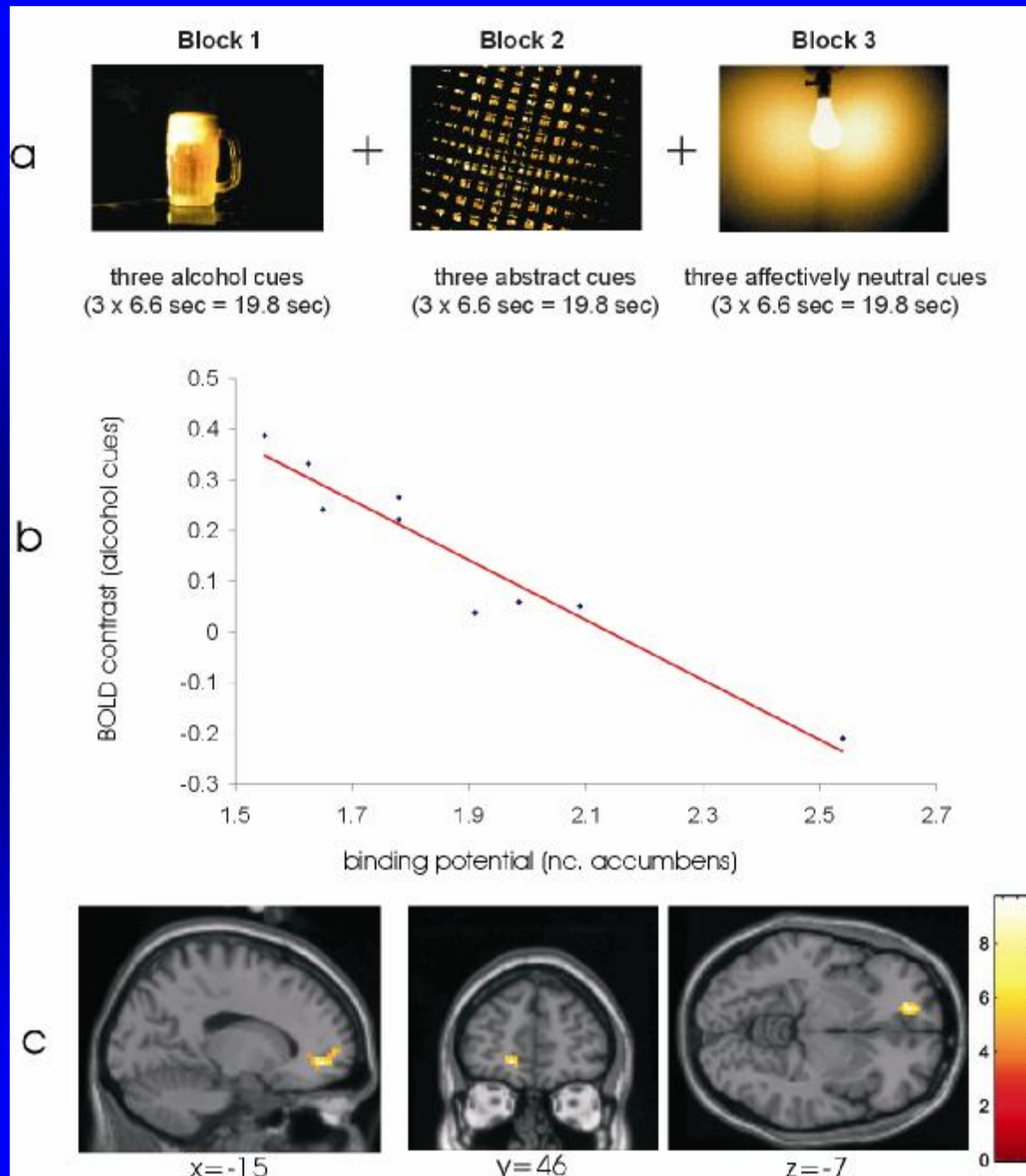


R received = 0,  
R expected = 1:  
 $0 - 1 = -1$





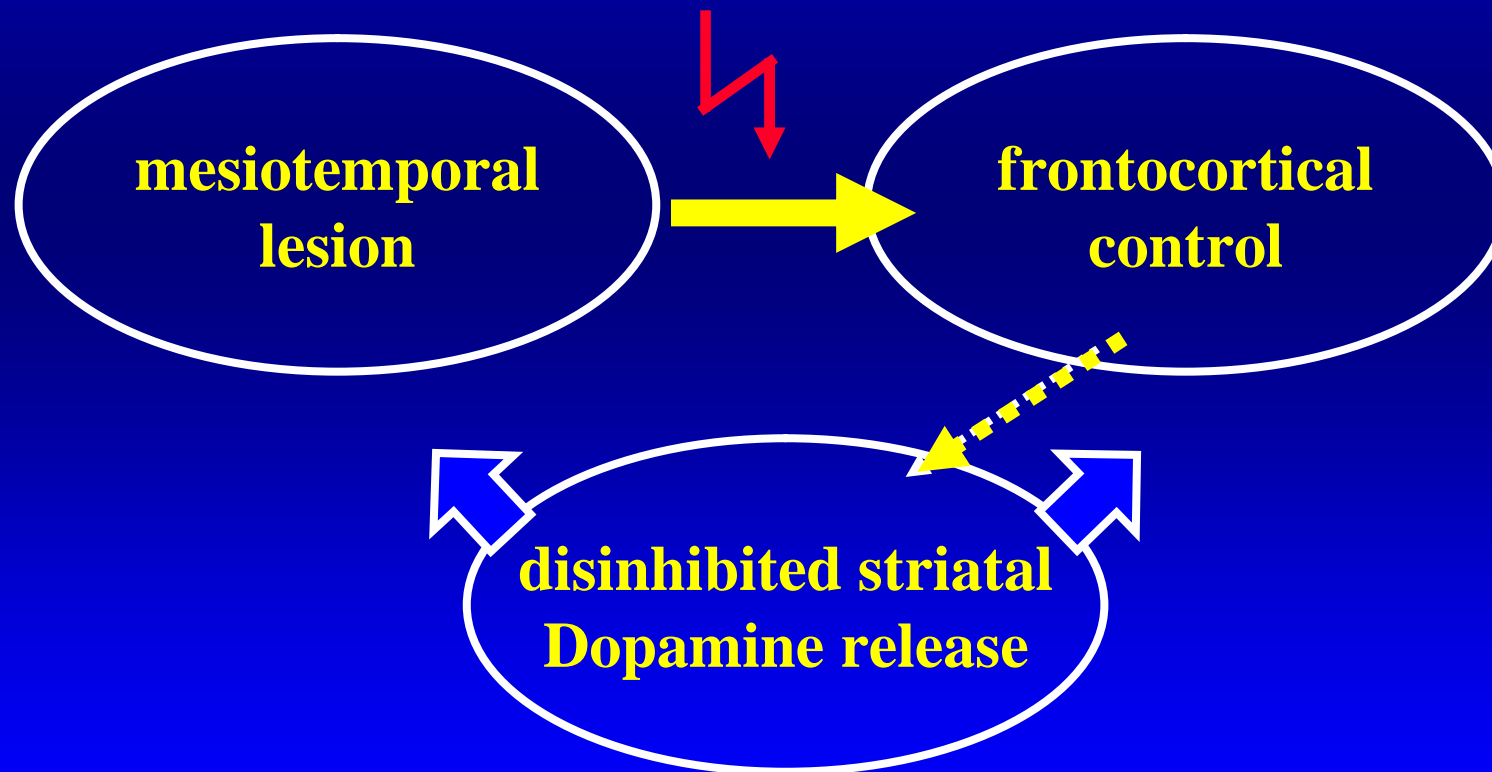


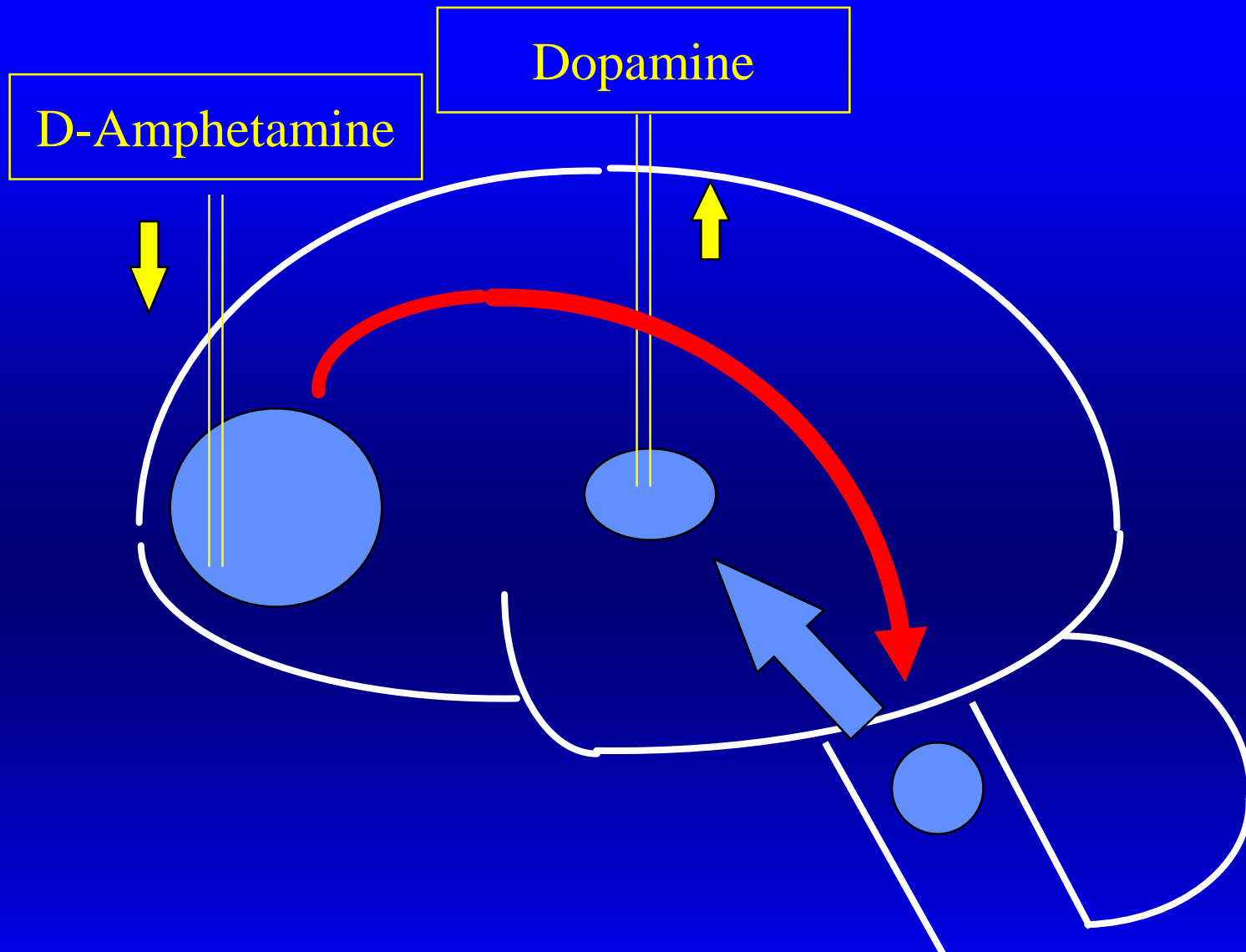


For  
presentation  
P<0.001  
uncorrected

*Charité*

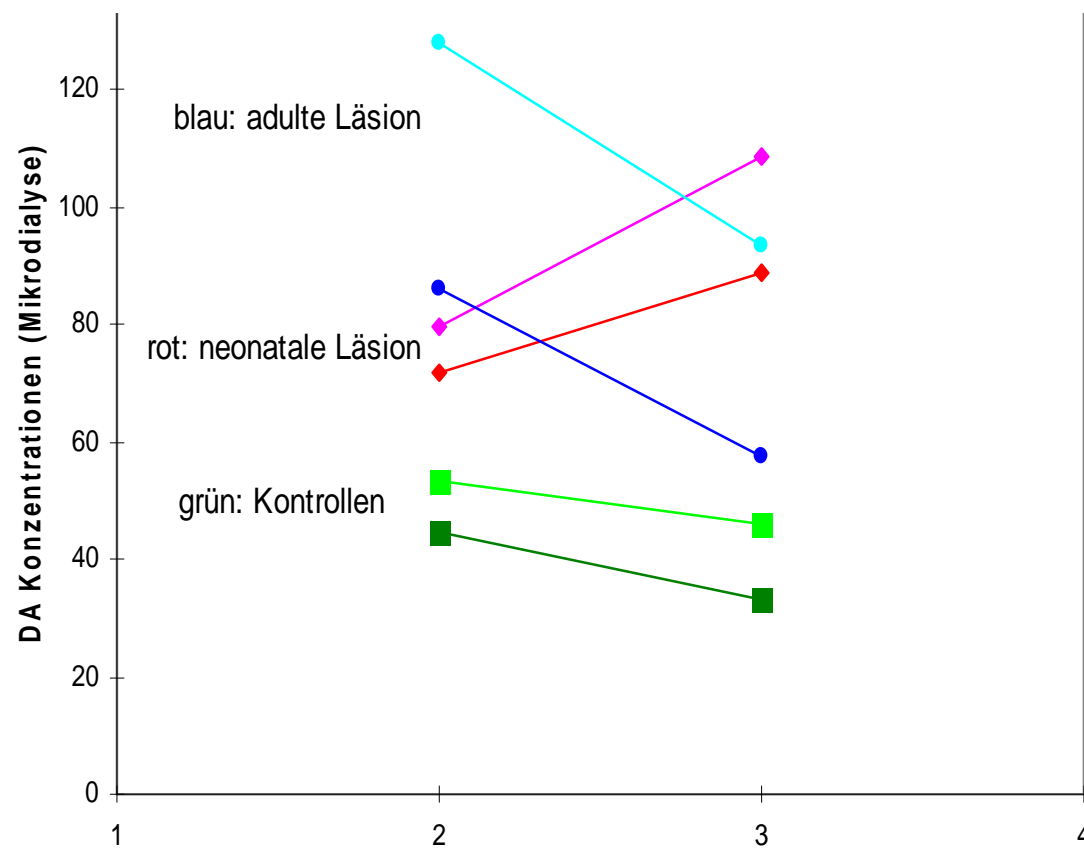
# Early developmental mesiotemporal lesion – disinhibition of striatal dopamine release?





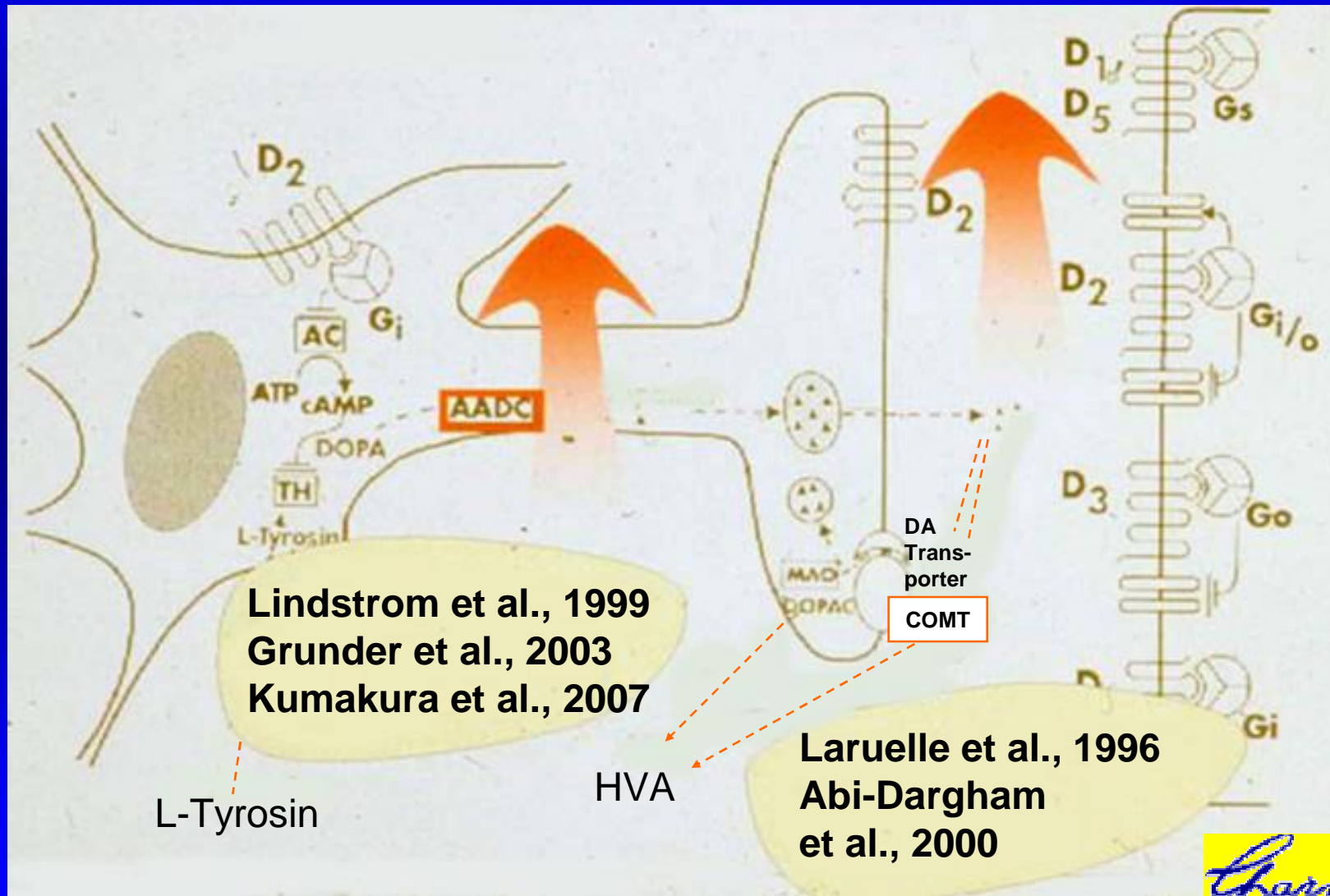
Microdialyse: B. Kolachana; Saunders et al., 1998

## Basic DA and DA following PFC stimulation

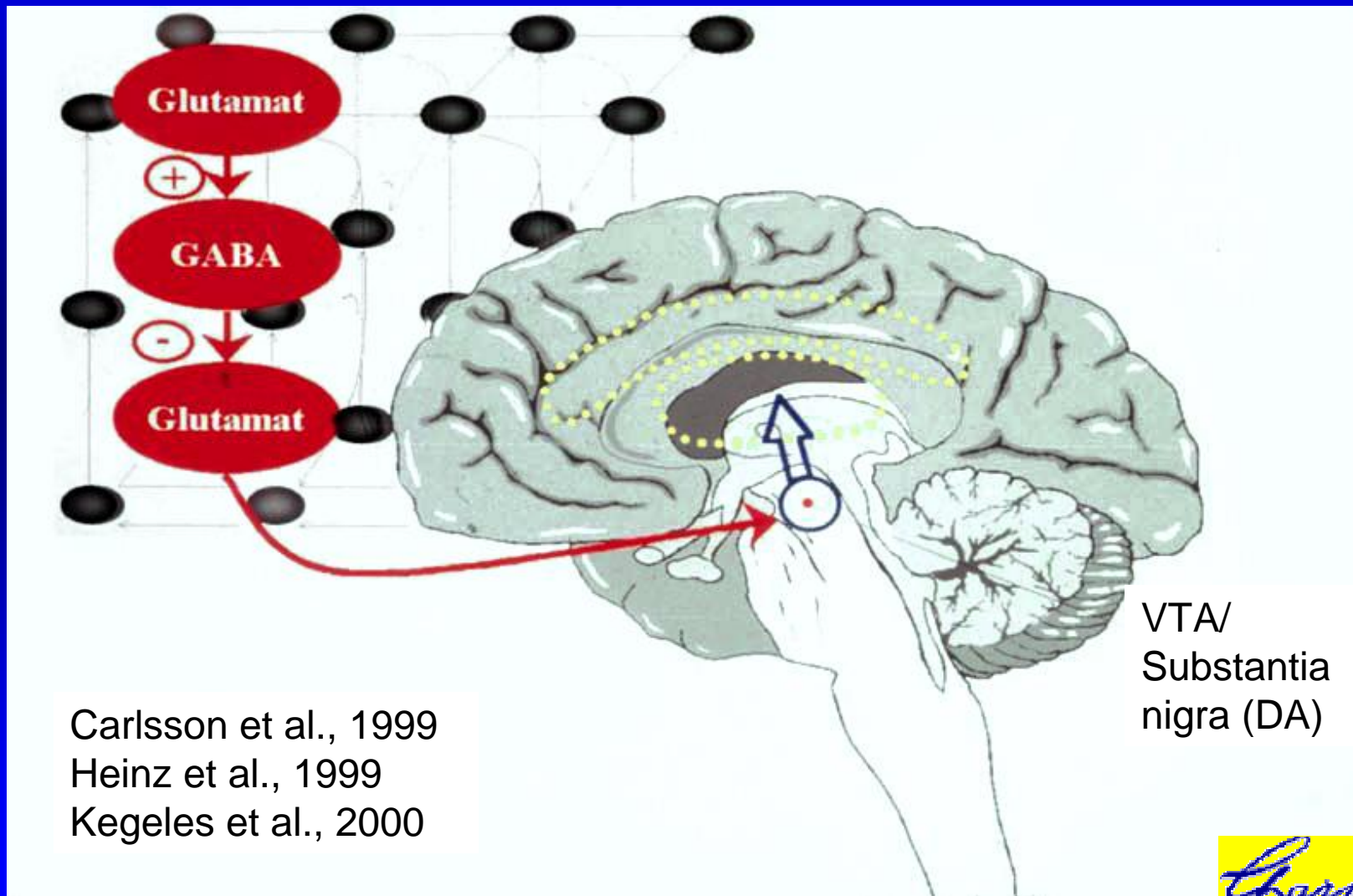


Heinz et al., Synapse 1999

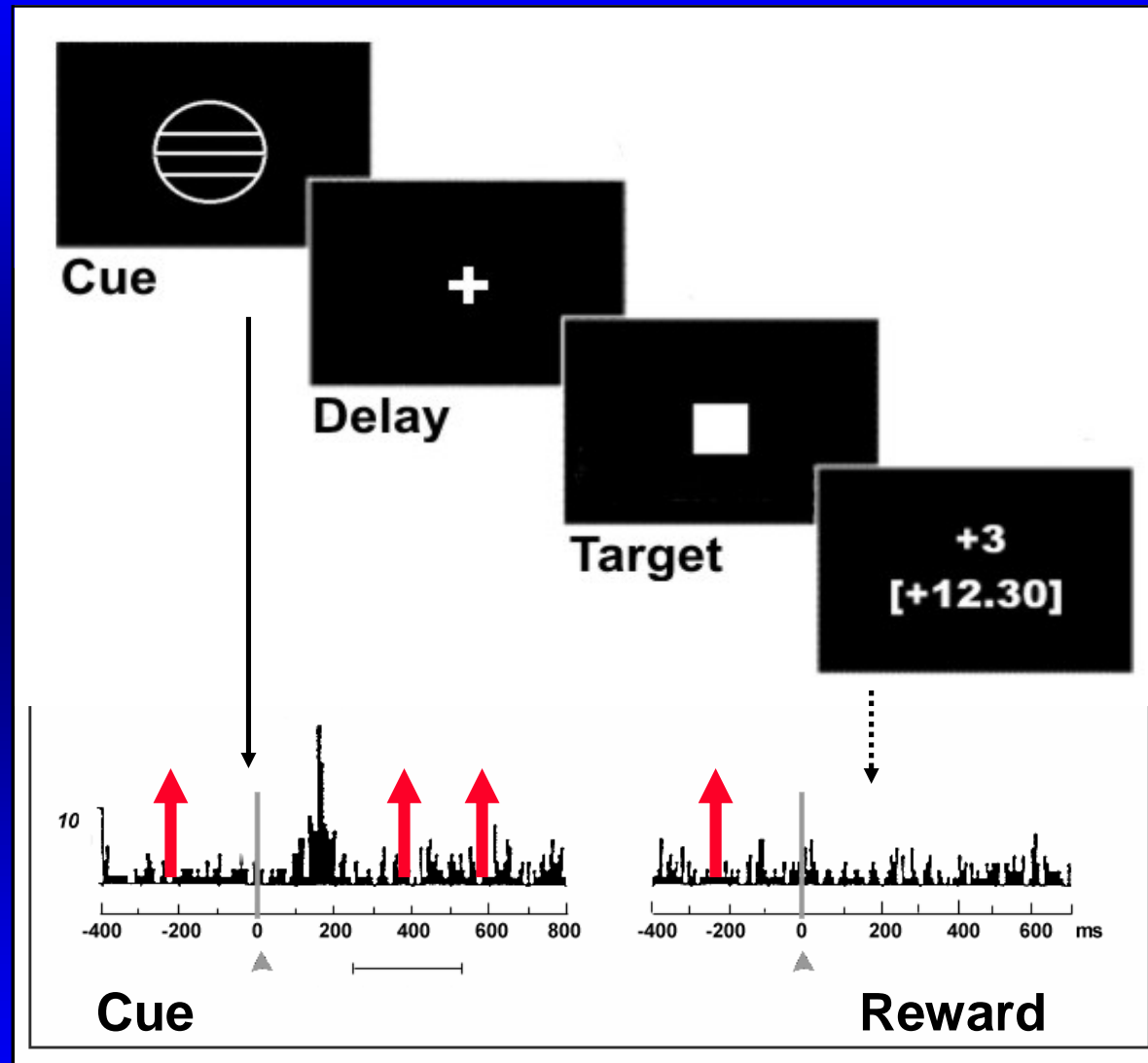
# Dopamine dysfunction in schizophrenia



# Cortical disconnectivity & disinhibition of subcortical dopamine release



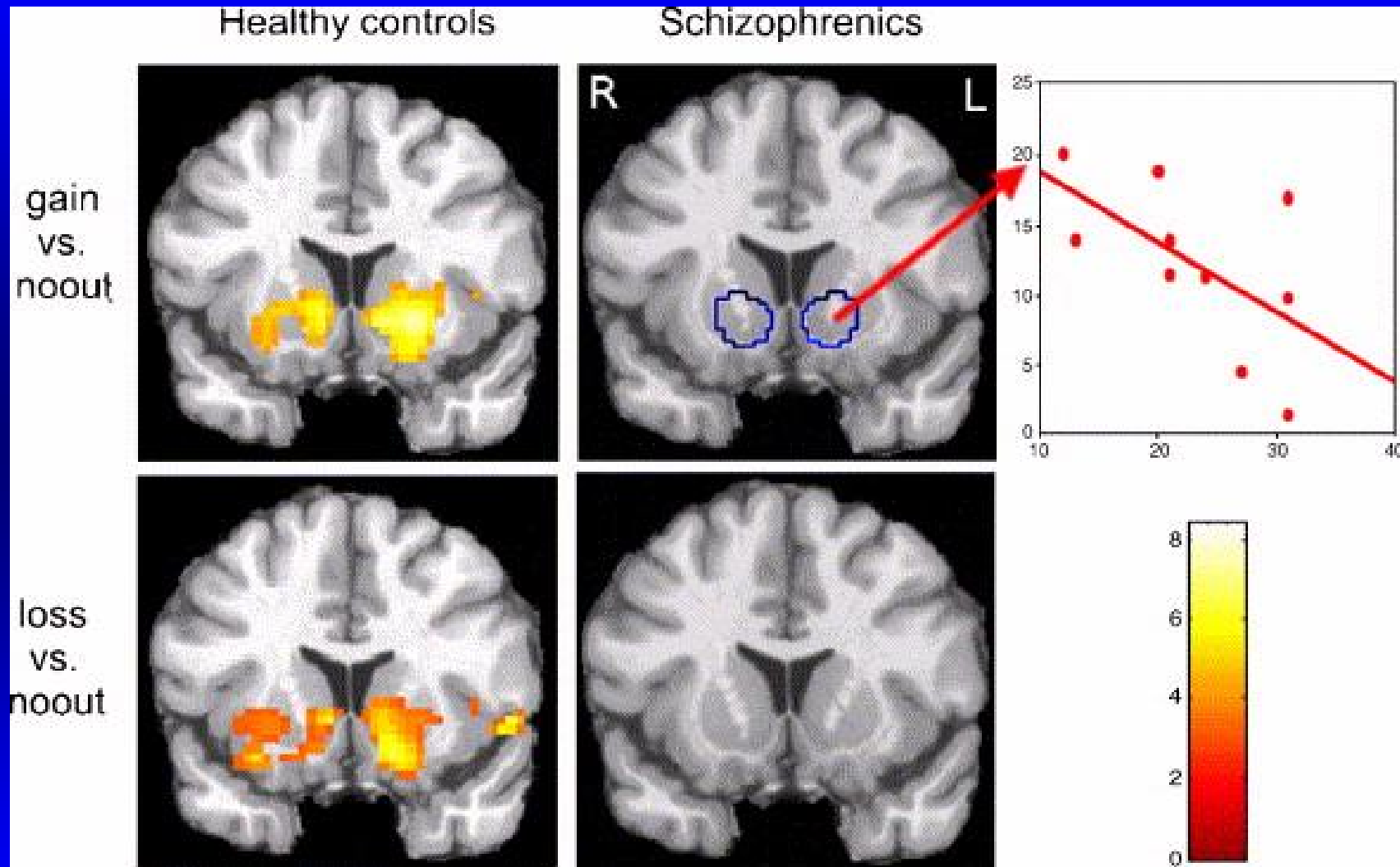
# Dopamine release can interfere with reward anticipation



Knutson et al., Neuron 2004

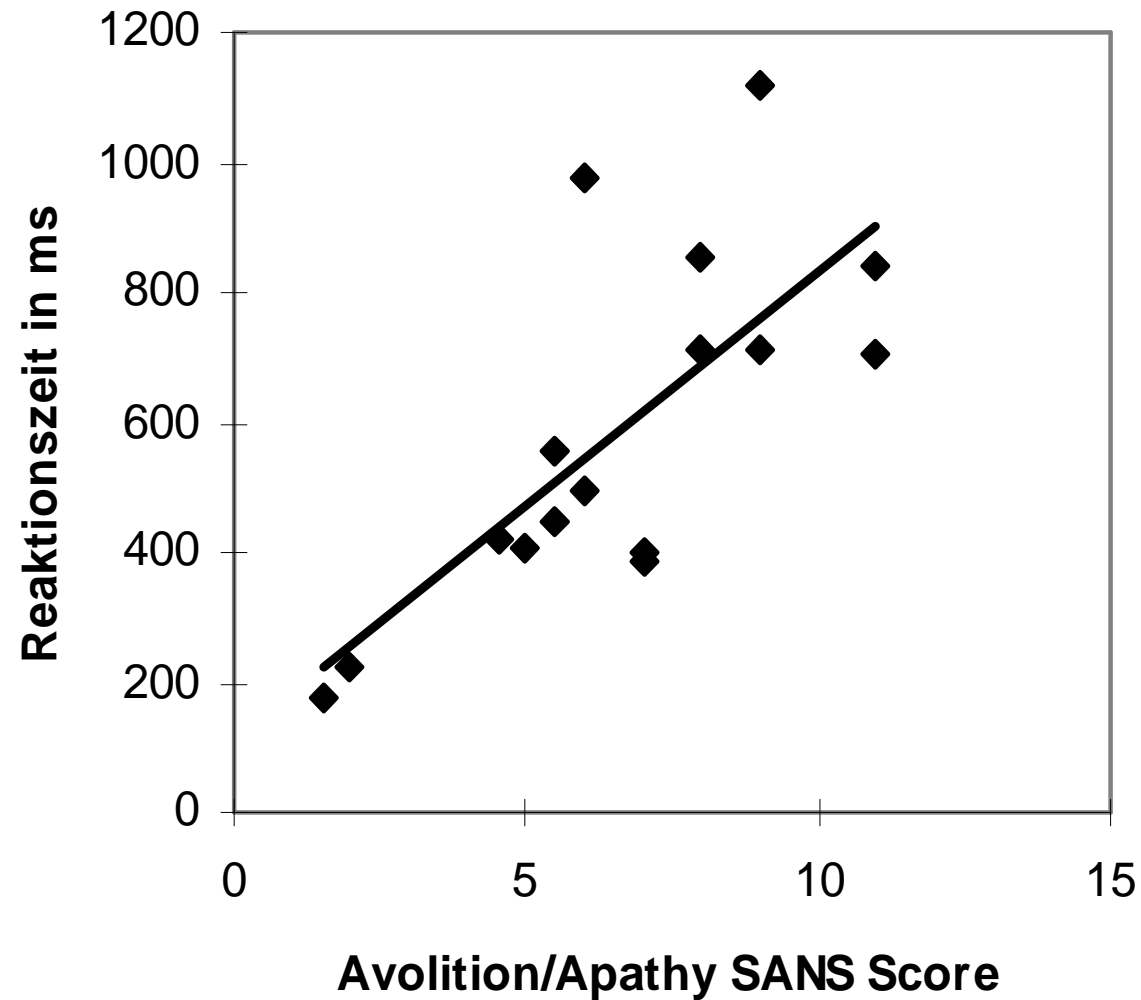
Schultz et al., Science 1996

# Dysfunction of ventral striatum during reward anticipation



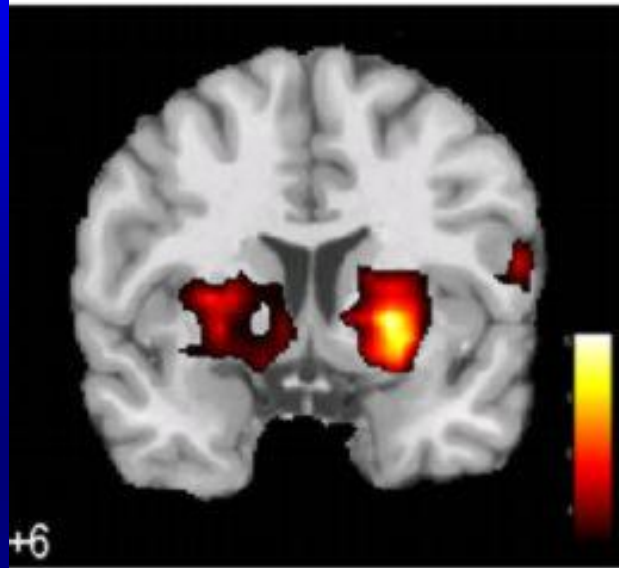
Juckel et al., Neuroimage 2006

Psychomotor slowing & apathy correlate with each other and with degree of D2 receptor blockade by neuroleptics

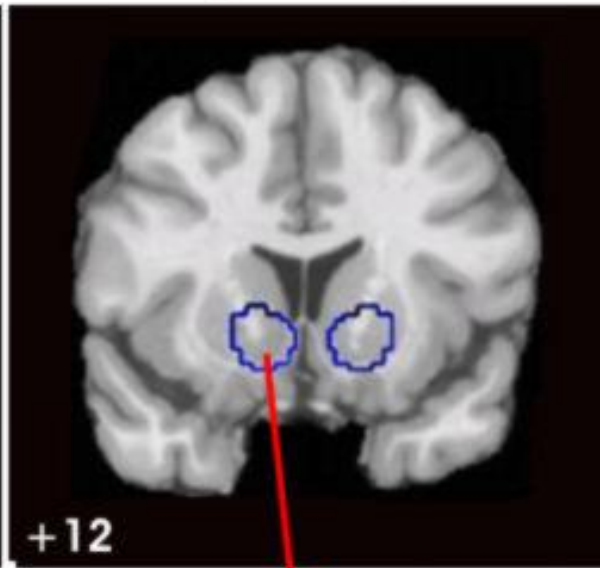


Heinz et al.,  
Schiz Res  
1998

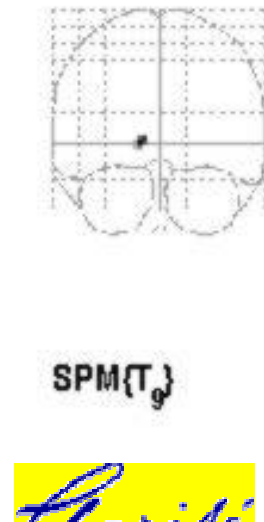
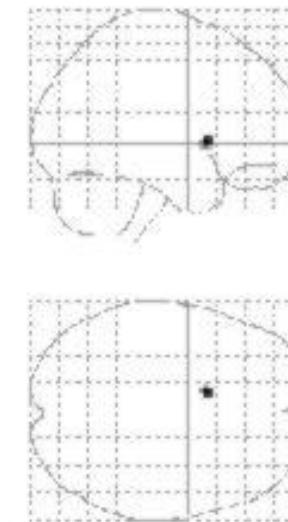
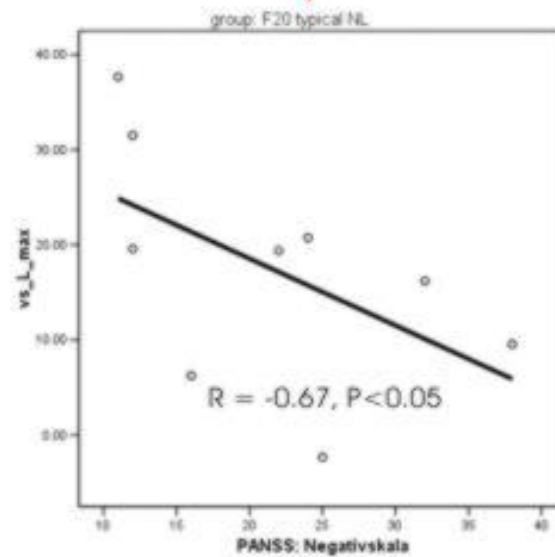
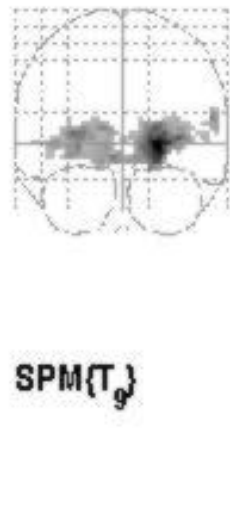
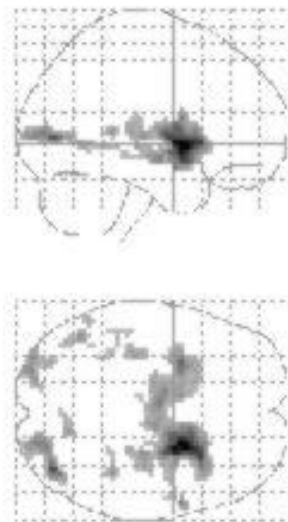
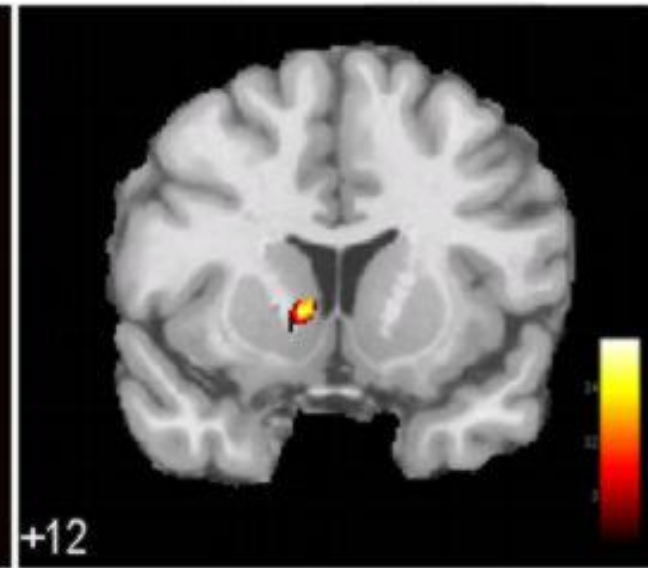
### Healthy controls



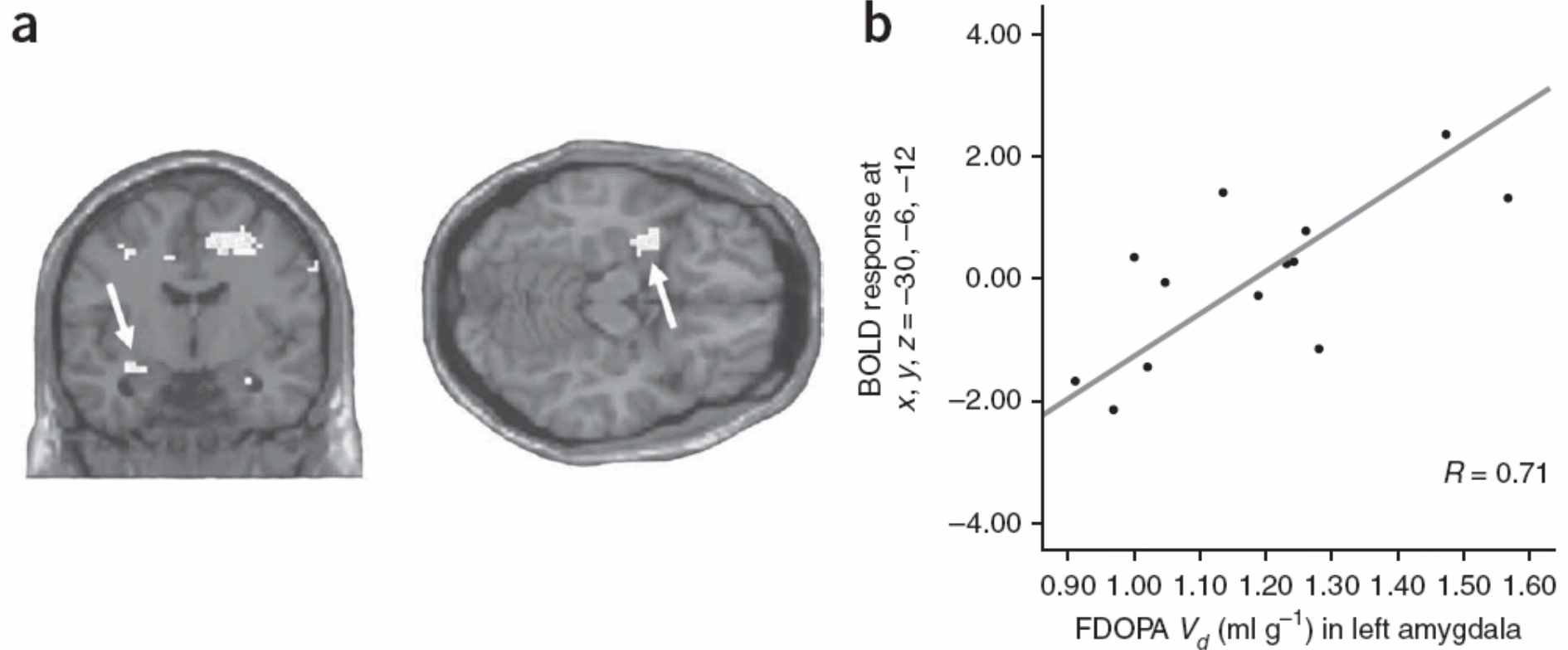
### Typical medicated schizophrenic patients



### Atypical medicated schizophrenic patients



# Dopamine synthesis in amygdala & limbic activation by aversive cues



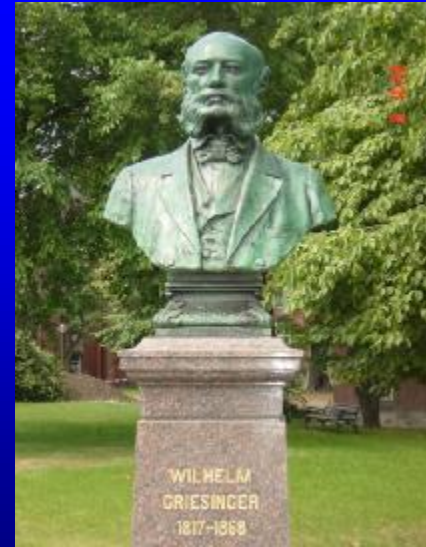
Kienast ... Heinz, Nature Neurosci 2008

# Summary

- Reduced dopamine D2 receptors in alcoholism: dysfunction during reward anticipation & problems to learn something new?
- Reduced dopamine D2 receptors in alcoholism: dysfunction during reward feedback & problems to unlearn something old?
- Increased phasic dopamine release in VS of unmedicated schizophrenia: aberrant salience attribution?  
(Heinz, *Eur Psychiatry* 2002; Kapur *AJP* 2003)
- Increased dopamine release in amygdala & anxiety?
- High blockade of D2 receptors with neuroleptics: dysfunction during reward anticipation & dysfunction of motivation = apathy?



*Charité*



**Schlagenhauf F, Wrase J, Beck A, Friedel E, Sterzer P, Gallinat J**

*Charité Campus Mitte*

**Cooperations:**

**Büchel C**

*Neuroimage Nord & Klinik für Psychiatrie, Universität Hamburg*

**Schumann G**

*Institute of Psychiatry, London*

**Bares R, Reimold M, Machulla HJ**

*PET Center Univ. Tübingen*

**Knutson B**

*Stanford University*

**Goldman D, Jones DW, Higley JD, Hommer D, Weinberger DR**

*National Institutes of Health, Bethesda, MD*