rTMS and neurofeedback

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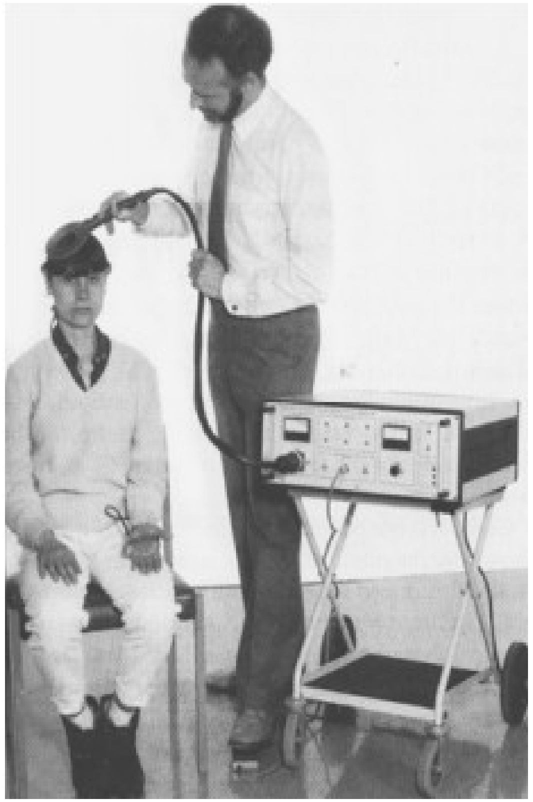
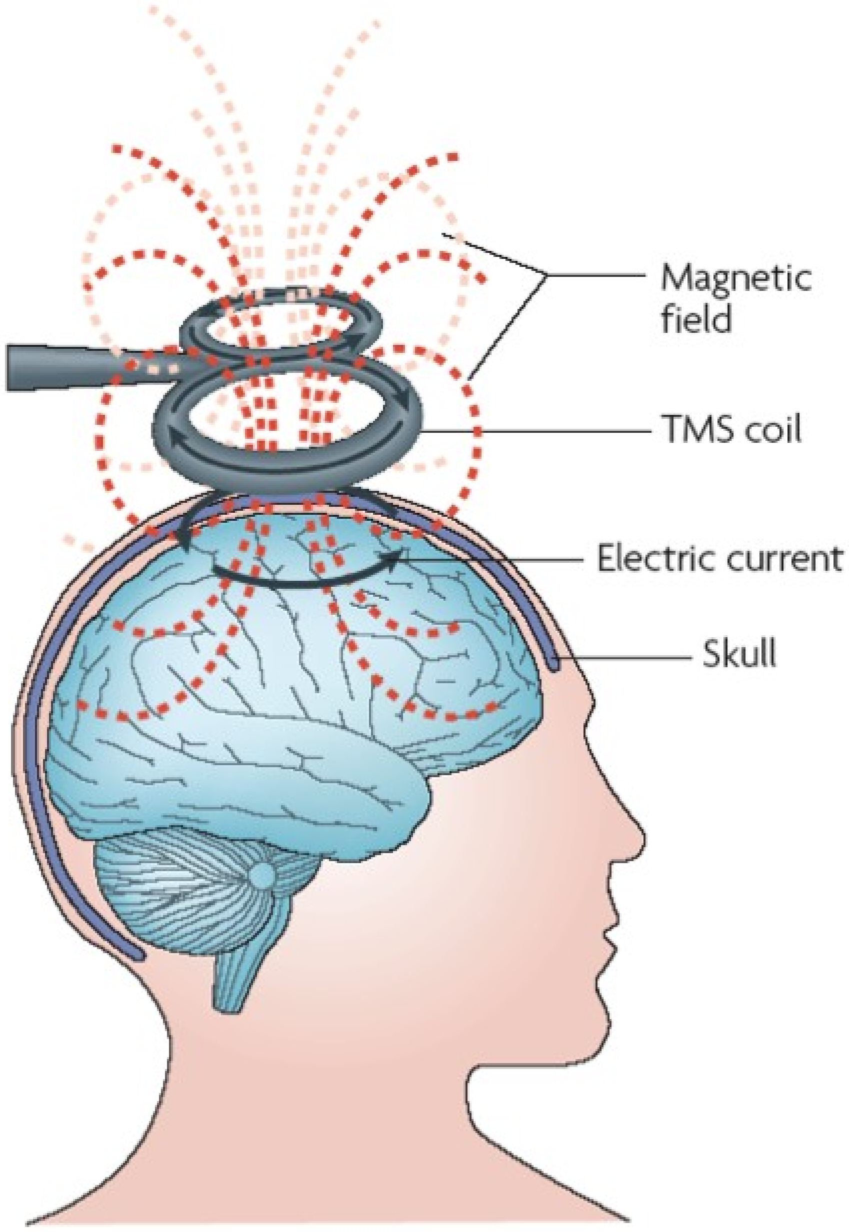
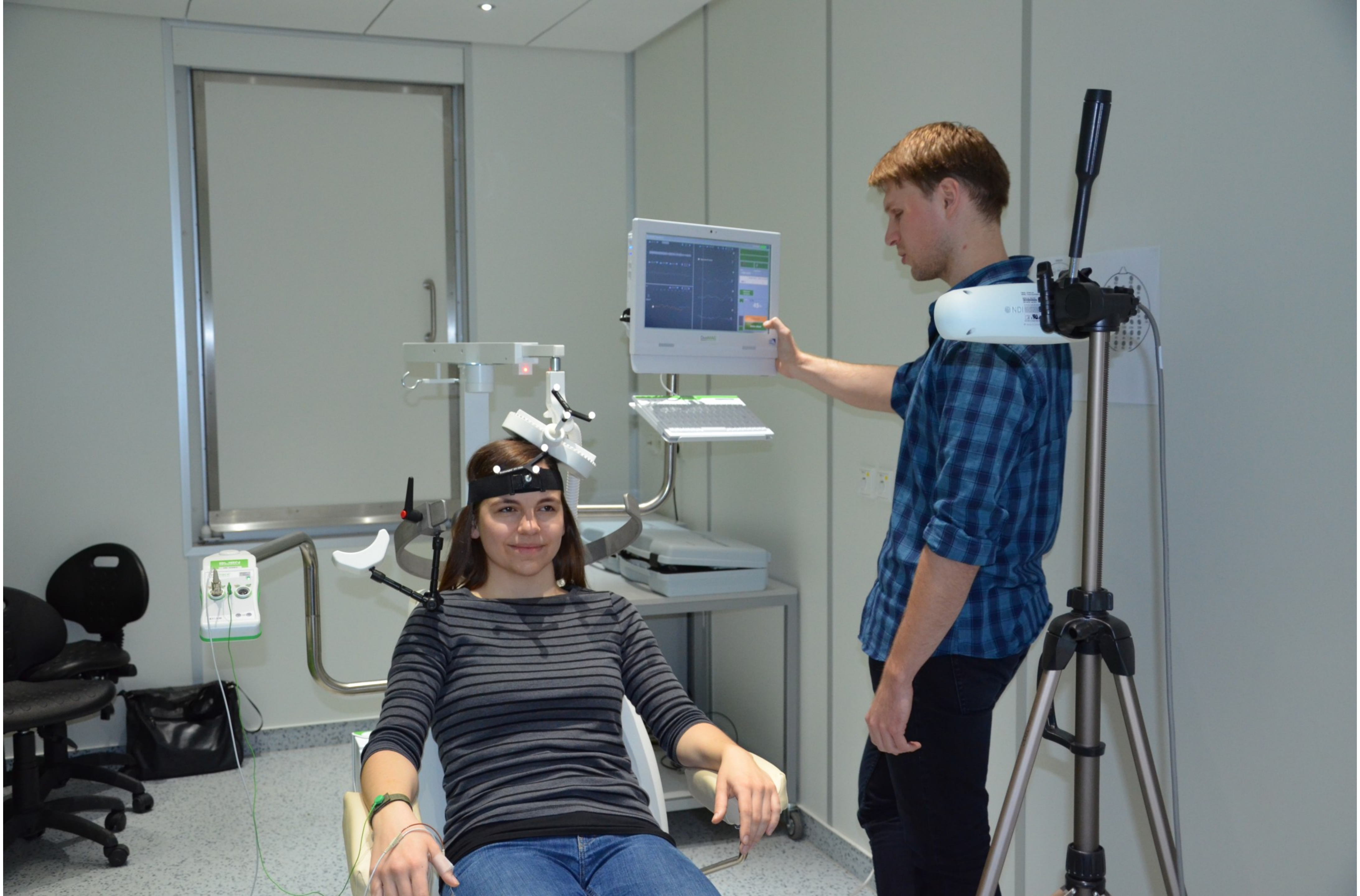
TMS

- Transcranial magnetic stimulation
- Non-invasive method of brain stimulation
- 1985, Anthony Barker
- Electromagnetic induction based on Faraday principle: magnetic field induced electrical current in the cortex



TMS





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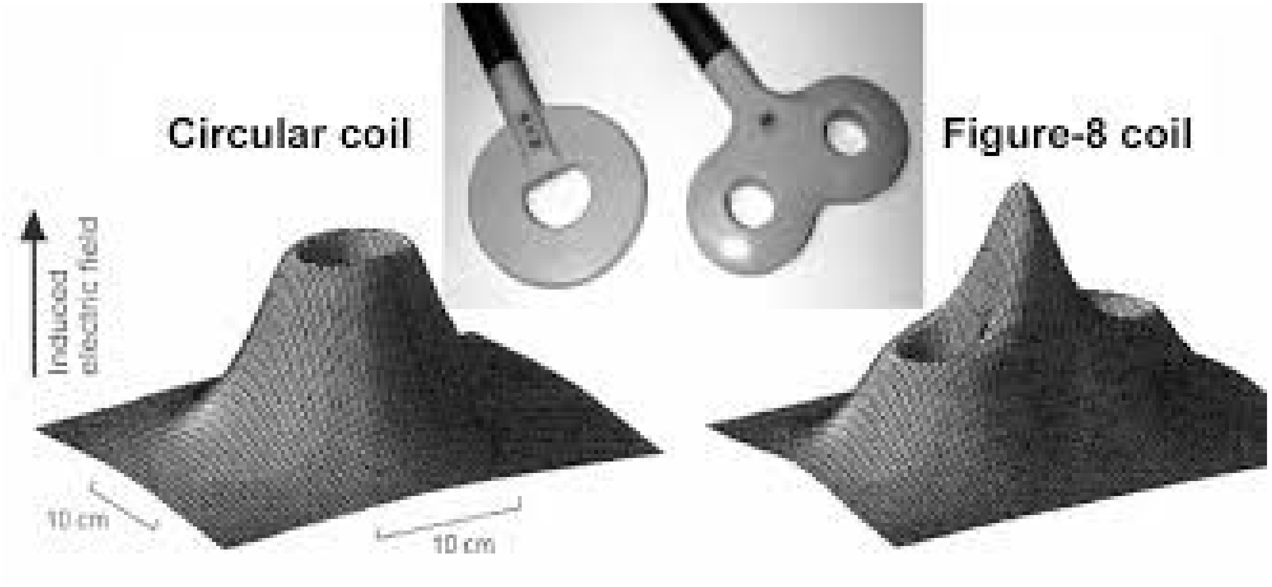
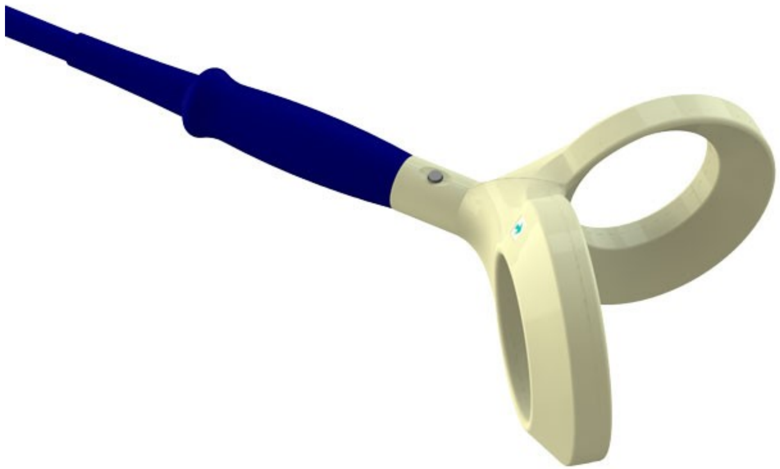
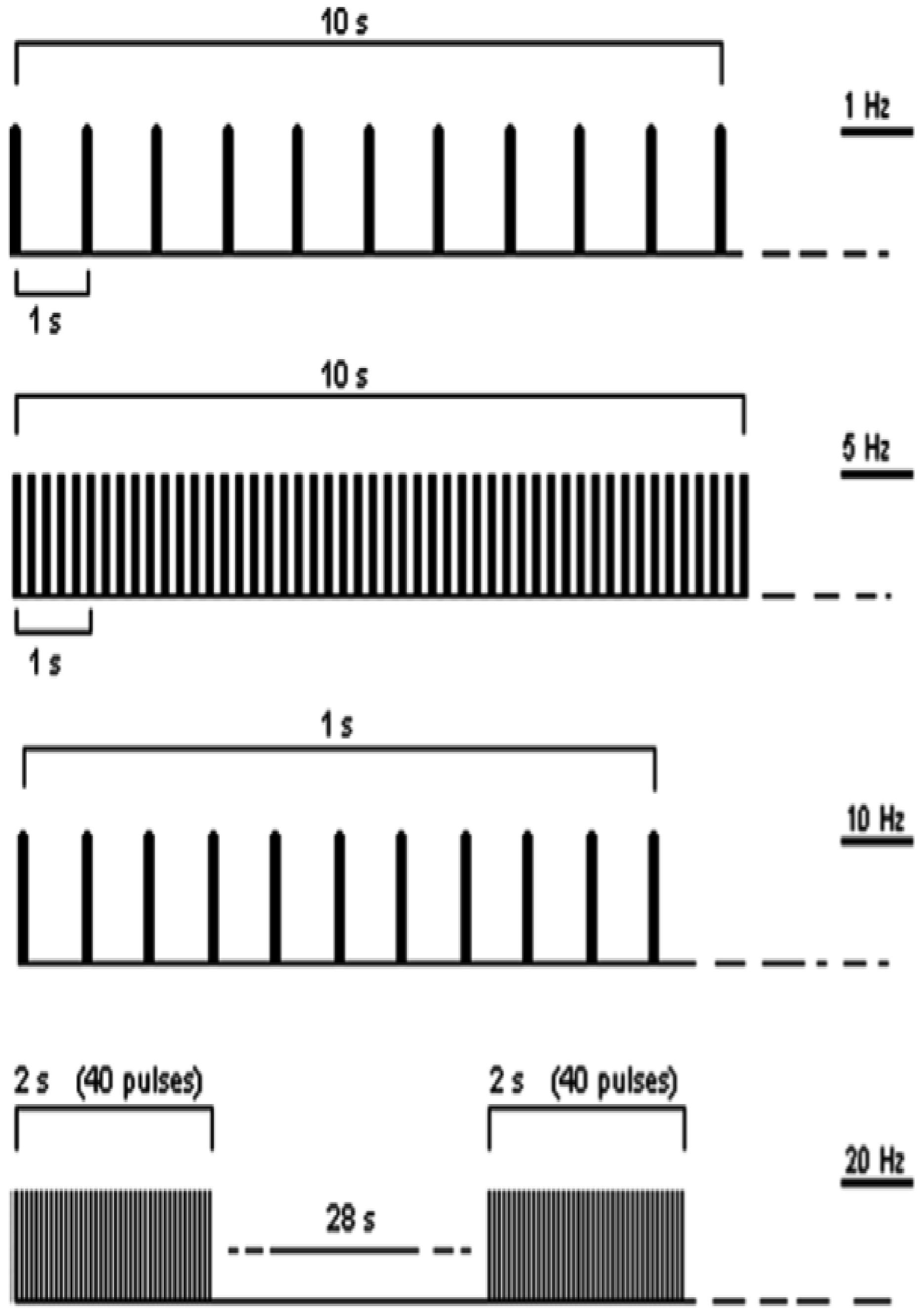
TMS coils


Circular coil
Figure-8 coil
Induced electric field
10 cm
10 cm



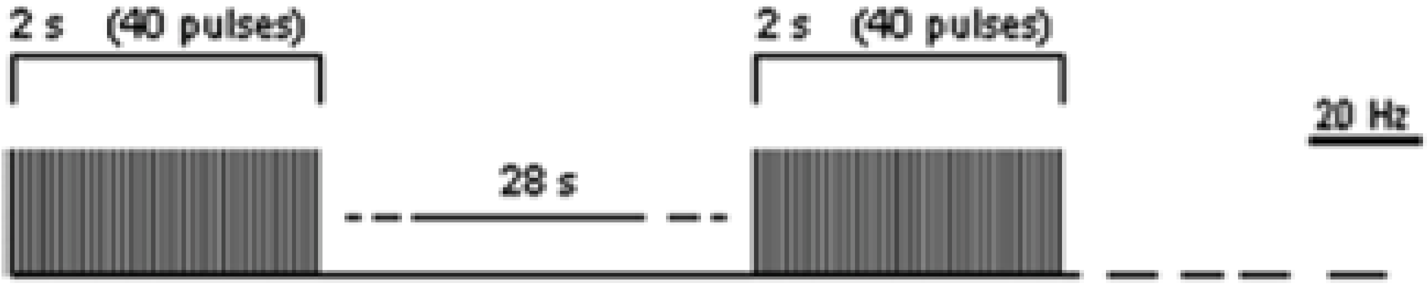
rTMS

- Repeptitive transcranial magnetic stimulation: therapeutical use
- Modulation of cortical excitability
- Modulation of metabolic activity



rTMS parameters

- Frequency (low, high)
- Number of pulses
- Length of train and inter-train
- Number of sessions and time between sessions
- Coil type, stimulated area



rTMS contraindication

- Epilepsy
- Pregnancy
- Alcohol
- Intracranial metal objects
- Pacemaker

rTMS in psychiatry

Depression

ADHD

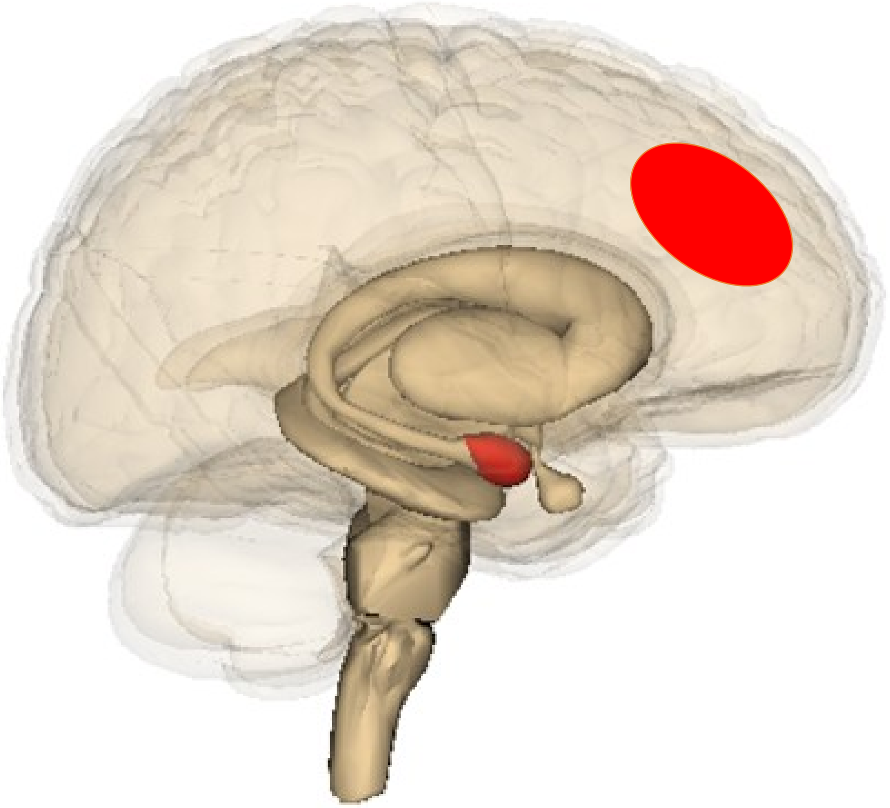
Auditory halluctionations

Other...

Addictions (cravingu)

Obsessive compulsive disorder

Neural substrates of emotion regulation



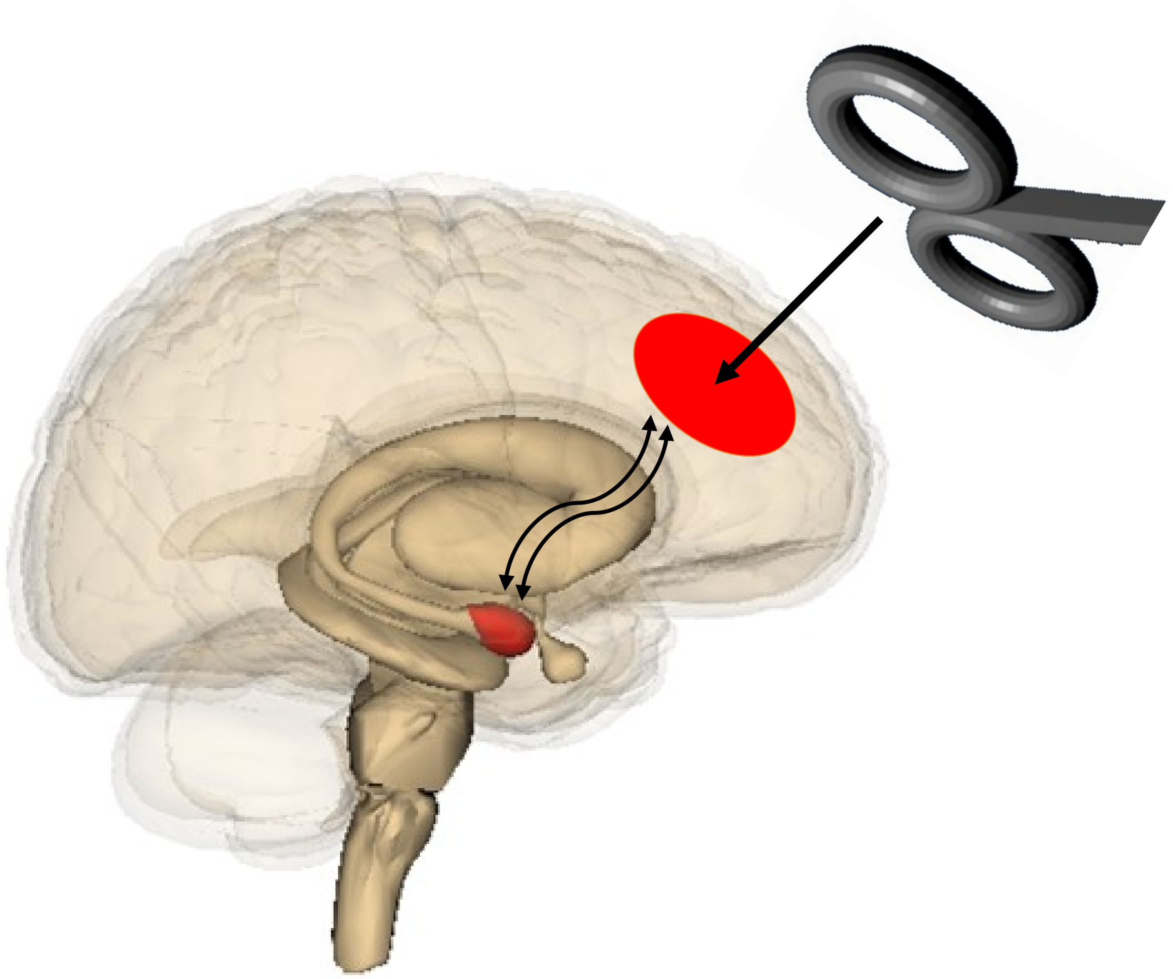
- Volitional „top-down“ cognitive emotion regulation: amygdala activity regulation by prefrontal cortex
- Petients with impaired emotion regulation:
    - Amygdala hyperactivity during emotion processing
    - Decreased lateral prefrontal activity during emotion processing
    - Impaired connectivity between amygdala and prefrontal cortex

Phillips, M.L., Ladouceur, C.D., Drevets, W.C. (2008). A neural model of voluntary and automatic emotion regulation. *Molecular Psychiatry, 13*(9), 829-857.

Schulze, L., Schmahl, C., Niedtfeld, I. (2016). Neural correlates of disturbed emotional processing in borderline personality disorder: A multimodal meta-analysis. *Biological Psychiatry, 79*(2), 97-106.

rTMS for emotion regulation

Targeting emotion regulation in BPD by rTMS



INCREASE IN

EMOTION AWARENESS
EMOTION REGULATION

DECREASE IN

DISSOCIATION
IMPULSIVITY

Previous studies of rTMS in BPD

- Arbabi et al. (2013). *Asian Journal of Psychiatry*, *6*(6), 614–617.
  - Case study, 22 year-old-patient
  - 10 Hz rTMS over lDLPFC, 10 sessions, 1500 pulses per session, 100% of RMT
  - Decrease in symptoms of depression (DBI-II), negative affect (PANASS) and impulsivity (BIS-11) directly after the treatment and one month after the treatment
- Cailhol et al. (2014). *Psychiatry Research*, *216*(1), 155–157.
  - 10 BPD patients, 5 in active and 5 in sham group
  - 10 Hz rTMS over rDLPFC, 10 sessions, 2000 pulses per session, 80% of RMT
  - Response rate defined as 30% reduction on Borderline Personality Severity Index and was reached by 2 patients in the active group
  - Lower scores in affective instability and anger after 3 months in the active group compared to sham group

Previous studies of rTMS in BPD

- De Vidovich et al. (2016). *Frontiers in Human Neuroscience*, *10,* 1–11.
  - 8 BPD patients and 8 controls
  - rTMS over left cerebellum based on cerebellar projections to prefrontal cortex through ventral striatum
  - 1 Hz rTMS for 10 minutes, 80% of RMT
  - Effect measured by an affective Go/NoGo Task, no difference was found between the groups after the stimulation as comapred to results before the stimulation
- Feffer et al. (2017). *Brain Stimulation*, *10*, 716–717.
  - 3 women with BPD and commorbid major depression
  - iTBS of DMPFC, 20 session, 600 pulses to each hemisphere per session
  - Reduction in BDI-II scores after the treatment

Previous studies of rTMS in BPD

- Reyes-López, J. et al. (2017). *Revista Brasileira de Psiquiatria*, *40*, 97–104.
  - 29 BPD patients, 2 stimulation designs
  - 1 Hz rTMS over the rDLPFC, 15 sessions, 900 pulses per session, 100% of RMT (15 patients)
  - 5 Hz rTMS over lDLPFC, 15 sessions, 900 pulses per session, 100% of RMT (14 patients)
  - Reduction in Clinical Global Impressions scale for BPD, BIS-11, BDI and Hamilton Anxiety Scale in both groups

Repetitive Transcranial Magnetic Stimulation Treating Impulsivity in Borderline Personality Disorder and Attention Deficit/Hyperactivity Disorder

Tomas Sverak, Pavla Linhartova, Adam Fiala and
Tomas Kasparek

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.72787

Abstract

The need for novel treatment approaches that target impulsivity symptoms in neuropsychiatric disorders is clear. Repetitive transcranial magnetic stimulation (rTMS) allows selective neuromodulation of regions involved in the functional neuroanatomy of neuropsychiatric disorders. This chapter presents impulsivity in psychiatry, especially in bor-

rTMS protocol

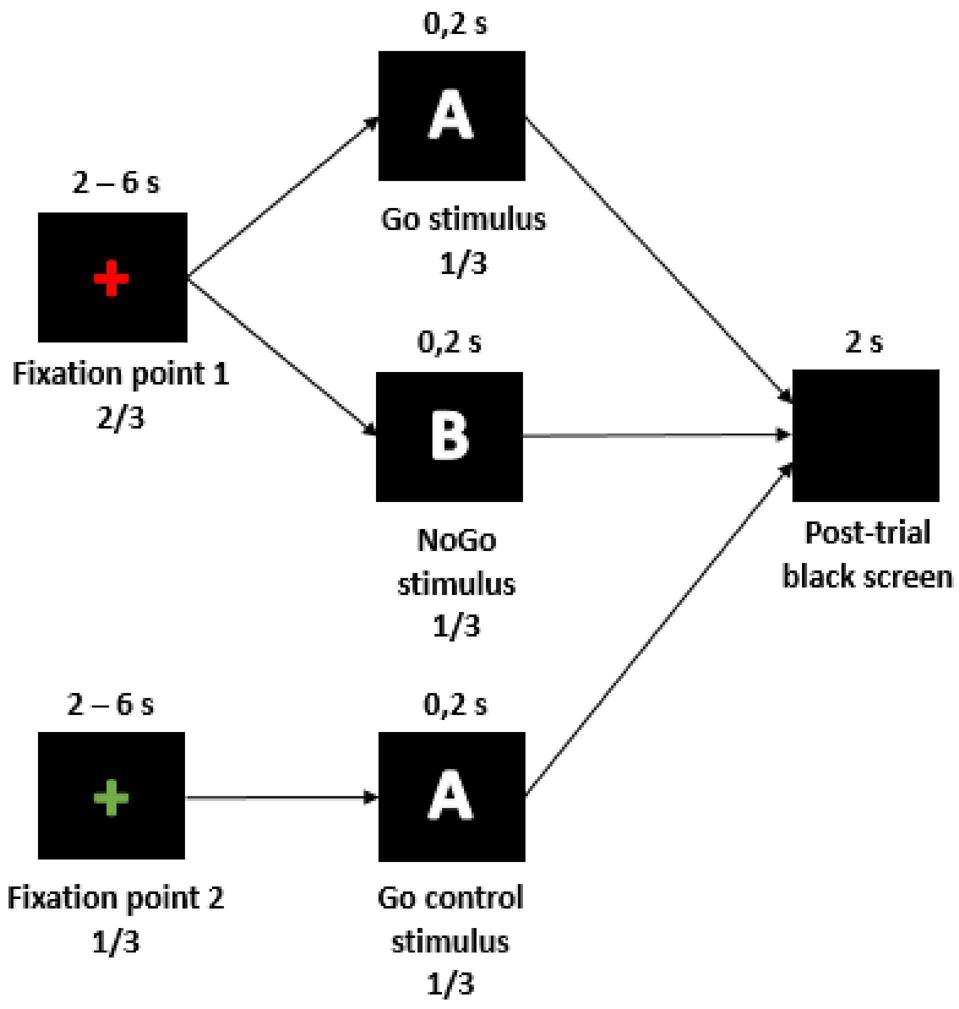
- fMRI based navigation using Brainsight within rDLPFC
- 10 Hz rTMS, 15 sessions, 1 session per day, 1500 pulses per session, 110% of RMT, 10 s trains and 30 s inter-train intervals
- Evaluation protocol:
  - Emotion awareness and regulation: DERS
  - Impulsivity: UPPS-P
  - Depression, anxiety: MADRS, Zung anxiety inventory
  - Borderline symptoms: BSL-23
  - ADHD symptoms – attention: Adult ADHD Symptoms Rating Scale (ASRS)
  - MR: T1, T2*, resting state, fMRI Go/NoGo Task, DTI
- Current sample: 14 patients, 2 men, mean age 23.4 years (SD = 5.4)

fMRI of behavioral inhibition in healthy people

- Healthy people, N = 32, 59% of men, age 18 to 33 years
- 3-T Siemens Prisma, Ceitec Brno
- BOLD sequences: res. 3x3x3 mm, TR=2280 ms, TE=35 ms

RESULTS

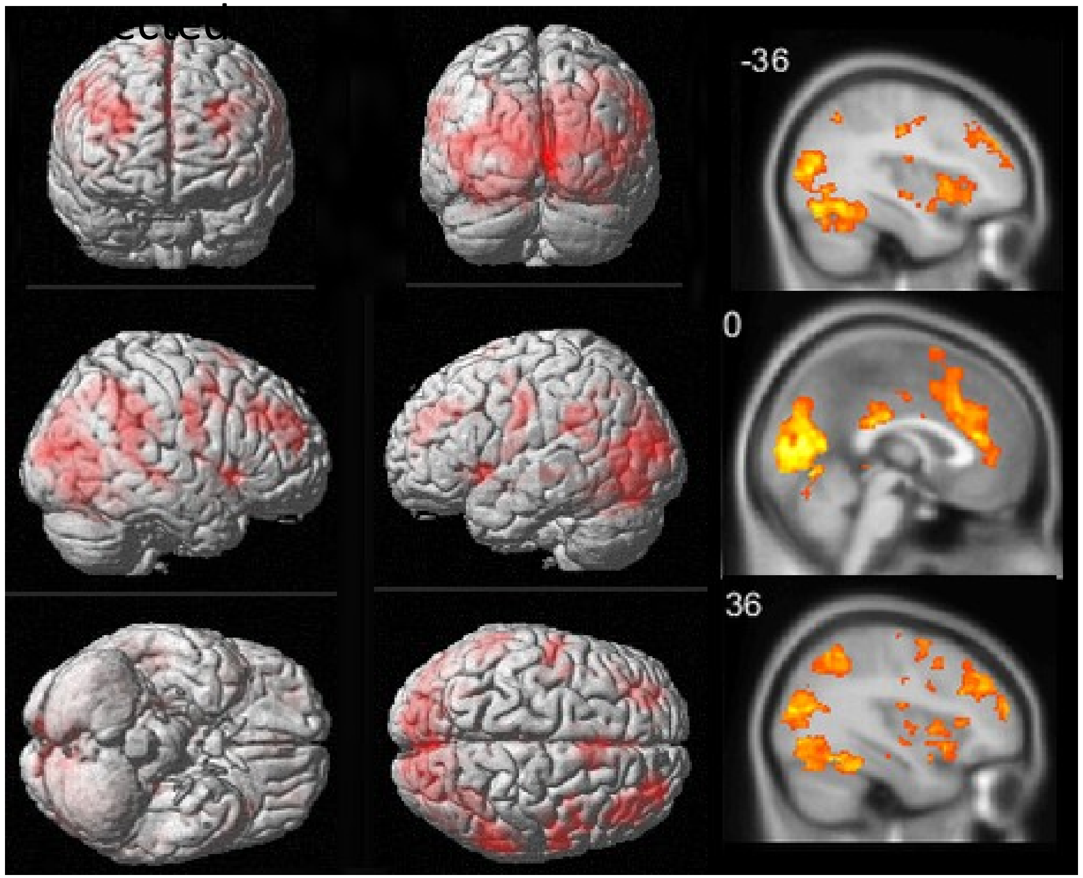
- Manipulation check:
  - Go stimuli RT: M=376,4; SD=47,2
  - Go Control stimuli RT: M=308,0; SD=47,1
  - paired t-test: **t(31)=13,126; p<0,001; d=1,45**
- Behavioral results:
  - NoGo commissions: **M=8,6%, SD=6,7%**



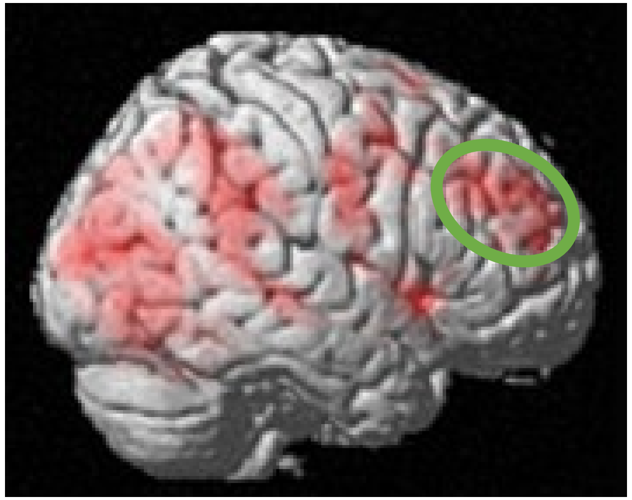
Current study: fMRI navigated rTMS

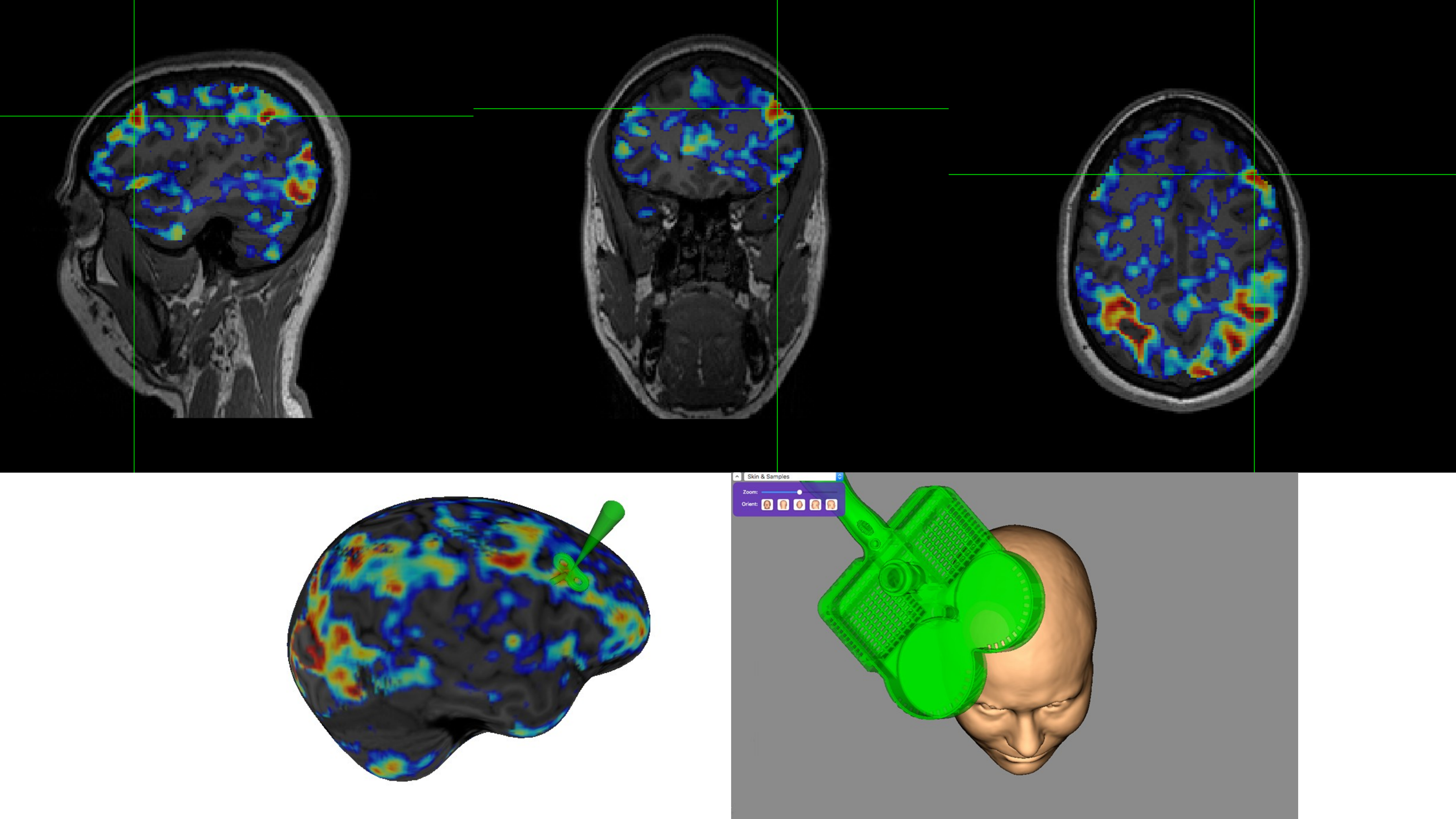
Neutral Go/NoGo Task: NoGo > Go

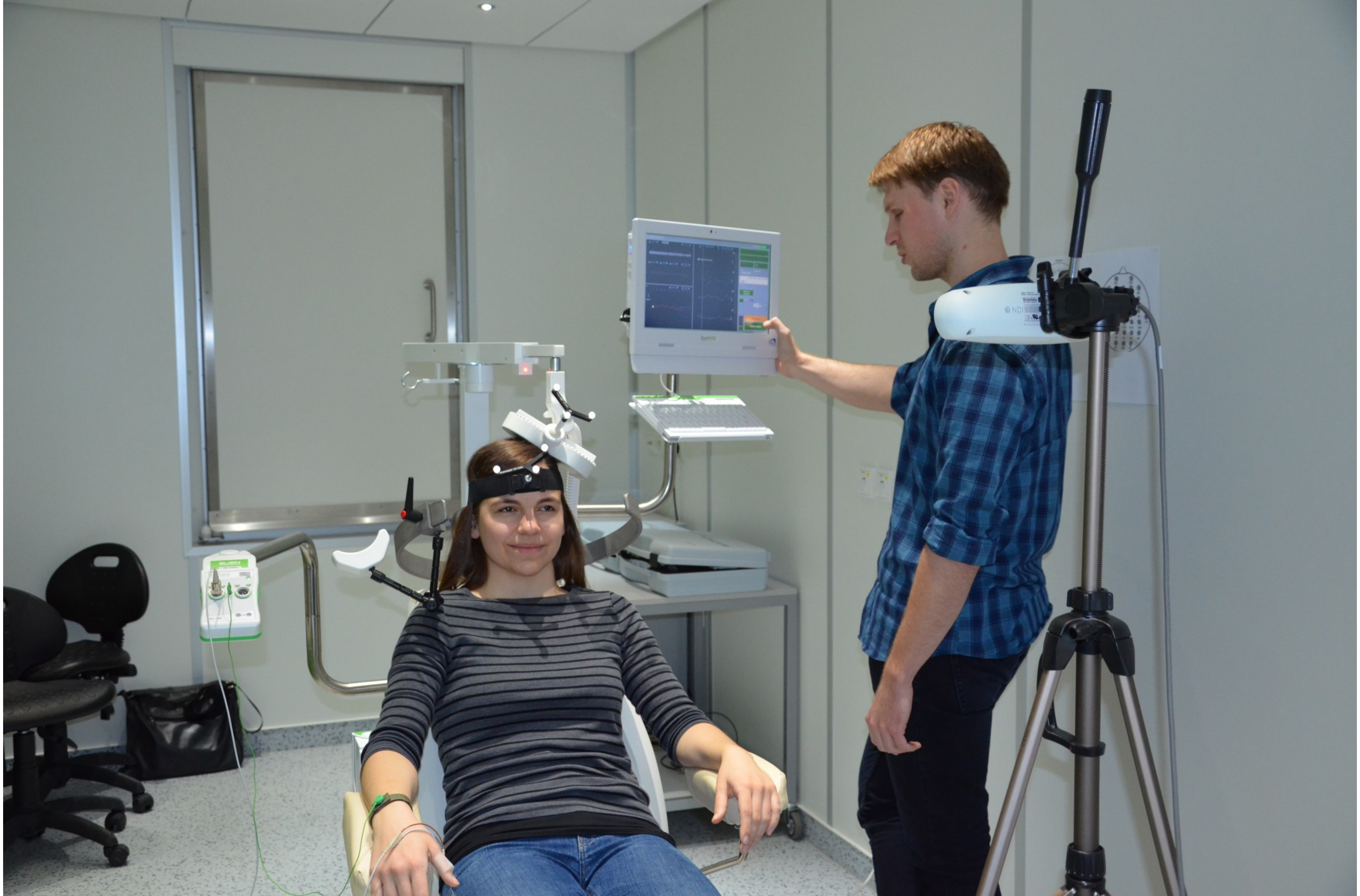
N=32, healthy subjects, p < 0.001 FDR



1. Task activated area within DLPFC used as a mask (through Freesurfer using Destrieux atlas)
2. Individual peak of NoGo > Go contrast taken as rTMS target




Skin & Samples
Zoom:
Orient:


NDI

Current results: before and right after rTMS

	before rTMS		after rTMS				
	M	SD	M	SD	t (df)	p	Cohen d
DERS	121.9	22.2	100.6	29.1	3.11 (11)	**0.01**	**0.93**
Lack of Premeditation	29.9	4.2	26.3	5.4	3.78 (11)	**0.003**	**1.16**
Lack of Perseverance	28.8	5.0	24.7	5.0	2.67 (11)	**0.022**	**0.77**
Sensation Seeking	32.8	6.5	30.9	7.9	1.56 (10)	0.152	-
Negative Urgency	36.6	5.6	34.3	7.8	1.01 (11)	0.335	-
Positive Urgency	37.8	11.2	34.2	8.4	1.24 (11)	0.242	-
MADRS	15.2	6.0	11.2	7.6	2.69 (12)	**0.020**	**0.78**
Zung (anxiety)	46.8	9.2	42.7	12.6	1.67 (11)	0.122	-
BSL-23	38.7	19.8	34.5	20.3	0.89 (11)	0.394	-
ASRS	57.5	7.3	49.2	9.4	3.54 (11)	**0.005**	**1.05**

Current results: subjective reports

- Positive effects reported by most patients
  - increased attention, improved mood and anxiety
  - less overwhelming emotions, „more time to think“ before acting in stressful situations
  - improved ability recognizing and describing emotion, less emotional outbursts
- Positive effects reported by some patients
  - less dissociative experiences
  - reduction of self-harm
- Adverse effects
  - increased anxiety in approx. 10% patients

Future directions

- Analysis of the neural effects
- Placebo effect: RCTs – problems with sham stimulation
- Intensive rTMS protocols
- Combination with other forms of treatment: neurofeedback, psychotherapy

Real-time fMRI neurofeedback

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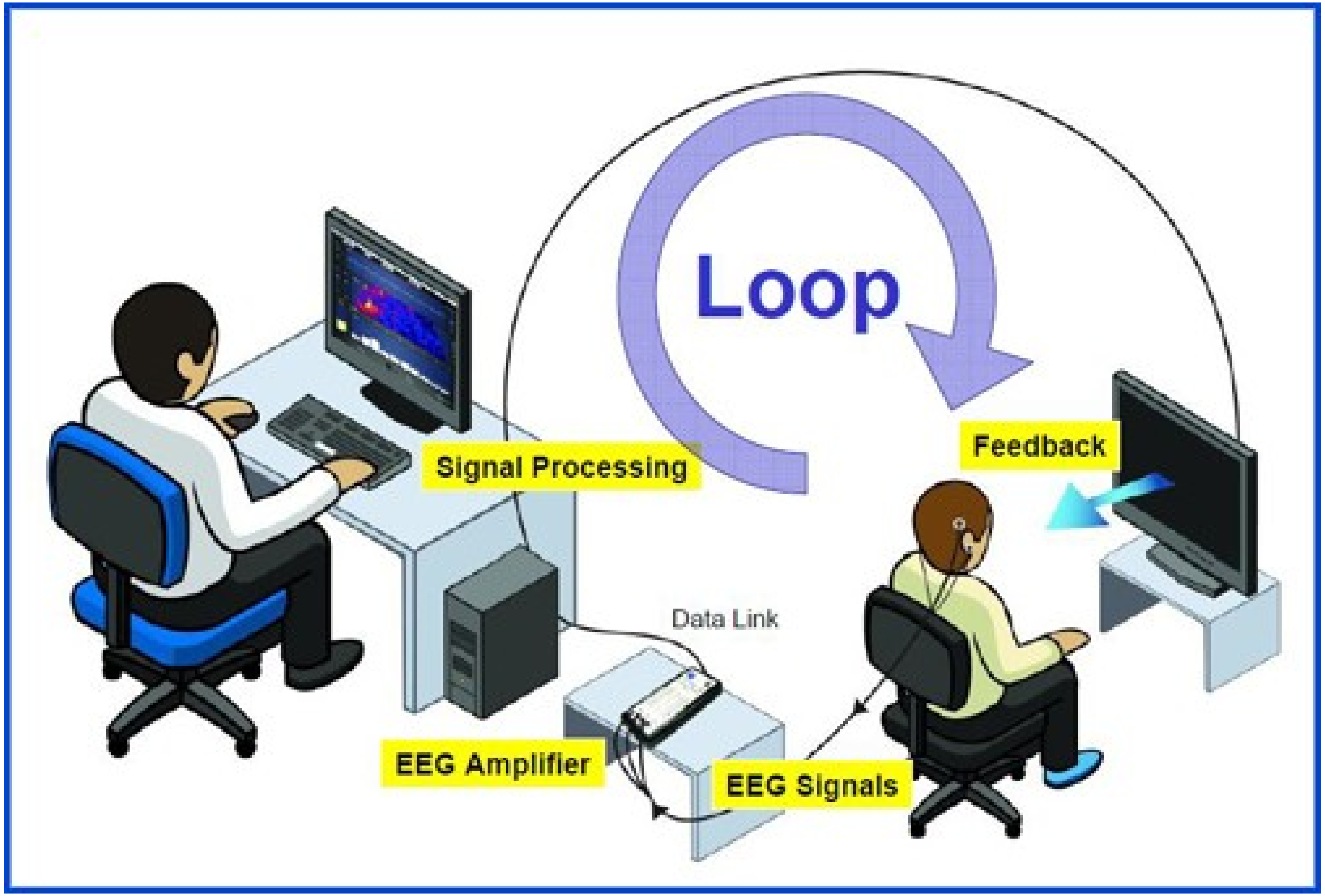
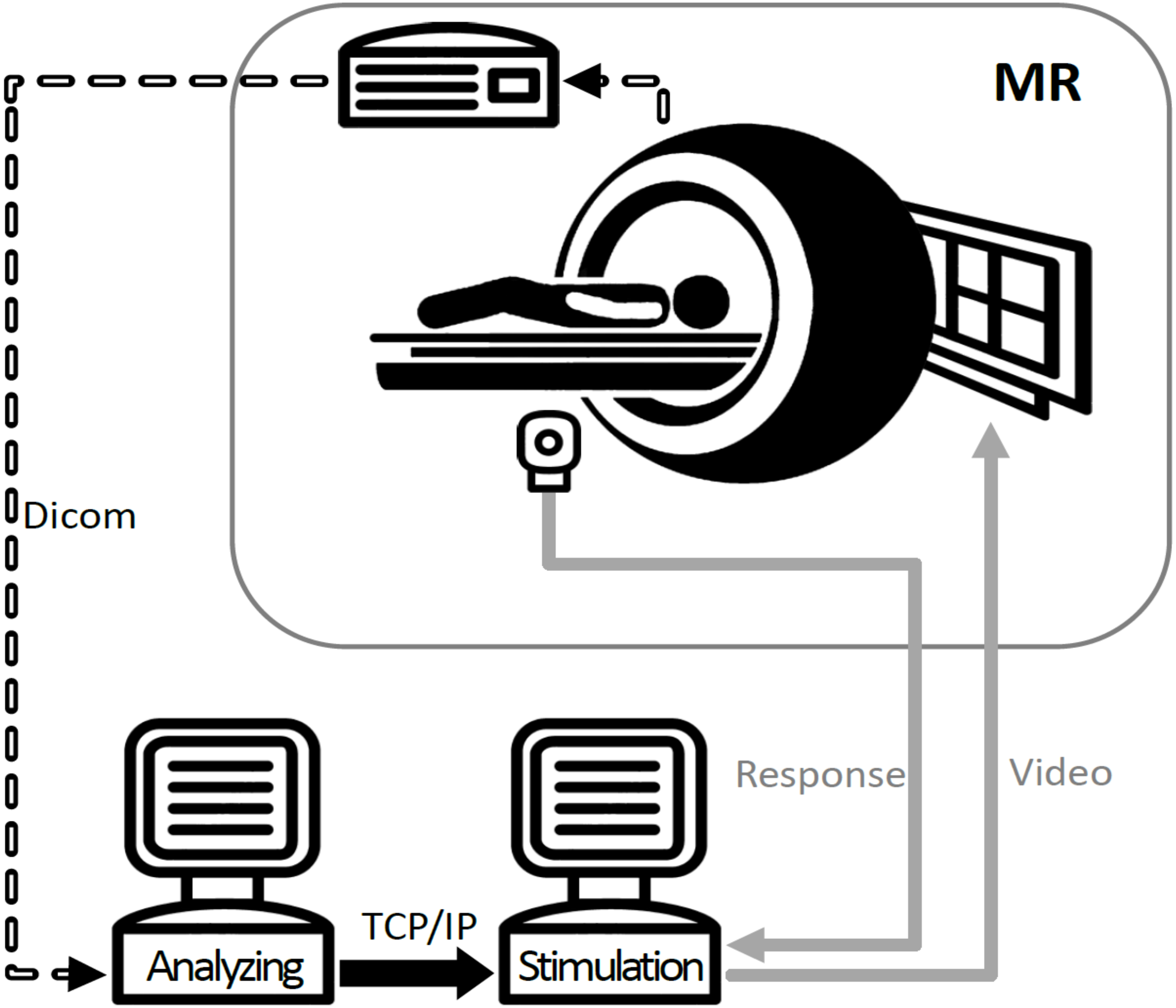
Neurofeedback



Real-time fMRI neurofeedback

1. dicom to nifti, realigment
2. Selection of ROI and control region based on masc
3. BOLD signal extraction
4. Filtering (Kalman filter)
5. Subtraction of the signals
6. Results evaluation




Ovládněte pocity vyvolané obrázkem
SIEMENS

fMRI neurofeedback application areas

- In the existing studies, fMRI neurofeedback was successfuly used for improvement of:
  - Tinnitus (Emmert K, Kopel R, Koush Y, et al. *NeuroImage Clin*. 2017;14:97-104 etc.)
  - Verbal hallucinations (Dyck MS, Mathiak KA, Bergert S, et al. *Front Psychiatry*. 2016;7:1-14 etc.)
  - Chronic pain (Guan M, Ma L, Li L, et al. *Ismrm*. 2014;22:5889 etc.)
  - Craving in nicotinism (Hartwell KJ, Hanlon CA, Li X, et al. *J Psychiatry Neurosci*. 2016;41(1):48-55 etc.)
  - Motor skills in Parkinson‘s disease (Subramanian L. et al. *Park Relat Disord*. 2016;22:e70 etc.)
  - Cognitive functions in healthy people and patients with schizophrenia (Ruiz S, Lee S, Soekadar SR, et al. *Hum Brain Mapp*. 2013;34(1):200-212 etc.)

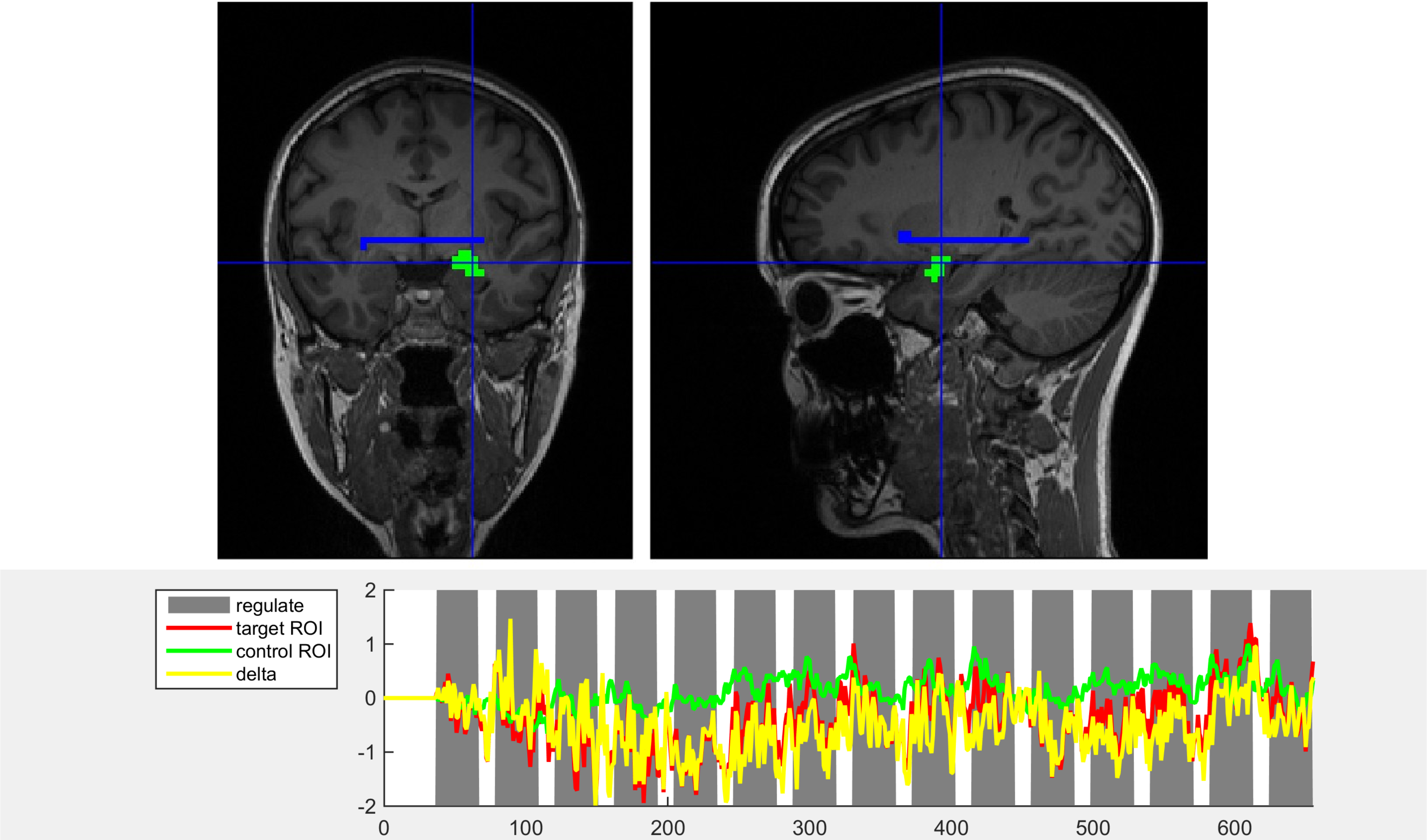
Stimulation parameters

- Stimulation type: visual, auditory, pain, memories, imagination
- Neurofeedback presentation: visual, auditory
- Brain area for real-time processing: depends on our goal
- Type of control group: sham, different region, no feedback
- Localizer type: anatomical, functional
- Instructions for signal change:
  - Signal change direction (upregulation and downregulation)
  - Signal change strategy

fMRI neurofeedback of amygdala for emotion regulation training

fMRI neurofeedback of amygdala

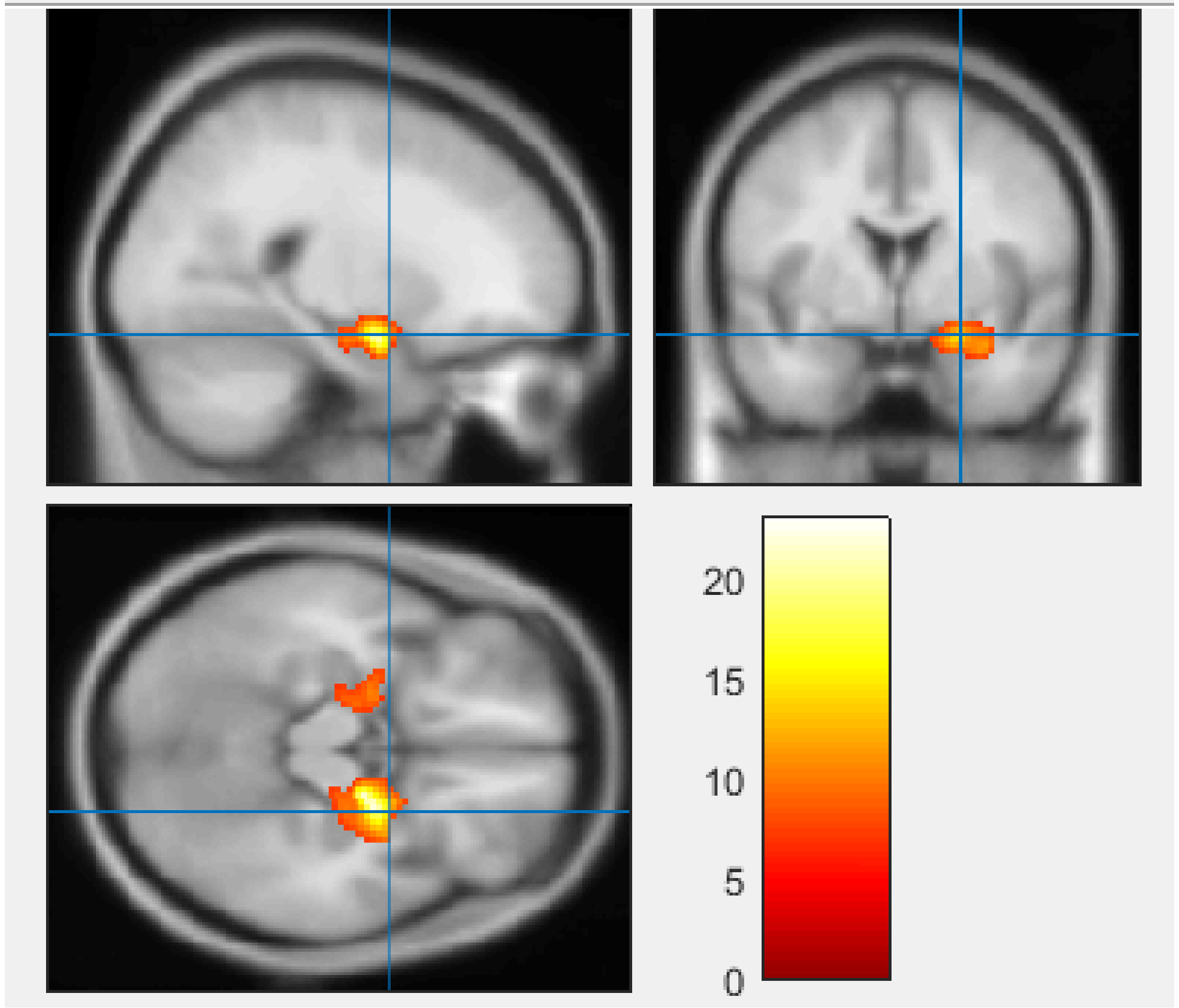
- Zotev et al., 2011, 2013 (PloS One), Young et al., 2014 (PloS One): fMRI NF effect on amygdala upregulation during retrieving positive autobiographical memories in healthy people and patients with depression (as compared to sham fMRI NF)
- Paret et al., 2014 (NeuroImage) a Paret et al., 2016 (Soc Cogn Affect Neurosci): fMRI NF effect on amygdala downregulation during watching aversive pictures and increase of amygdala-prefrontal cortex connectivity in healthy people and patients with borderline personality disorder (as compared to sham fMRI NF)
- Nicholson et al., 2017 (HBM): fMRI NF efect on amygdala downregulation and increase of amygdala-prefrontal cortex connectivity during processing of individualized trauma-related words in patients with PTSD



regulate
target ROI
control ROI
delta
2
1
0
-1
-2
0
100
200
300
400
500
600

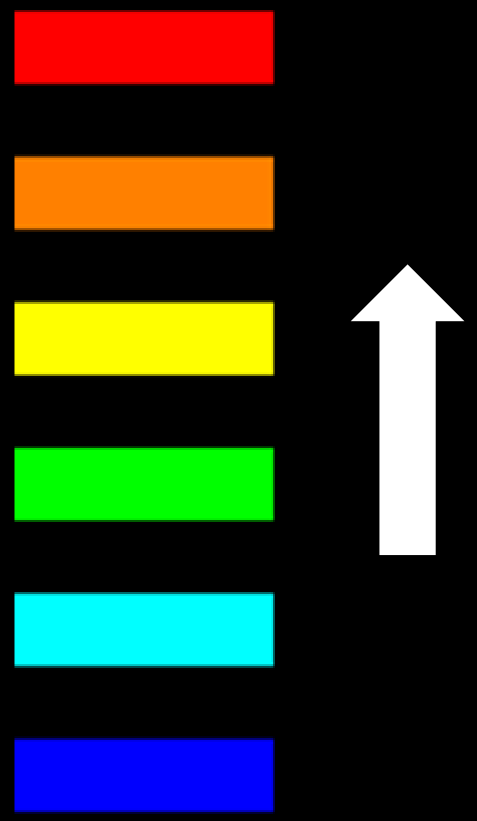
Corresponding brain activation

- N = 17
- FWE = 0.05




amygdala downregulation


amygdala upregulation



Effect analysis

- Amygdala regulation during neurofeedback vs. without neurofeedback
- Amygdala regulation with active neurofeedback vs. sham neurofeedback
- Correlation with physiological parameters (skin conductance etc.)
- Neural effects of neurofeedback training
- Feedback on regulation success from the subject
- Behavioral and clinical changes

fMRI neurofeedback of amygdala and the current project

- Patients with borderline personality disorder
- Looking for and training in different emotion regulation strategies
- Use of individualized stimuli
- Different strategies for emotion regulation have different neural correlates (e.g. cognitive reapraisal, acceptance, supression, distraction… např. Murakami et al., 2015, *PLoS One;* Smoski et al., 2014, *Soc Cogn Affect Neurosci*)

Thanks for your attention