Biofeedback mittels rtfMRI beim Tinnitus - und bei Schmerz?

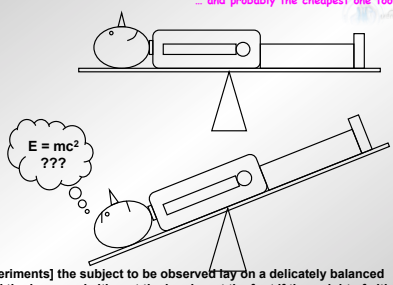
Sven Haller

"Standard" fMRI

The First "Brain Imaging Experiment"

... and probably the cheapest one too!

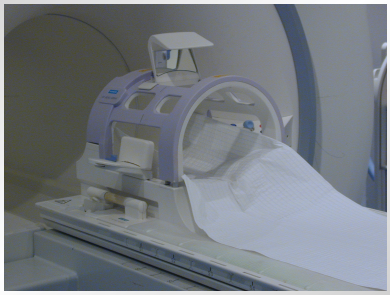
Angelo Mosso
Italian physiologist
(1846-1910)



"[In Mosso's experiments] the subject to be observed lay on a delicately balanced table which could tip downward either at the head or at the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head-end, in consequence of the redistribution of blood in his system."

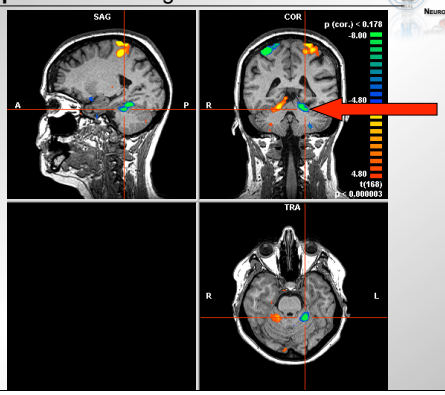
-- William James, *Principles of Psychology* (1890)

NeuroImaging Methods: fMRI setup

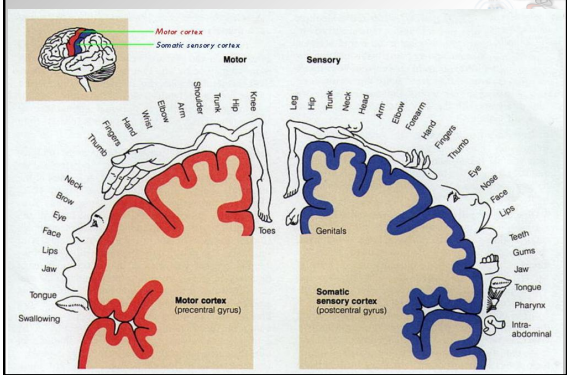


NeuroImaging Methods: fMRI setup

fMRI & pain: methodological considerations



Anatomy: homunculus



Pain: types and domains

- Temporal dimension of pain
  - **acute pain** versus **chronic pain**
- Perceptual dimensions of pain
  - **sensation** and **emotion**
- From a basic research point of view,
  - **inflammatory** versus **neuropathic** pain
  - (however rarely observed independently in the clinical setting)

Apkarian, A. V. (2008) Pain perception in relation to emotional learning. *Curr Opin Neurobiol, 4, 464-468.*

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fMRI & pain: methodological considerations

- **acute pain**
- ON-OFF paradigm
  - externally triggered
    - heat
    - electric stimulation
    - tactile stimulation (CAVE motion, sensation)
    - laser (no sensory stimulation)

fMRI of pain: the beginning in late 1990s

- electric shock (20.8 mA, 2 Hz)
- heat (48° C)
- mechanical stimulus

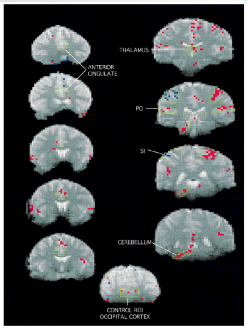

Figure 1.
Consecutive coronal EPI images (top left → rostral) from a typical subject, showing the responses to noxious electrical stimulation. Green lines delineate predetermined regions of interest. Red voxels indicate significant activation in phase with the noxious stimulus. Blue voxels represent significant activation that is 180° out of phase.

Disbrow, E., Buonocore, M., Antognini, J., Carstens arison of the response to noxious thermal, mechanical, and elec ng. *Hum Brain Mapp, 3, 150-159.*

Pain: types and domains

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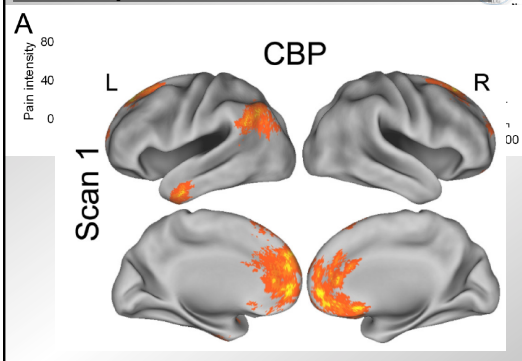
Chronic pain and fMRI: methods



Baliki, M. N., Geha, P. Y., Jabakhanji, R., Harden, N., Schnitzer, T. J., Apkarian, A. V. (2008) A preliminary fMRI study of analgesic treatment in chronic back pain and knee osteoarthritis. *Mol Pain, 47.*

Brain & pain: review

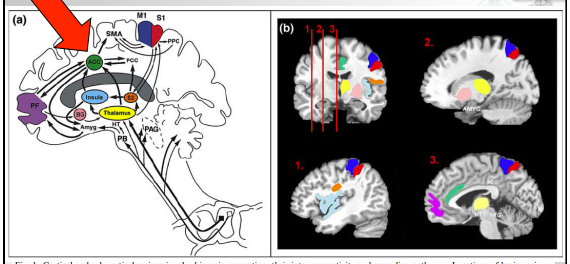
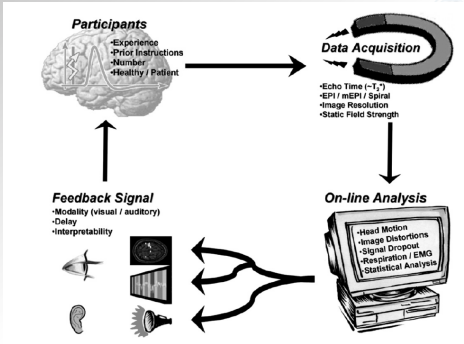


Fig. 1. Cortical and sub-cortical regions involved in pain perception, their inter-connectivity and ascending pathways. Locations of brain regions involved in pain perception are color-coded in a schematic drawing and in an example MRI. (a) Schematic shows the regions, their inter-connectivity and afferent pathways. The schematic is modified from Price (2000) to include additional brain areas and connections. (b) The areas corresponding to those shown in the schematic are shown in an anatomical MRI, on a coronal slice and three sagittal slices as indicated on the coronal slice. The six areas used in meta-analysis are primary and secondary somatosensory cortices (S1, S2, red and orange), anterior cingulate (ACC, green), insula (blue), thalamus (yellow), and prefrontal cortex (PF, purple). Other regions indicated include: primary and supplementary motor cortices (M1 and SMA), posterior parietal cortex (PPC), posterior cingulate (PCC), basal ganglia (BG, pink), hypothalamus (HT), amygdala (AMYG), parabrachial nuclei (PB), and periaqueductal gray (PAG).

Apkarian, A. V., Bushnell, M. C., Treede, R. D., Zubieta, J. K. (2005) Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain, 4, 463-484.*

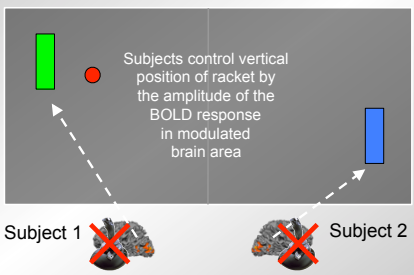
REAL-TIME FMRI NEUROFEEDBACK

Neurofeedback: principles



Weiskopf, N., Sitaram, R., Josephs, O., Veit, R., Scharnowski, F., Goebel, R., Birbaumer, N., Deichmann, R., Mathiak, K. (2007) Real-time functional magnetic resonance imaging: methods and applications. *Magn Reson Imaging, 6, 989-1003.*

BOLD Brain Pong: Experimental logic



Up-and-down movement of racket requires ***graded control*** !

Brain Pong: Example game (real-time movie)

'Standard' fMRI – rtfMRI feedback

- 'Standard' fMRI
  - *independent variable*: stimulation / behavior
  - *dependent variable*: brain activity
- rtfMRI neurofeedback
  - *independent variable*: voluntarily controlled brain activity
  - *dependent variable*: behavior

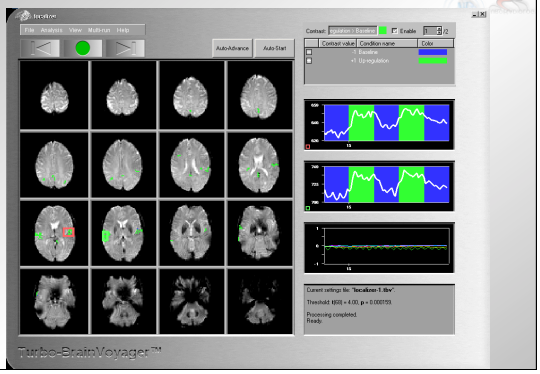
rtfMRI neurofeedback: tinnitus

- Tinnitus -> excess auditory activations
  - Muhlnickel W, Elbert T, Taub E et al (1998) Reorganization of auditory cortex in tinnitus. Proc Natl Acad Sci U S A 17:10340-10343
  - Andersson G, Lyttkens L, Hirvela C et al (2000) Regional cerebral blood flow during tinnitus: a PET case study with lidocaine and auditory stimulation. Acta Otolaryngol 8:967-972
  - Kleinjung T, Eichhammer P, Langguth B et al (2005) Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 4:566-569
- rTMS may reduce tinnitus
  - Kleinjung T, Eichhammer P, Langguth B et al (2005) Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 4:566-569
  - Rossi S, De Capua A, Ulivelli M et al (2007) Effects of repetitive transcranial magnetic stimulation on chronic tinnitus. A randomised, cross over, double blind, placebo-controlled study. Journal of neurology, neurosurgery, and psychiatry
  - Plewnia C, Reimold M, Najib A et al (2007) Dose-dependent attenuation of auditory phantom perception (tinnitus) by PET-guided repetitive transcranial magnetic stimulation. Hum Brain Mapp 3:238-246

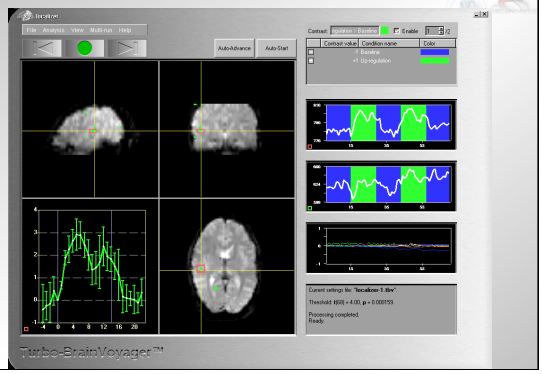
rtfMRI neurofeedback: tinnitus

- **Hypothesis**
  1. rtfMRI neurofeedback may reduce auditory activations
  2. this may improve tinnitus

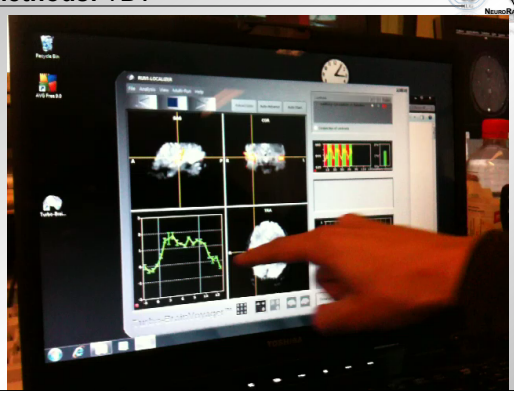
Methods: auditory localizer



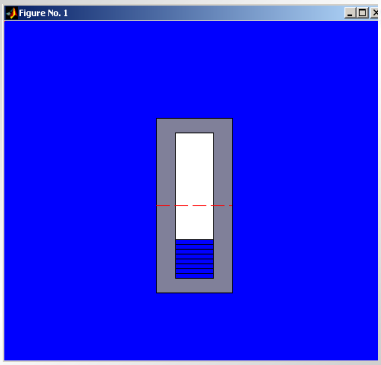
Methods: auditory localizer



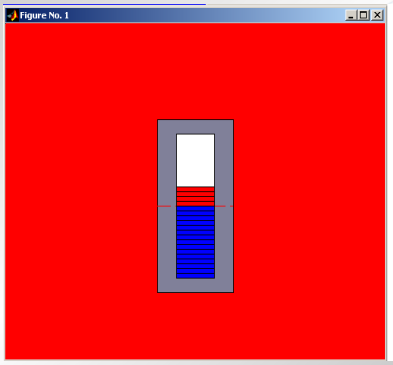
Methods: TBV



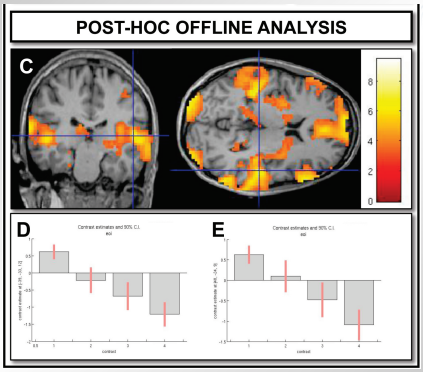
Methods: visual feedback



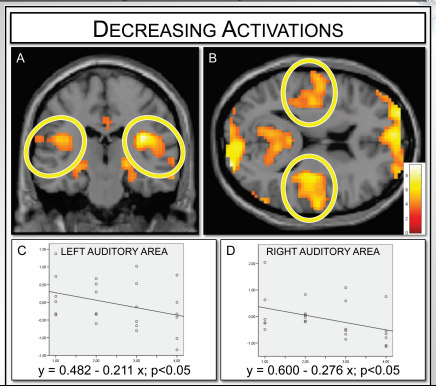
Methods: visual feedback



Initial results: single subject



Initial results: group analysis (N=6)



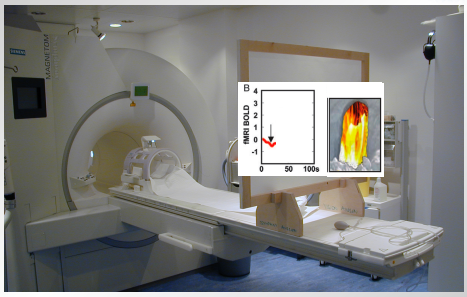
rtfMRI: previous literature

- Clinical rtfMRI
  - **tinnitus**
  - pain
- Research rtfMRI
  - approximately 20 papers
  - ACC, motor, language, ..

rtfMRI in chronic pain: hypothesis

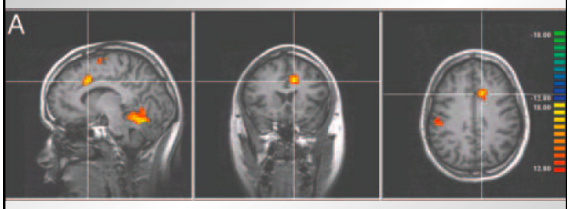
1. It is possible to learn **voluntary control** over 'pain areas' using rtfMRI neurofeedback
2. this will reduce the subjective pain

rtfMRI feedback in chronic pain



deCharms, R. C., Maeda, F., Glover, G. H., Ludlow, D., Pauly, J. M., Soneji, D., Gabrieli, J. D., Mackey, S. C. (2005) Control over brain activation and pain learned by using real-time functional MRI. *Proc Natl Acad Sci U S A, 51, 18626-18631.*

rtfMRI feedback in chronic pain



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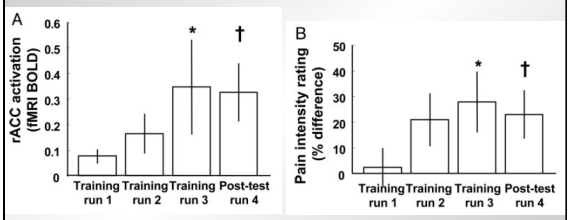
rtfMRI feedback in chronic pain

- 8 chronic pain patients (not specified)



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rtfMRI feedback in chronic pain

- Patient control group (n 4)
  - autonomic biofeedback (skin conductance, heart rate, and respiration)

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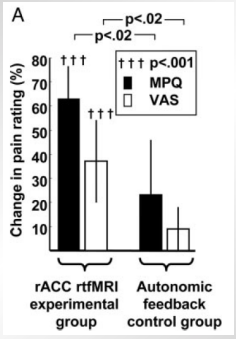

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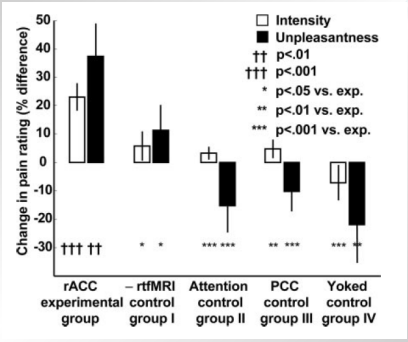
rtfMRI feedback in chronic pain

- Patient control group (n 4)
  - autonomic biofeedback (skin conductance, heart rate, and respiration)
- Group I (8 healthy controls)
  - no rtfMRI information
- Group II (8 healthy controls)
  - purely behavioral training
- Group III (8 healthy controls)
  - rtfMRI information from a different brain area
- Group IV (4 healthy controls)
  - rtfMRI information from a previous subject

deCharms, R. C., Maeda, F., Glover, G. H., Ludlow, D., Pauly, J. M., Soneji, D., Gabrieli, J. D., Mackey, S. C. (2005) Control over brain activation and pain learned by using real-time functional MRI. *Proc Natl Acad Sci U S A, 51, 18626-18631.*

rtfMRI feedback in chronic pain



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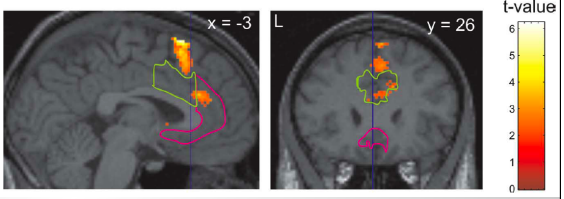
rtfMRI: characteristics

- Increase and decrease activations
  - gradual -> BRAIN PONG
- Regionally specific activation changes

rtfMRI: regionally specific

- Differential activation of two adjacent areas
  - dorsal ACC (ACcd) “cognitive” division
  - rostral–ventral ACC (ACad) “affective” division

b) Positive change of signal increase across sessions



Weiskopf, N., Veit, R., Erb, M., Mathiak, K., Grodd, W., Goebel, R., Birbaumer, N. (2003) Physiological self-regulation of regional brain activity using real-time functional magnetic resonance imaging (fMRI): methodology and exemplary data. *Neuroimage, 3, 577-586.*

rtfMRI: characteristics

- Increase and decrease activations
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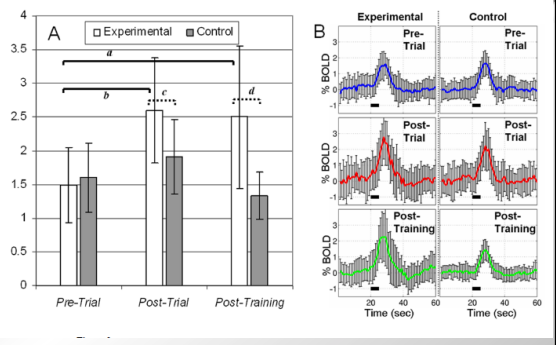
- Regionally specific activation changes
  - e.g. dorsal ACC (ACcd) and rostral–ventral ACC (ACad)
- Activation changes persist over time

rtfMRI of M1: Consolidation after 2 weeks



Yoo, S. S., Lee, J. H., O'Leary, H., Panych, L. P., Jolesz, F. A. (2008) Neurofeedback fMRI-mediated learning and consolidation of regional brain activation during motor imagery. *Int J Imaging Syst Technol, 1, 69-78.*

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- Increase and decrease activations
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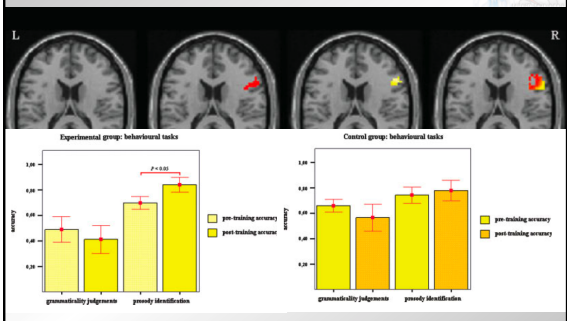
  - e.g. dorsal ACC (ACcd) and rostral–ventral ACC (ACad)
- Activation changes persist over time
  - rtfMRI of M1 persists after 2 weeks
- rtfMRI neurofeedback may change behavior
  - reduced pain

rtfMRI: right IFG and language



Rota, G., Sitaram, R., Veit, R., Erb, M., Weiskopf, N., Dogil, G., Birbaumer, N. (2008) Self-regulation of regional cortical activity using real-time fMRI: The right inferior frontal gyrus and linguistic processing. *Hum Brain Mapp,*

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- Activation changes persist over time
  - rtfMRI of M1 persists after 2 weeks
- rtfMRI neurofeedback may change behavior
  - reduced pain
  - improved linguistic processing

clinical rtfMRI: challenges

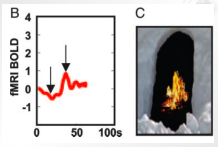
- rtfMRI embedded in clinical treatment concept
- Simple and robust

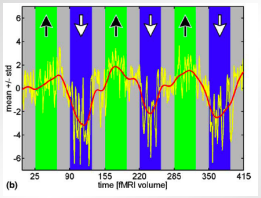
clinical rtfMRI: challenges

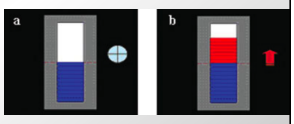
clinical rtfMRI: challenges

- rtfMRI embedded in clinical treatment concept
- Simple and robust
- Adapted to individual patients
- Optimization to achieve maximum effect
  - type of feedback
  - cognitive strategies
  - duration of session
  - number of sessions
  - strategies to transfer training into everyday life
  - …

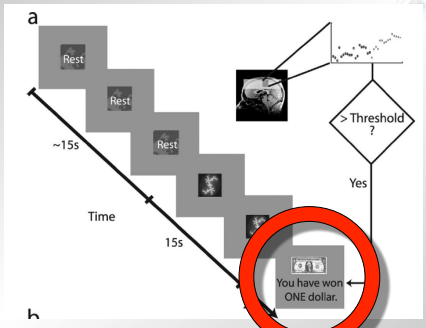
rtfMRI: feedback types







rtfMRI: feedback types



Bray, S., Shimojo, S., O'Doherty, J. P. (2007) Direct instrumental conditioning of neural activity using functional magnetic resonance imaging-derived reward feedback. *J Neurosci, 28, 7498-7507.*

Conclusions

- standard fMRI
  - Verhalten -> Gehirn Aktivierungen
- real-time fMRI neurofeedback
  - Gehirn Aktivierungen -> Verhalten
  - Raum
  - Zeit
  - Tinnitus und chronischer Schmerz
- **rtfMRI feedback in der Zukunft**
  - einfacher Versuchsaufbau
  - Verbesserungen (z.B. feedback, Dauer, Strategien, …)
  - Eingebunden in interdisziplinäre Behandlung

The End

THANK YOU!