

## **Addiction Therapy-2014**

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# The effect of HF-rTMS in alcohol-dependent patients: Results from an fMRI study

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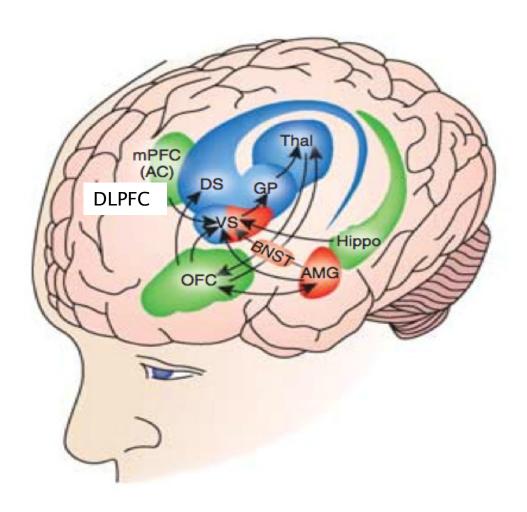
Introduction

Study design & results

Conclusions



## Key structures in addiction





# rTMS & alcohol craving in detoxified alcoholic patients

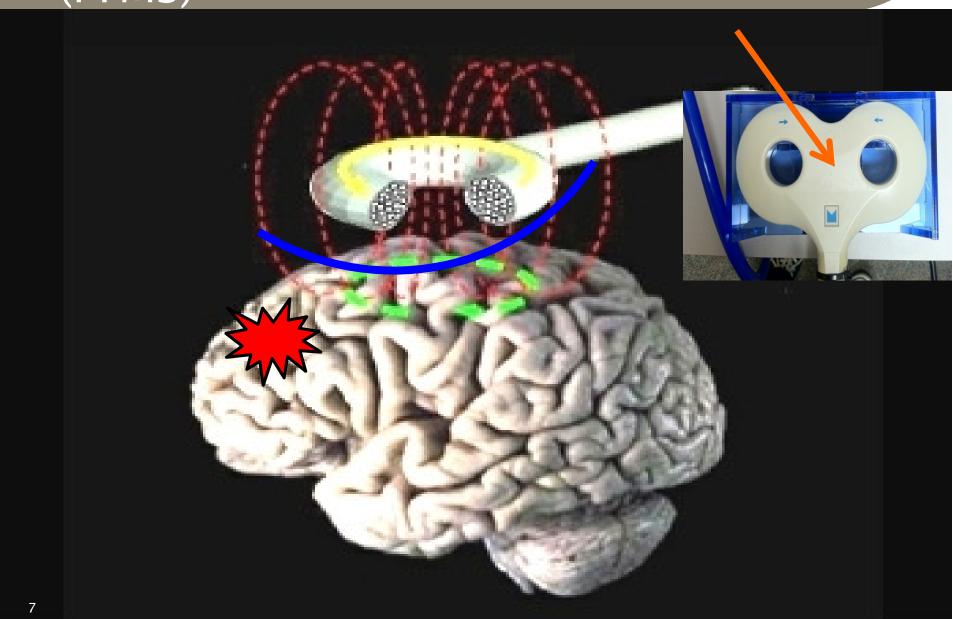
- Mishra et al., 2010:
- -> 10 daily sessions, HF-rTMS (10 Hz) right DLPFC, 1000 pulses per day, SHAM-controlled
- =>  $\Psi$  subjective craving,  $\Psi$  relapse rate
- Herremans et al., 2012:
- -> 1 session, HF-rTMS (20 Hz) right DLPFC, 1560 pulses, sham (=PLACEBO)-controlled
- → No effect on subjective craving
- ⇒ Increase of attentional control during Go-NoGo task



Repetitive transcranial magnetic stimulation (rTMS)



# transcranial magnetic stimulations (rTMS)



Can one and fifteen HF-rTMS sessions influence the craving neurocircuitry in detoxified alcohol dependent patients during a cue-exposure?



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#### Demographic data

- 20 alcohol-dependent patients
- Detoxified < CIWA-AR</li>
- 11 males / 9 females
- Age: 46,5 y (SD: 10,0)
- Duration alcohol problem: 13.0 y (SD:9.9)

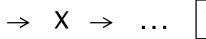
#### Study design - evaluation of 1 HF-rTMS session

#### fMRI Event Related design









VAS

one sha 12 pts -8 pts - "How much do you crave for an alcoholic beverage right now on a scale from 0 to 10?"

ssion

FC

#### fMRI Event Related design





$$\rightarrow$$
 X  $\rightarrow$ 



$$\rightarrow$$
 X  $\rightarrow$  ...

**VAS** 

# Study design – ACCELERATED evaluation of 15 HF-rTMS sessions

#### fMRI Event Related design







HF-rTMS: 20Hz 1560 p/session 110% MT Right DLPFC

15 active HF-rTMS sessions

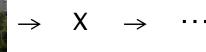
20 patients -> 2 drop-outs

#### fMRI Event Related design





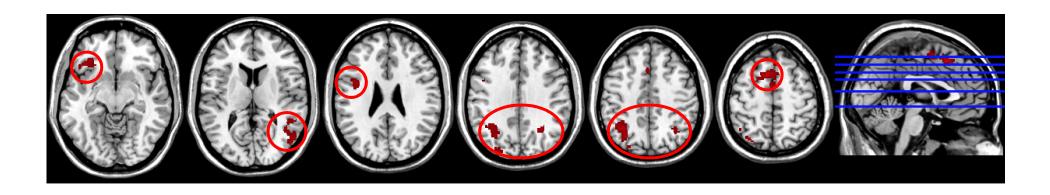




## Results: Baseline



#### Baseline Alcohol cue > Neutral cue



Inferior frontal gyrus (BA47) left Inferior temporal gyrus (BA37) right Medial Frontal gyrus (BA6) left Superior parietal lobule (BA7) left/right *P*<0.001; AlphaSim corrected voxel: 176

No increase in craving



# Results: one sham-controlled HF-rTMS session

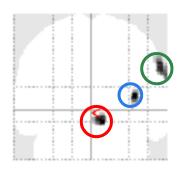


## Demographic data

	Real stimulation (12)	Sham stimulation (8)
Age	M=48.0 SD=9.9	M=44.4 SD=8.7
Gender (M/F)	8/4	4/4
Benzodiazepine free days before stimulation	M=15.1 SD=5.2	M=12.5 SD=2.7
% MT	M=57.6 SD=10.6	M=64.1 SD=6.4
VAS before cue-exposure (0=>10)	M=2.3 SD=2.7	M=2.6 SD=3.4
VAS after cue-exposure (0=>10)	M=2.5 SD=3.0	M=2.8 SD=3.5

#### Results: 1 sham controlled session



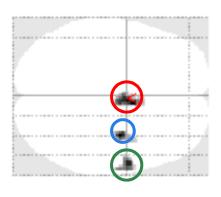


INTERACTION: Pre\_Post x Sham\_Real

F=7.4; *p*<0.01;

AlphaSim corrected voxel: 71

**SPM**\*\*\*; [0,0,0]



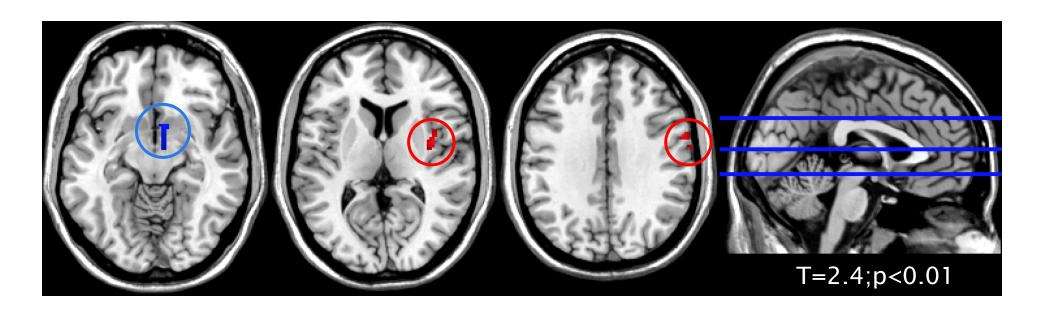
 $\mathsf{SPM}\{\mathsf{F}_{1,34}^{}\}$ 

Nucleus Accumbens Insula BA6

**SPMresults:** ./full factorial\_isessie\_ER\_age\_gender Height threshold F = 7.444136 {p<0.01 (unc.)} Extent threshold k = 71 voxels



#### Results: 1 REAL stimulation







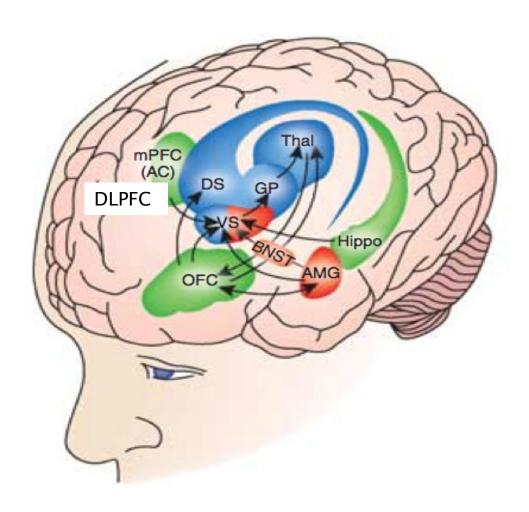




No effect of sham stimulation

No effect on VAS-craving (deltaVAS)

## Key structures in addiction





Koob & Volkow, 2010

#### Results: 15 active HF-rTMS sessions

in an accelerated paradigm



# Treatment effect of 15 active rTMS sessions



2 drop-outs

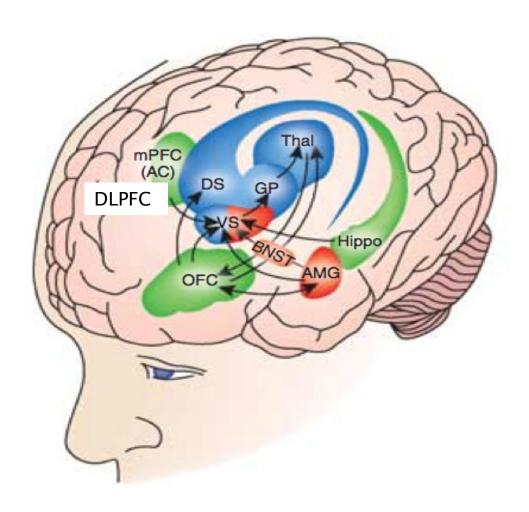
T=2.6; p<0.01 alphaSim voxel corrected: 482

Superior Parietal Iobule (BA7)





## Key structures in addiction





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#### 1 active HF-rTMS session

- Placebo controlled design
- No effect on cue-induced craving
- Vucleus Accumbens
- Insula
- **↑** BA 6
- No effect of sham stimulation

#### 15 active HF-rTMS sessions

- Accelerated HF-rTMS protocol
- Open study: 

   ✓ craving outside fMRI
- No effect on cue-induced craving
- superior parietal lobule



#### General conclusions

- HF-rTMS ★> cue-induced craving
- HF-rTMS > craving neurocircuit (Koob & Volkow, 2010)

#### **But:**

- HF-rTMS => salience and attention network
- HF-rTMS => subjective craving

salience attribution to & attention at alcoholic stimuli





#### Limitations

- Relatively small sample
- No control group for the treatment part
- Hospitalized patients seldom report craving when confronted with alcoholic stimuli (Wilson et al., 2004)



### Thank you for your attention!

#### **QUESTIONS?**

#### **Collaborators:**

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Frieda Matthys, MD
Rudi De Raedt, PhD





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