Neurofeedback
eeg & fMRI

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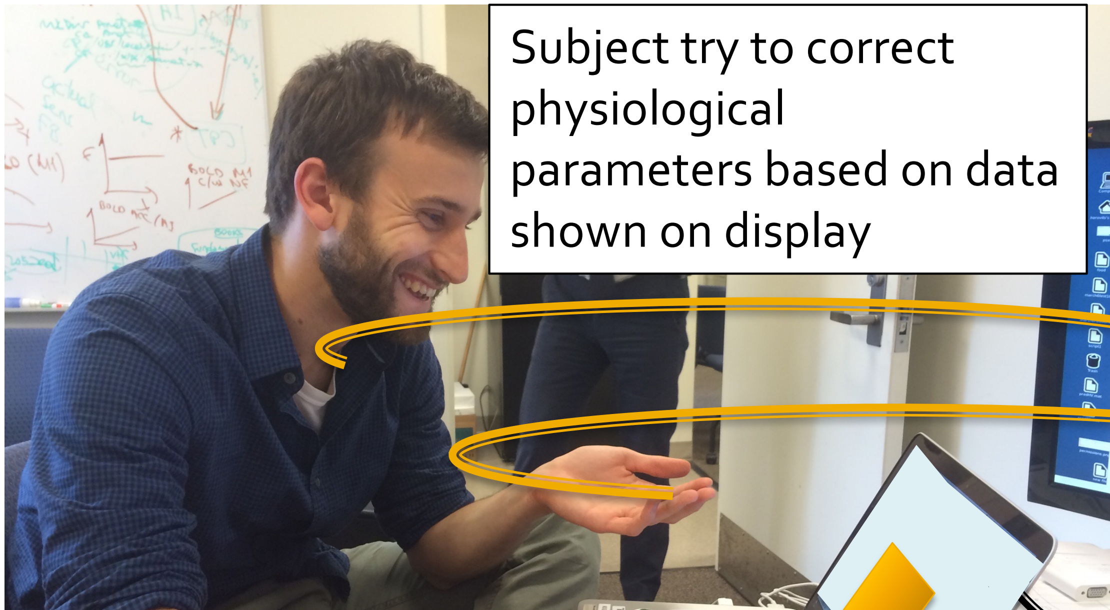
biofeedback principle



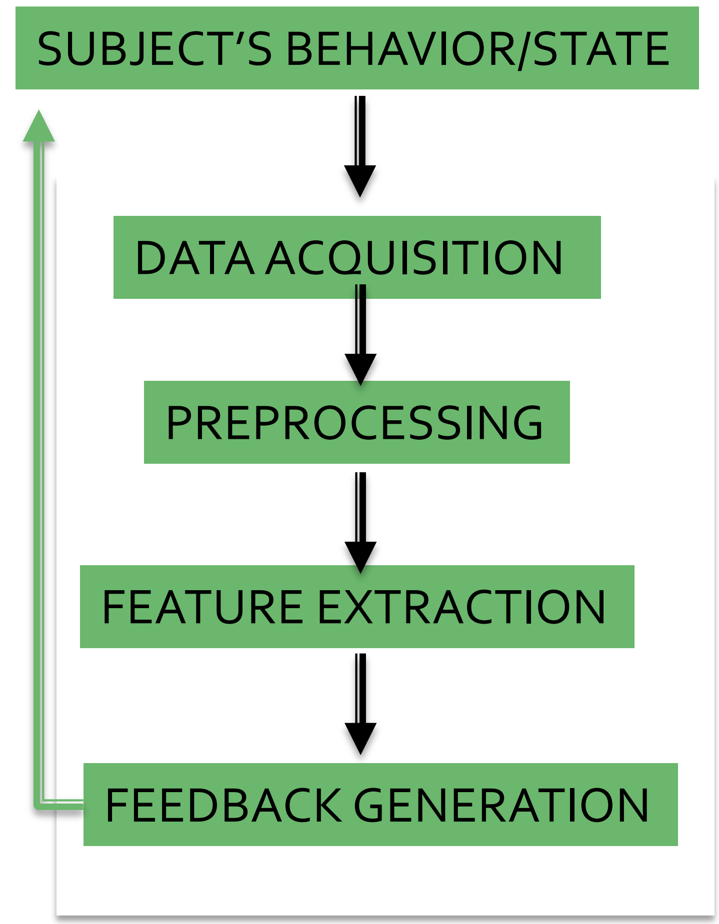
Subject try to correct physiological parameters based on data shown on display

Measure Physiological parameters

Data sent to computer for analysis and Feedback display

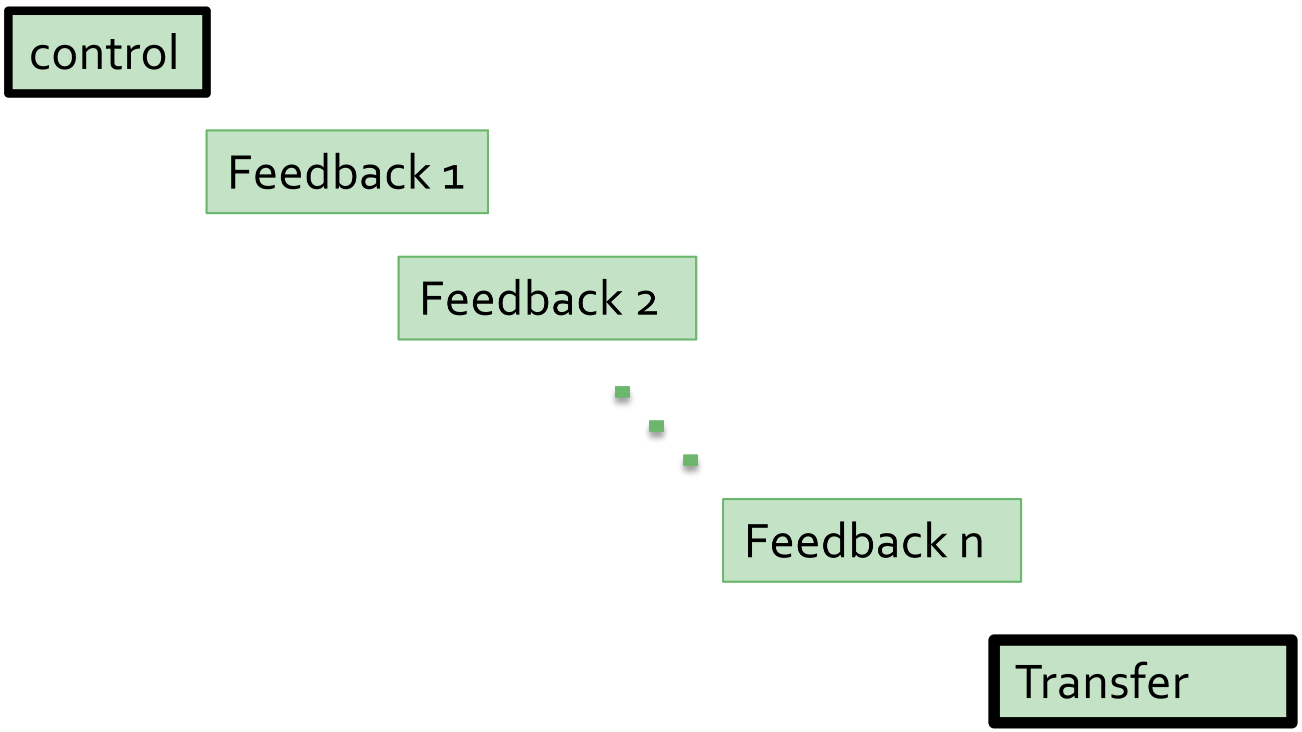
NEUROFEEDBACK

- Neurofeedback >> self-regulation of brain activity or state
  - **GOAL:** alter behavior or performance by modifying underlying neuronal "mechanism"

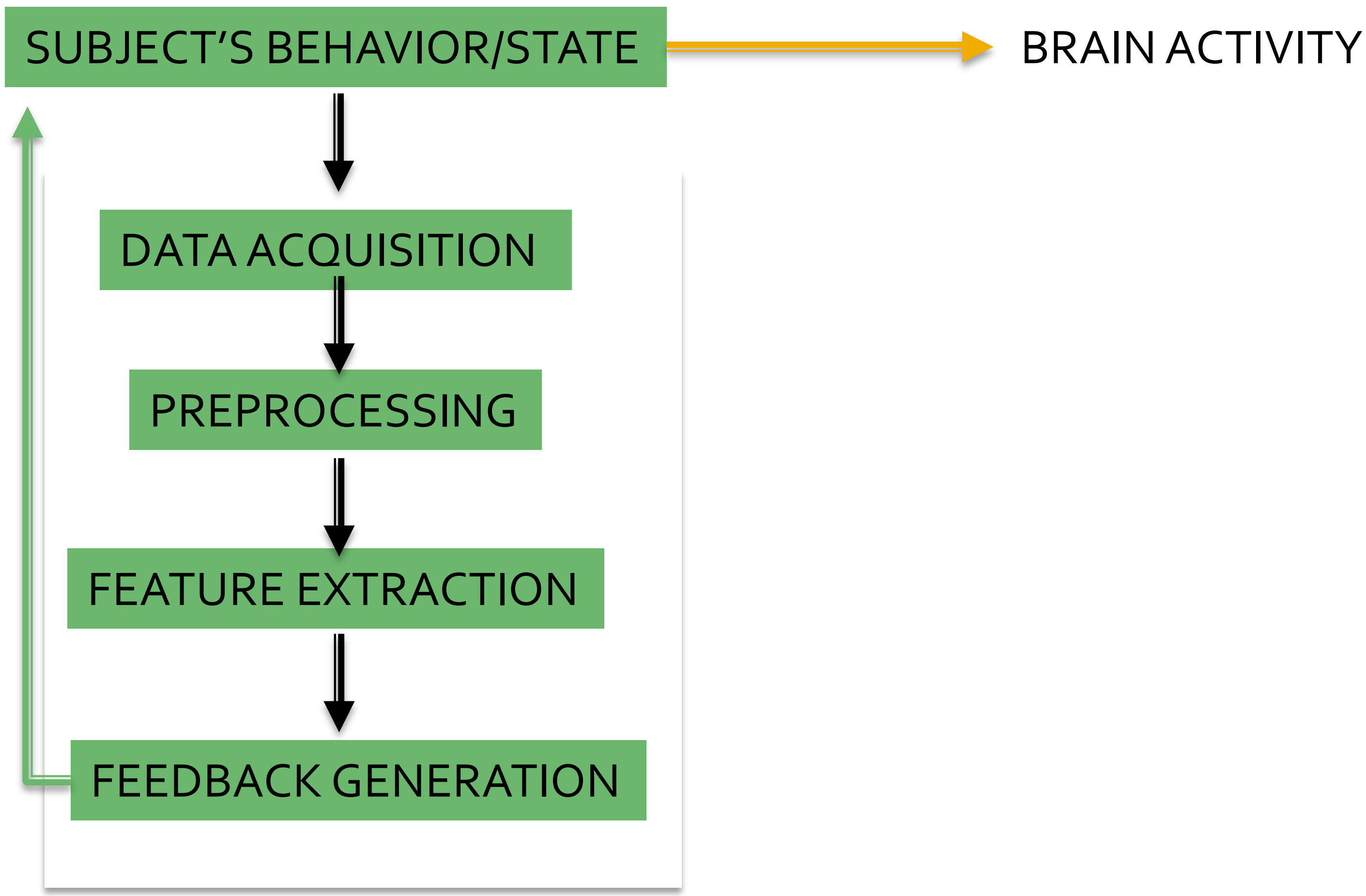


study design

Study design



NEUROFEEDBACK



BRAIN ACTIVITY (DATA)

BRAIN ACTIVITY
f(x,t)

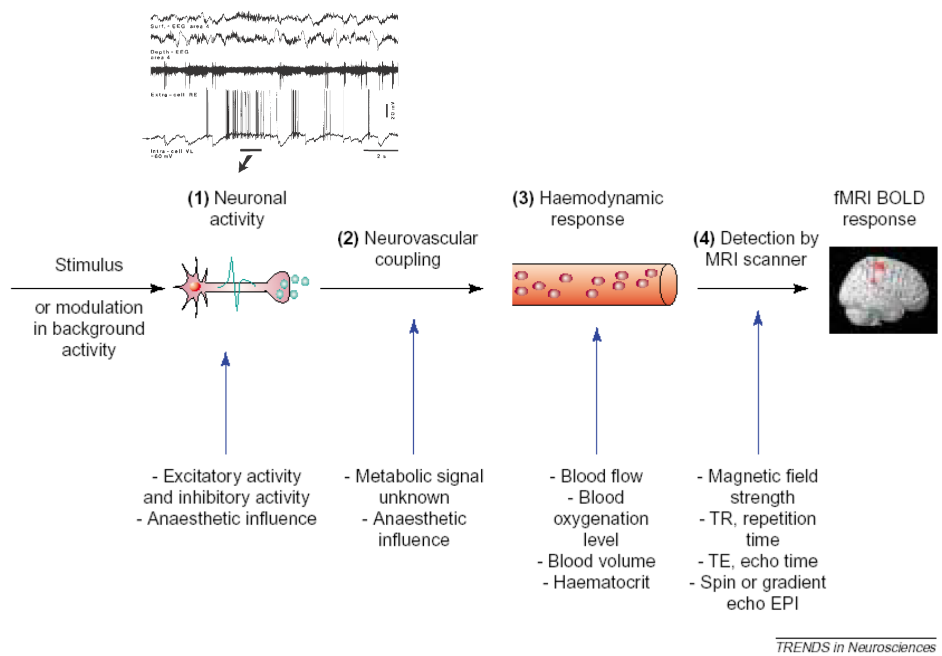
Metabolic/ vascular responses
g[f(x,t)]

fMRI
k{g[f(x,t)]}

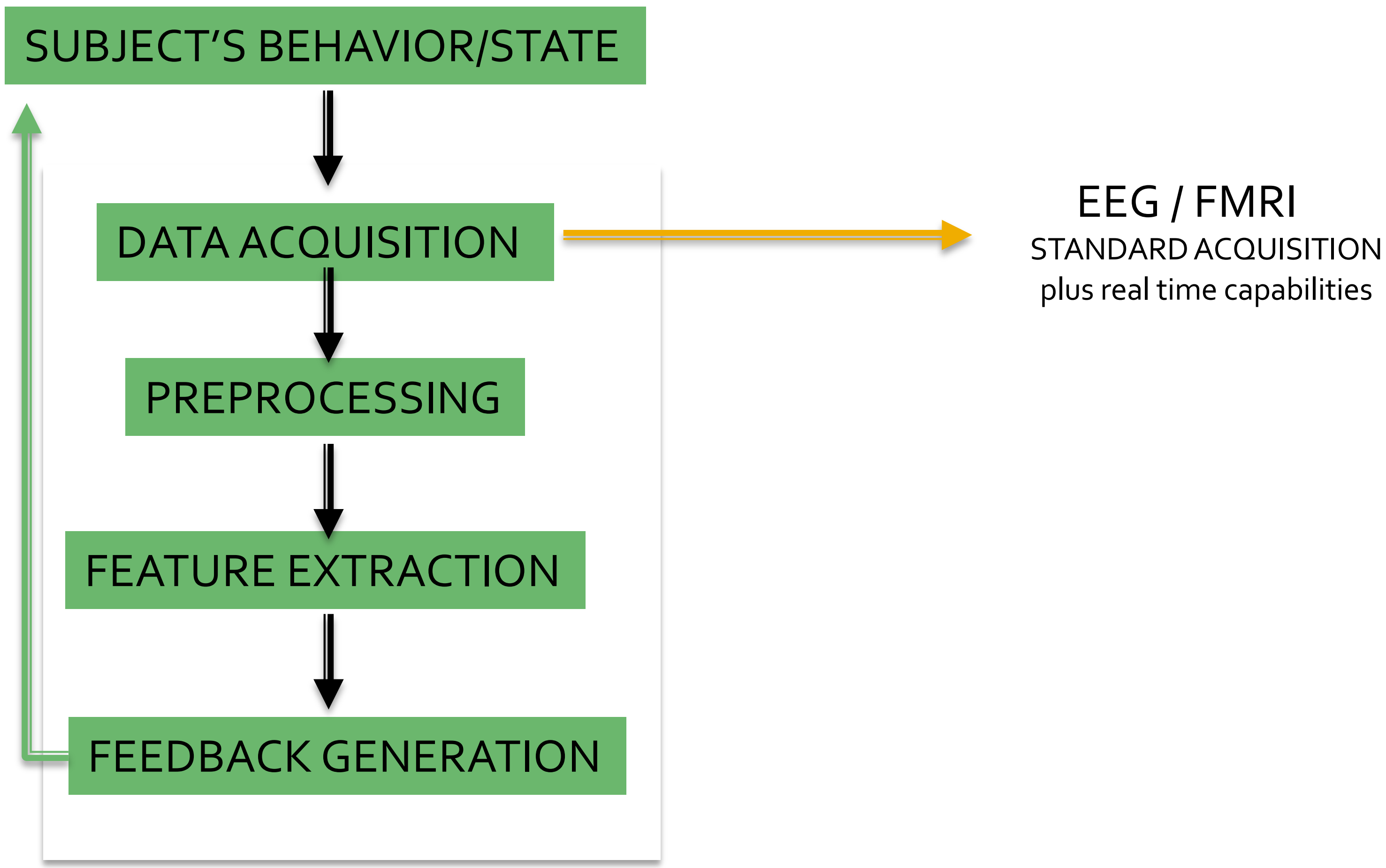
Poor time resolution (s)
Good spatial resolution (mm)

electrical EEG, MEG
m[f(x,t)]

Good time resolution (ms)
Poor spatial resolution



NEUROFEEDBACK



comparison nf-EEG /nf- fMRI

- Nf EEG is
- low cost equipment

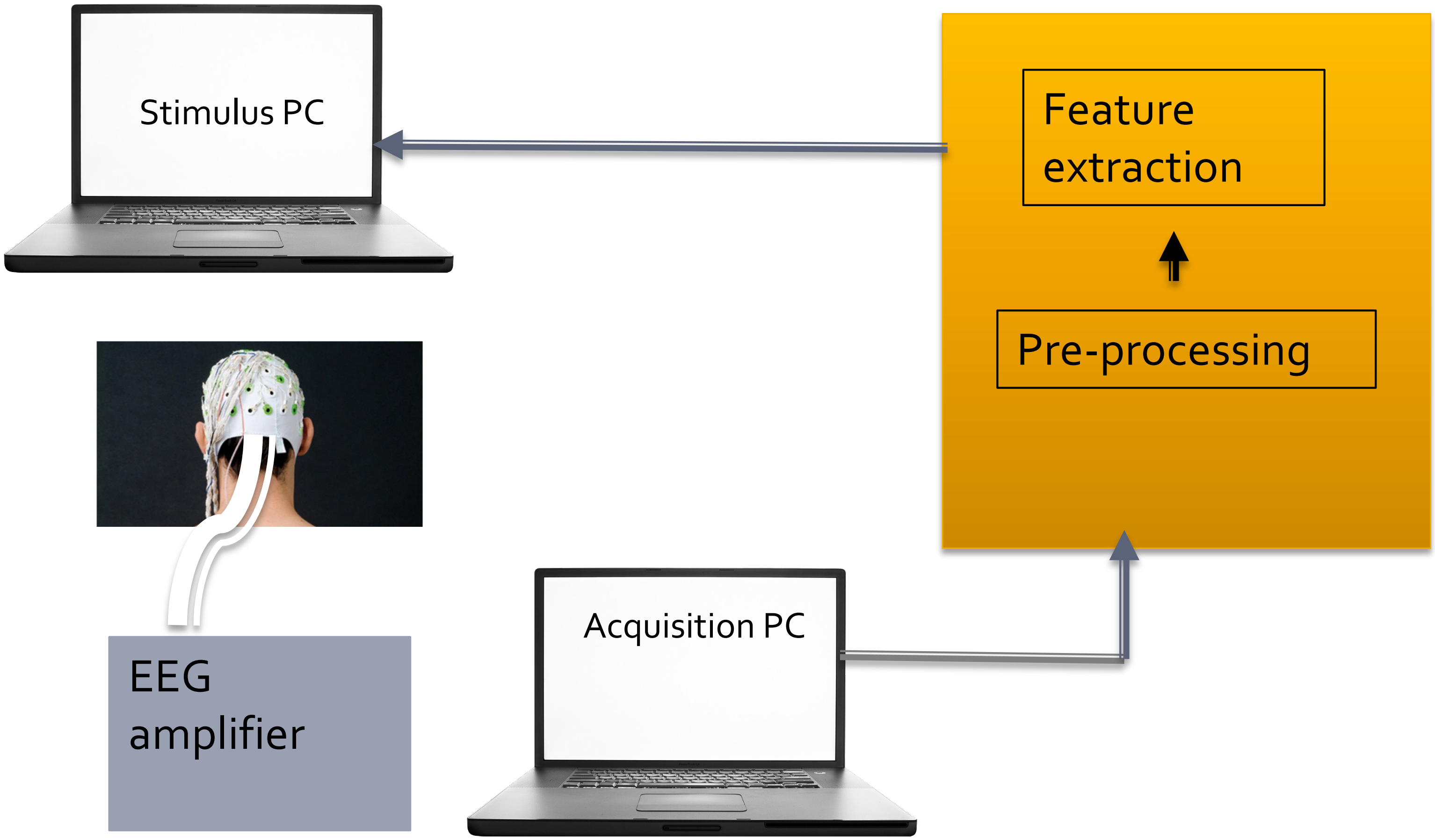
- Hard to extract features

- Nf fMRI
- high cost equipment

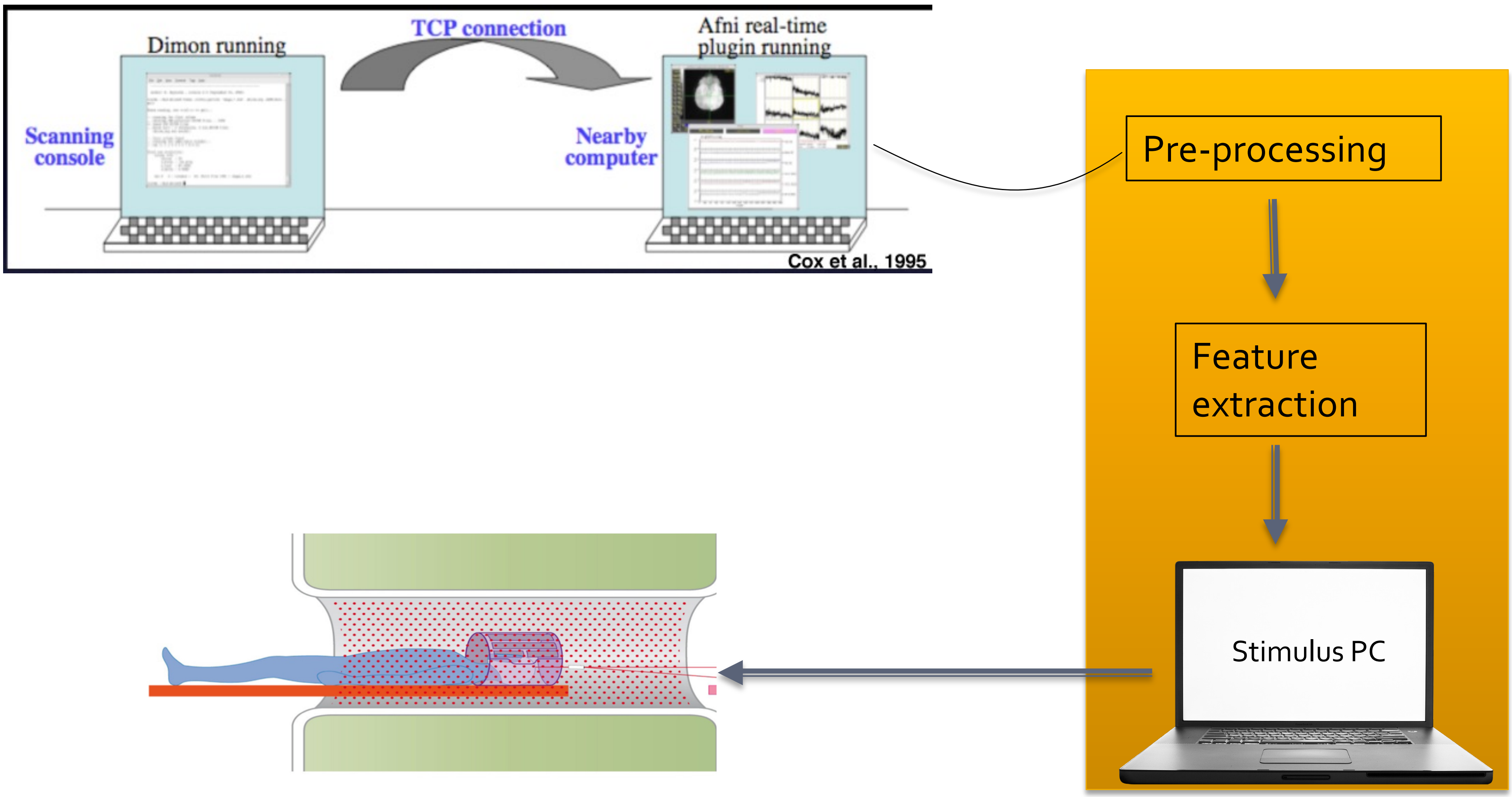
- Smooth signal

- ”easier” to extract feature

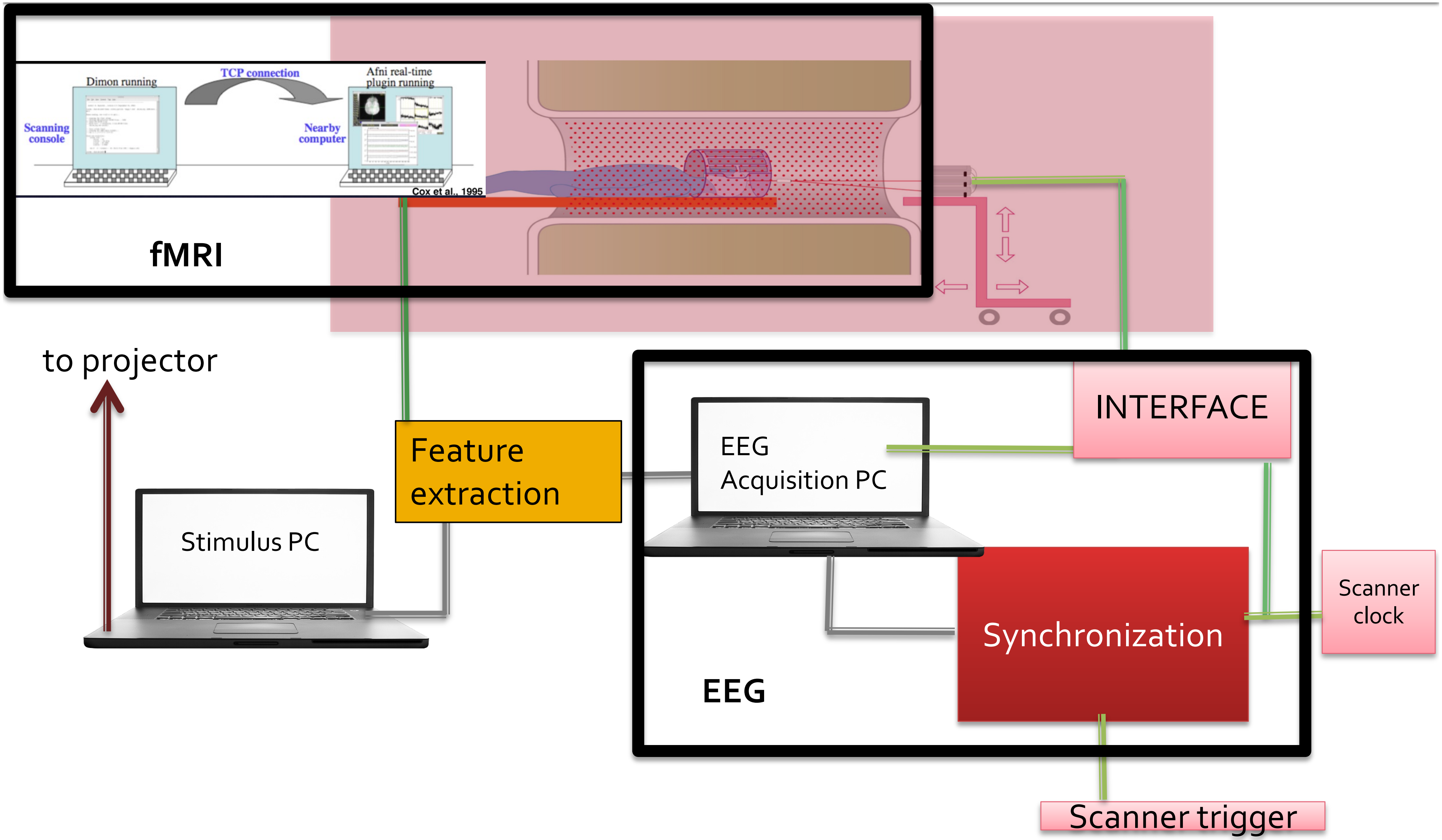
EEG neurofeedback setup



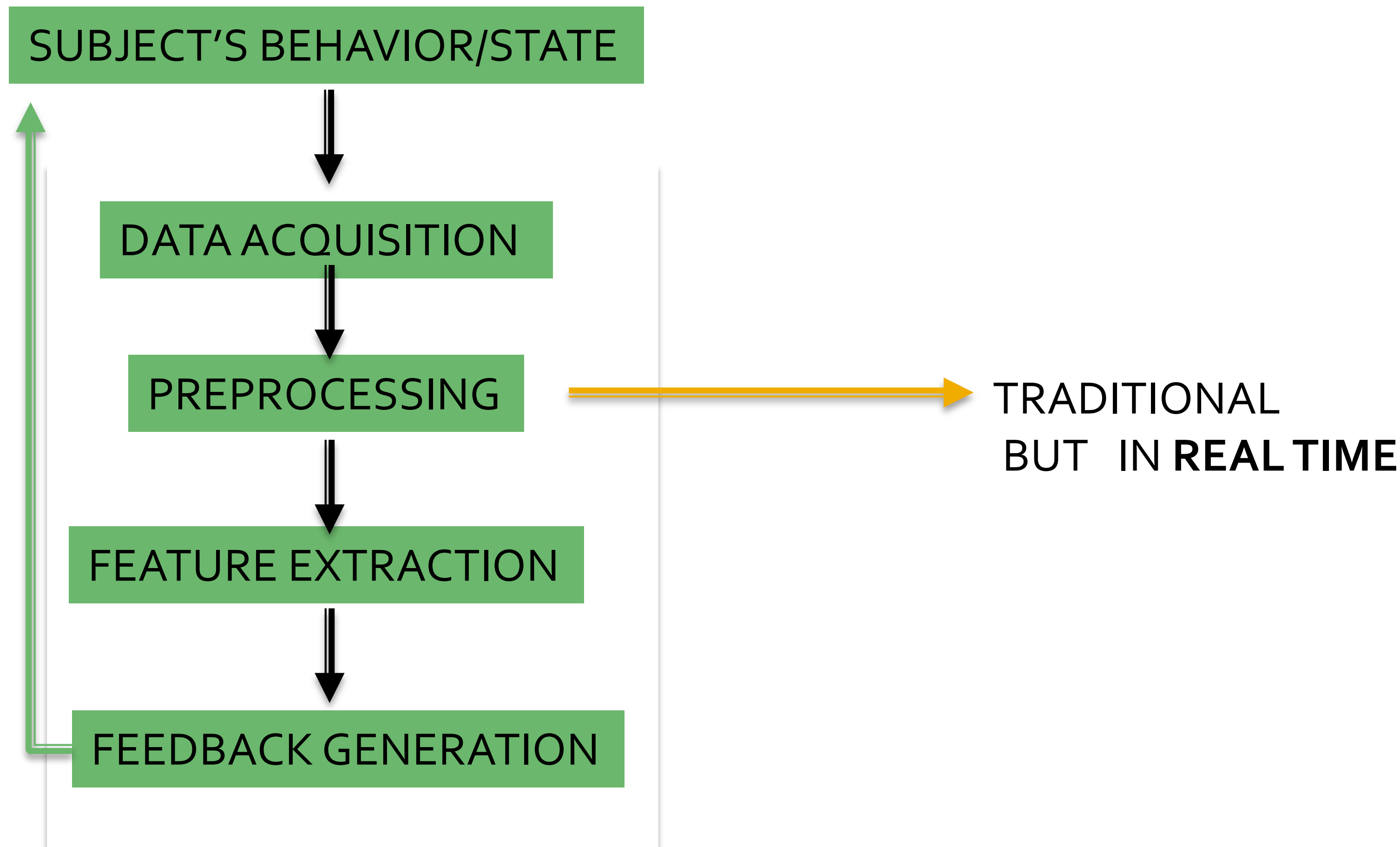
FMRI Neurofeedback setup



EEG-fMRI neurofeedback setup



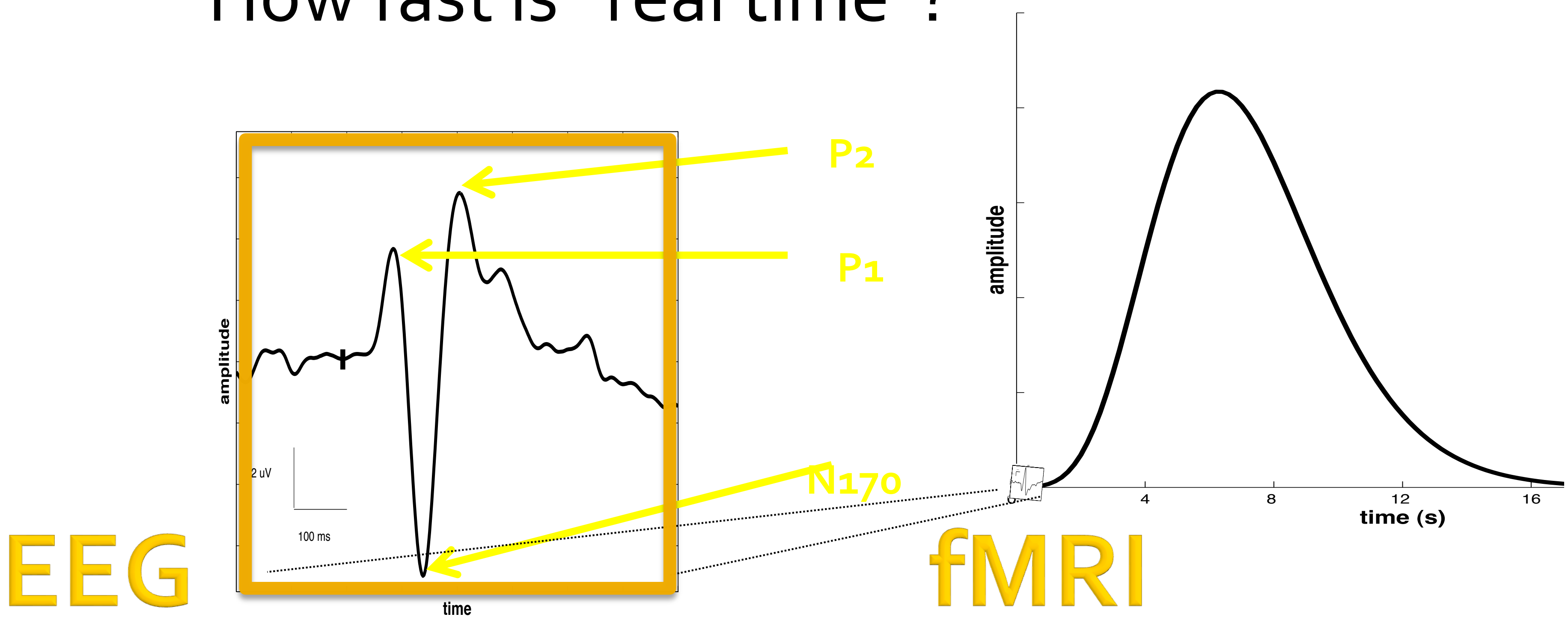
NEUROFEEDBACK



preprocessing

- Typical EEG or fMRI preprocessing needs to be performed in **real time**

How fast is "real time"?



Data preprocessing (EEG)

Channel(s) selection

- **Time domain**
  - Event Related Potentials (ERPs)

    pre-processing:

    detrend - filtering

    baseline correction

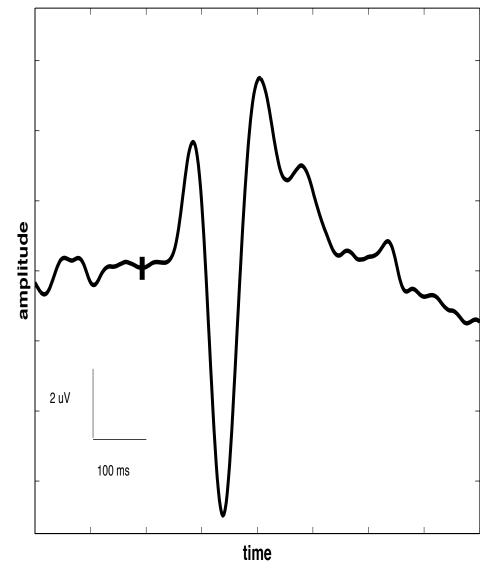
    ocular artifact reduction

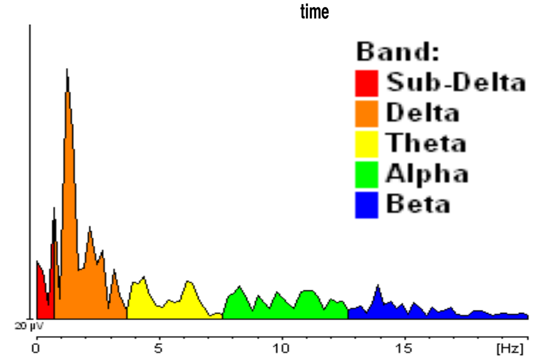
    (common grounded, laplacian, artifact rejection)

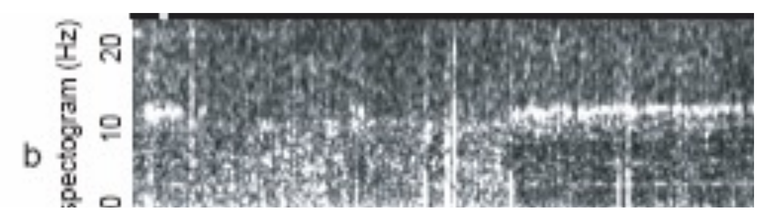
- **Frequency domain**
  - Power at different bands
  - Power spectra density (FFT)
  - Cross-spectra

    (correlation among different electrodes)
  - Coherence

    (measure of stability of the phase shift between electrodes)
  - Event related desynchronization







EEG neurofeedback limitations

- Difficulty detecting single events
  - Low signal to noise.
  - Hard to train on

Rt-fMRI neurofeedback limitations

- Motion
- BOLD is not an absolute measure
- Hemodynamic delay (slow)

fMRI requirements

- Structural /functional dataset for ROI definition
- EPI reference volume for ROI registration and motion correction
- Reference signal (since BOLD is not absolute)

Data preprocessing (fMRI)

- Motion correction

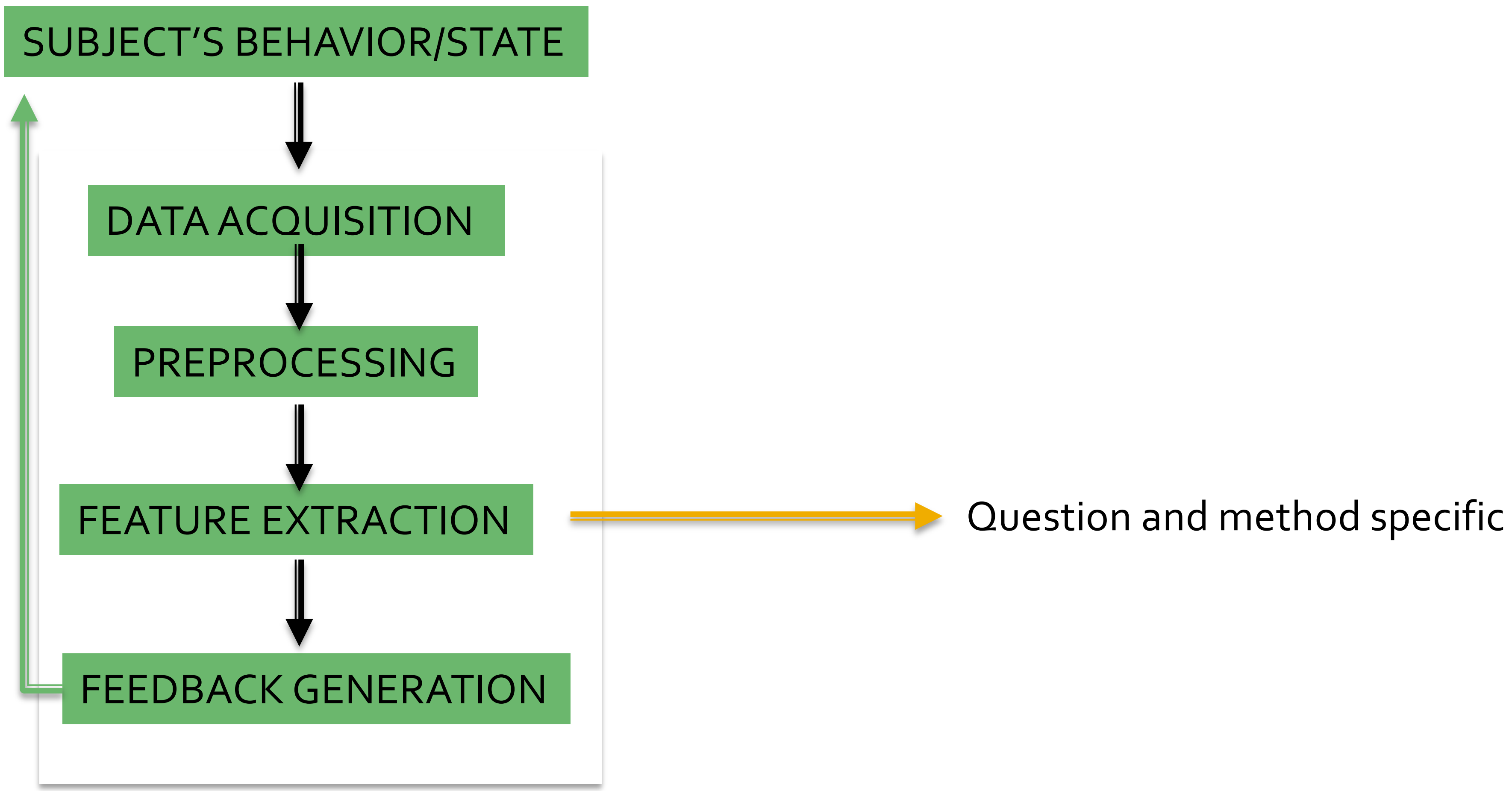
    Registering data to space where the ROI were defined

- Some proxy for physiological correction

    Reference ROI

- Voxel value extraction

NEUROFEEDBACK



Feature extraction in real time

EEG

- Event Related Potential peak
- Power at a particular band
- (de)Synchronization
- Coherence

fMRI

- Activation
- Connectivity
- Pattern

EEG neurofeedback example

Frontal alpha asymmetry neurofeedback for the reduction of negative affect and anxiety.

Mennella, Patron, Palomba. Behav Res Ther. 2017 May;92:32-40. doi: 10.1016/j.brat.2017.02.002. Epub 2017 Feb

Frontal alpha asymmetry neurofeedback for the reduction of negative affect and anxiety.

- Frontal alpha asymmetry has been proposed to underlie the balance between approach and withdrawal motivation associated to each individual's affective style.

- **neurofeedback training** to increase frontal alpha asymmetry (R/L)

- GOAL: to evaluate
  - discrete changes in alpha power at left and right sites,
  - in positive and negative affect, anxiety and depression.

- SUBJECTS: Thirty-two right-handed females

- DESIGN:
  - neurofeedback on frontal alpha asymmetry (N = 16).
  - active control training (N = 16).

Mennella, Patron, Palomba. Behav Res Ther. 2017 May;92:32-40. doi: 10.1016/j.brat.2017.02.002. Epub 2017 Feb

Frontal alpha asymmetry neurofeedback for the reduction of negative affect and anxiety.

From pre-to post-training the NF group showed

- an **increase in alpha asymmetry** driven by higher alpha at the right site ($p < 0.001$)

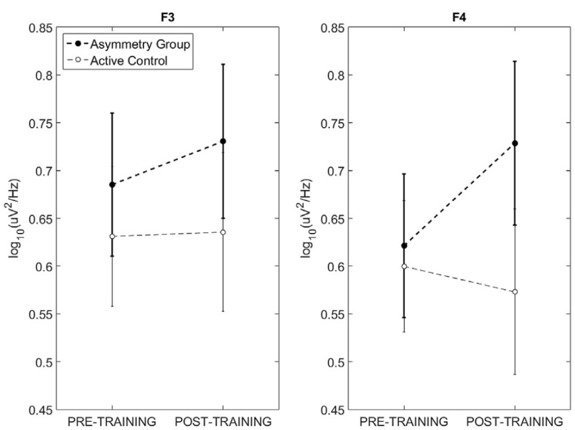


Fig. 2. Neurofeedback modulation of left and right alpha power: the Asymmetry Group, but not the Active Control, showed a significant increase in resting alpha power at F4, but not F3, from pre-to post-training. Error bars represent the standard error of the mean.

- **reduction in both negative affect and anxiety symptoms** (ps < 0.05)

Table 2
ANOVA on positive and negative affect, anxiety and depression scores from pre-to post-training in asymmetry group and Active control.

Variables	Pre-training	Post-training	*p*	η_p^2
PANAS Positive Affect Score			0.73[a]	0.004[a]
Asymmetry Group	27.56 (10.35)	29.19 (6.53)		
Active Control	29.94 (8.87)	30.75 (10.20)		
PANAS Negative Affect Score			0.05[a]	0.12[a]
Asymmetry Group	19.25 (9.03)	14.69 (6.46)	<0.01[b]	
Active Control	18.44 (6.64)	17.88 (8.58)	0.69[b]	
BAI			<0.05[a]	0.16[a]
Asymmetry Group	11.38 (9.56)	6.00 (5.56)	<0.001[b]	
Active Control	10.19 (9.39)	9.13 (8.00)	0.42[b]	
BDI-II			0.19[a]	0.06[a]
Asymmetry Group	9.75 (12.38)	6.00 (7.90)		
Active Control	8.13 (7.30)	7.19 (9.59)		

Notes: Data are *M* (*SD*). [a] = p-values and partial eta-squared referred to the Group × Time interaction for the corresponding measure. [b] = p-values associated to post-hoc comparisons in the context of a statistically significant Group × Time interaction (not reported for non-significant interactions). ANOVA = analysis of variance; PANAS = Positive and Negative Affect Schedule; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory II.

- No training-specific modulation emerged for positive affect and depressive symptoms.

Rt-fMRI-Based Neurofeedback some examples

Target brain areas:

Primary motor area (Yoo et al. 2002, 2004; de Charms et al. 2004, Berman 2012)

Primary Sensory area (Yoo et al. 2002, 2004; de Charms et al. 2004,)

Supplementary motor contex (Weiskopfs et al 2004)

Anterior insular cortex (Caria et al. 2007)

Emotion networks (Johnston et al.2010)

Connectivity

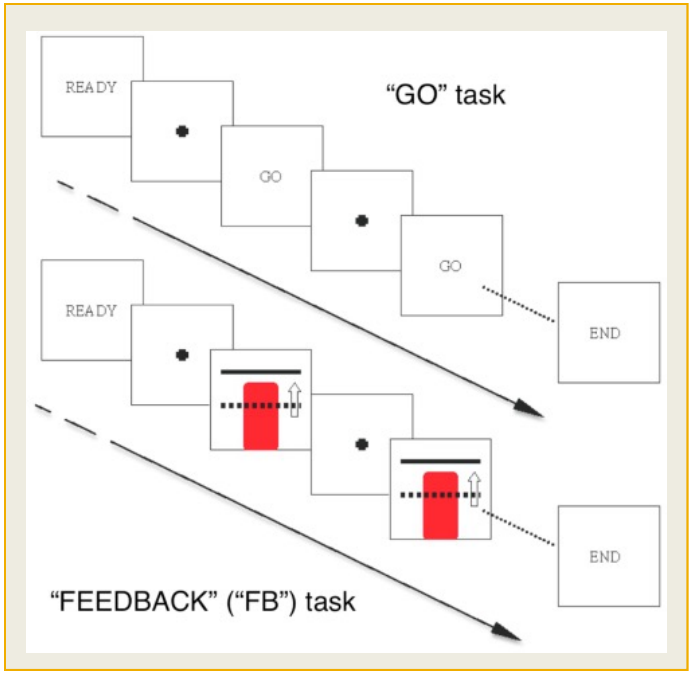
Motor system (Horovitz et al 2010)

SMA (Hampson et al 2011)

Insula (Berman et al, 2013)

Experiment

Task: block design movement imagery with and without neurofeedback. Control task was finger tapping in both conditions

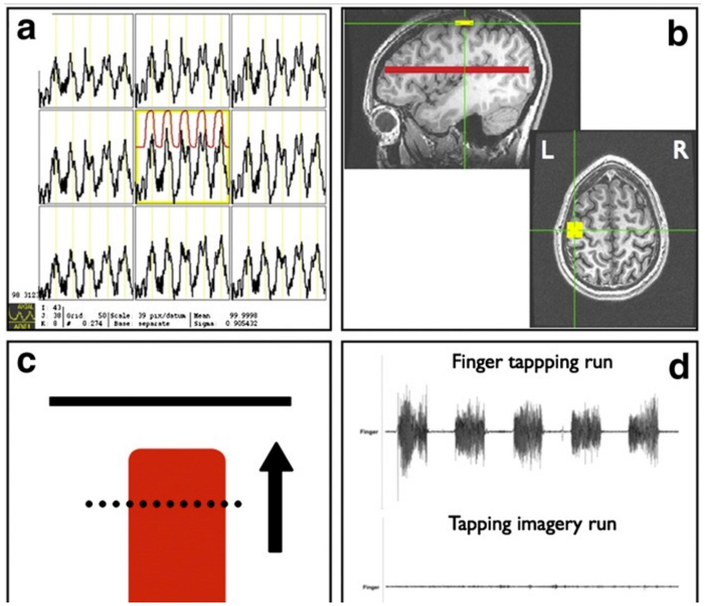


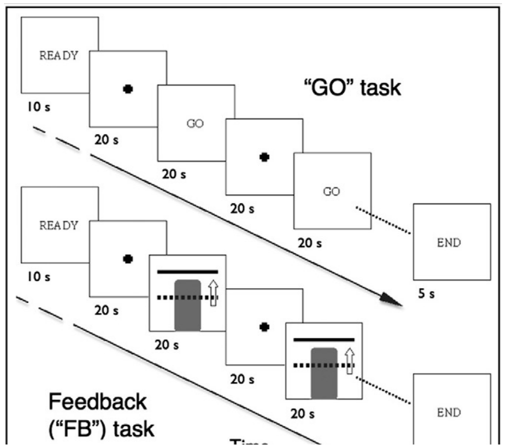
Acquisition: 3T GE scanner

- EPI sequence
- 17 slices 64x64
- Slice thickness 5.0mm
- gap=0.5mm
- Flip angle 70
- Repetitions: 294
- TR: 1.0s

Subjects: 9HV (25-34yo)

Motor system





Our findings suggest that while the ability to self-modulate M1 proper using rtfMRI-based NF can be quickly acquired using a simple finger tapping motor task, this was not the case when subjects used a motor imagery task

B.D. Berman et al. / NeuroImage 59 (2012) 917–925

POST processing

Do changes in functional connectivity occur during neurofeedback training?

Connectivity Analysis

- Define a seed region

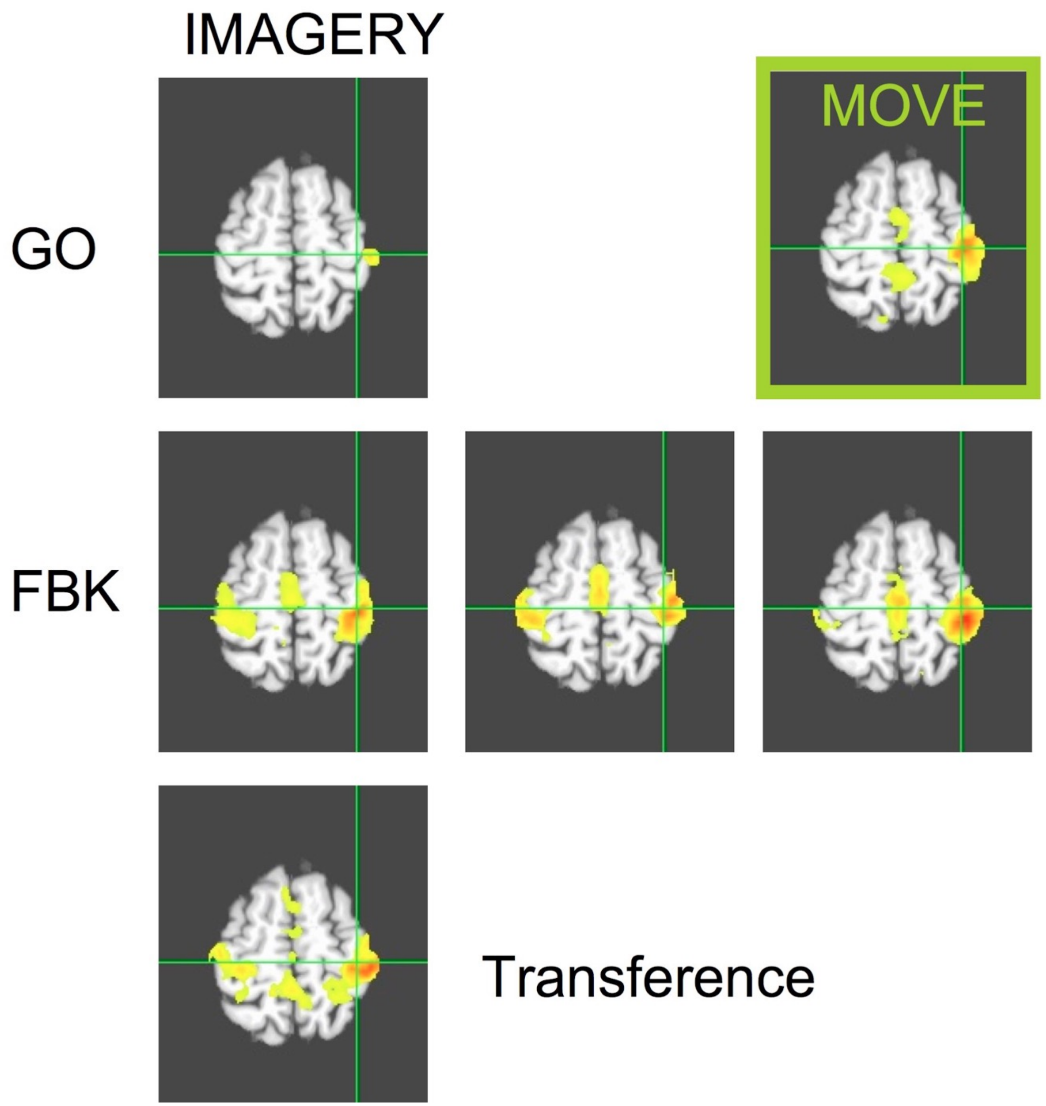
  Motor area defined by a block design finger tapping run

- Correlate the time course of the seed during task performance with the whole brain

- Compare connectivity values for the feedback and non-feedback runs, and non-feedback runs before and after training

Horovitz et al. / IEEE(2010)

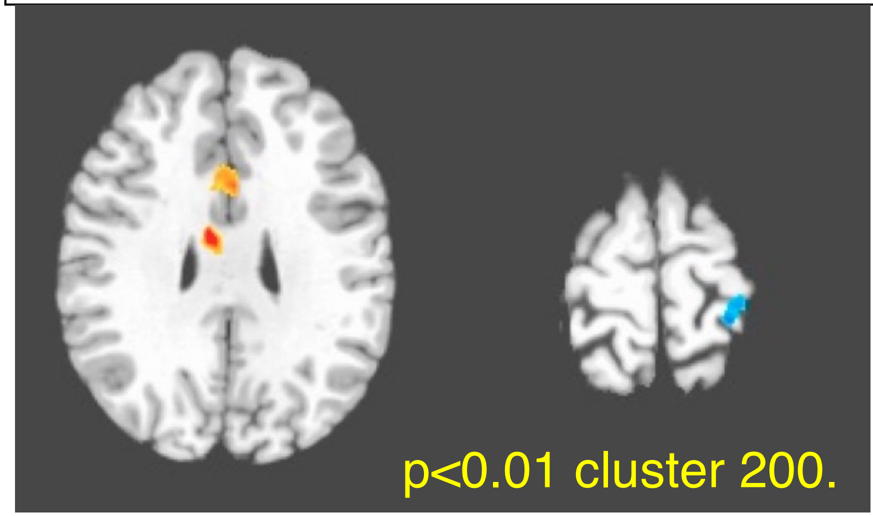
left sensorimotor cortex seed: connectivity maps



Connectivity maps for each task. P<0.001, cluster 200

RESULTS

t-test of connectivity for GO vs Transfer: Imagery task

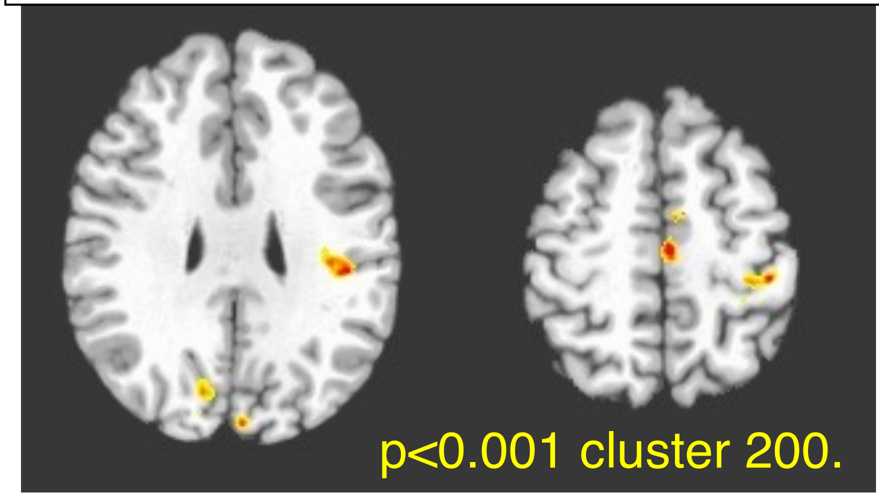


Before feedback training, seed strongest connectivity was with the Anterior Cingulate Cortex

After training, seed strongest connectivity was with the left anterior Putamen/globus pallidus, and bilateral parahippocampal gyri.

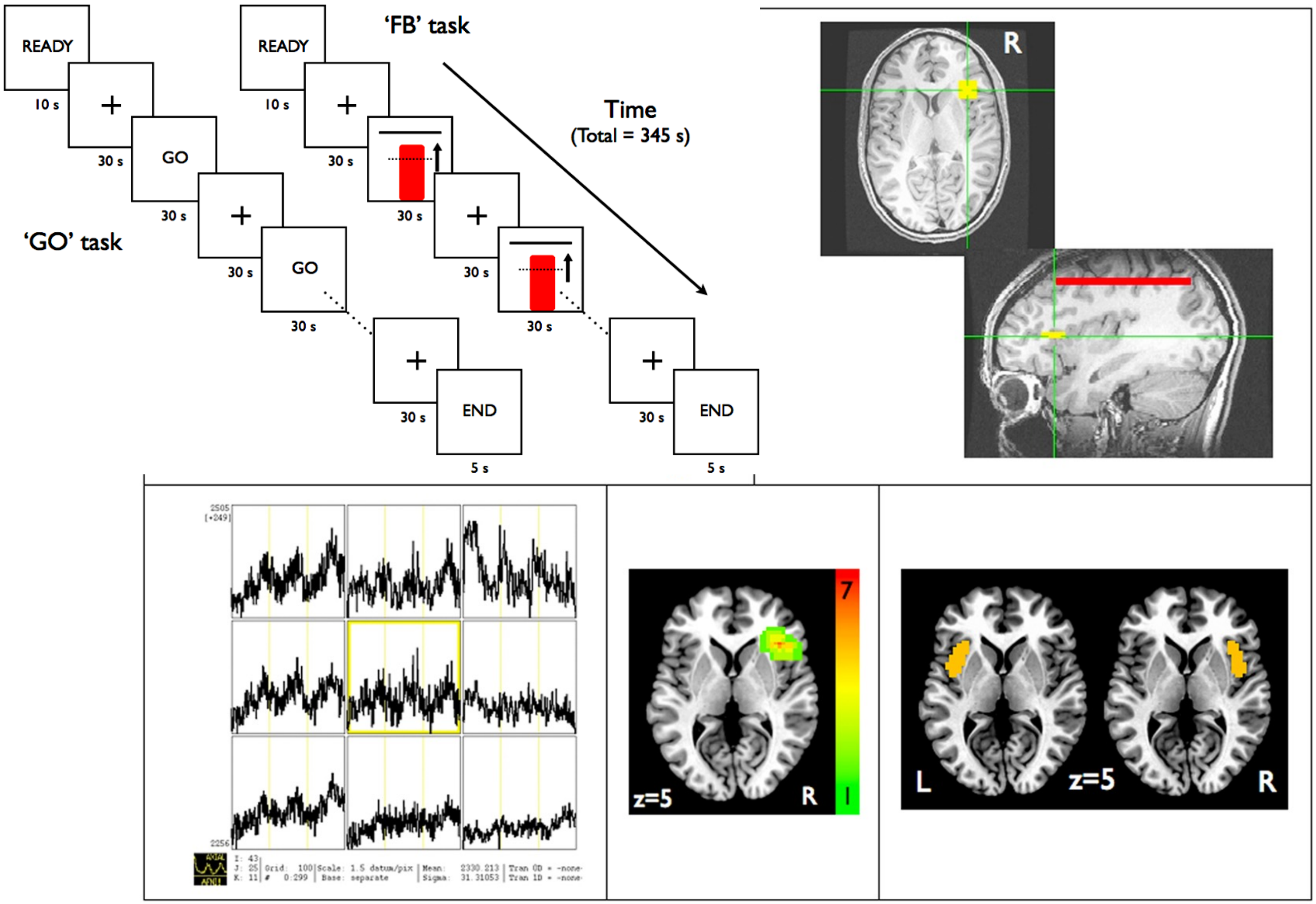
Anterior cingulate region (GO > Transfer) and left postcentral gyrus (Transfer > GO)

Task (IMAGINE/TAP) x Method (FEEDBACK /NON FEEDBACK) Interaction.



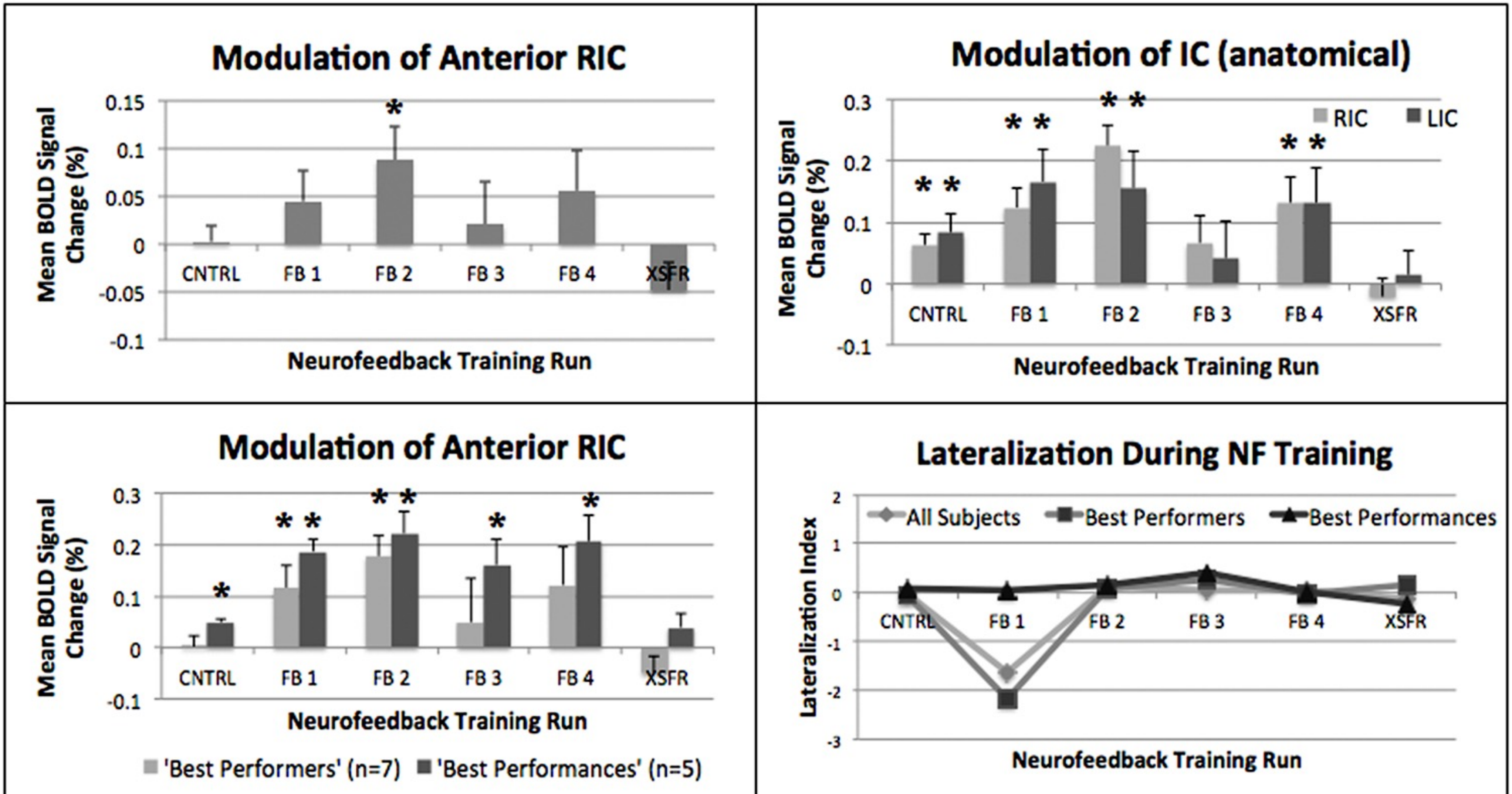
Connectivity with post-central cortex and Supplementary motor area was different for the different conditions.

Modulation of functionally localized right insular cortex activity using real-time fMRI-based neurofeedback



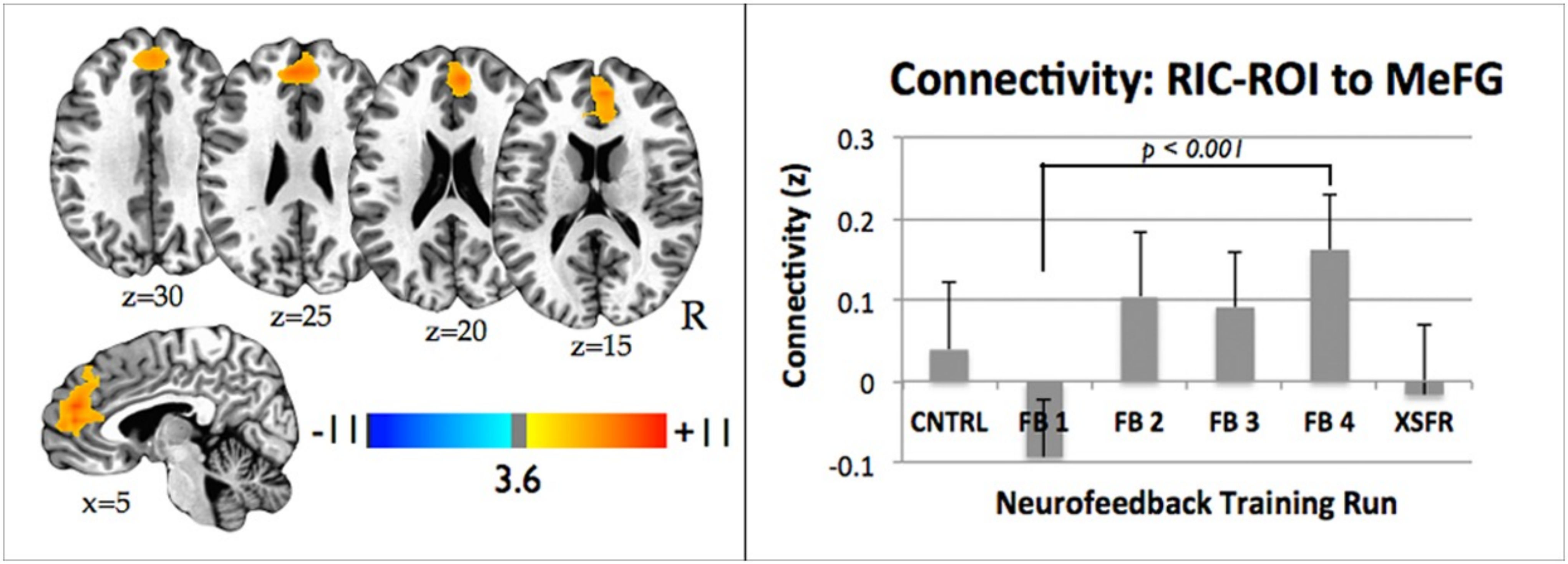
Berman, Horovitz ,Hallett Frontiers in Human Nsci 2013

Modulation of functionally localized right insular cortex activity using real-time fMRI-based neurofeedback



Berman, Horovitz ,Hallett Frontiers in Human Nsci 2013

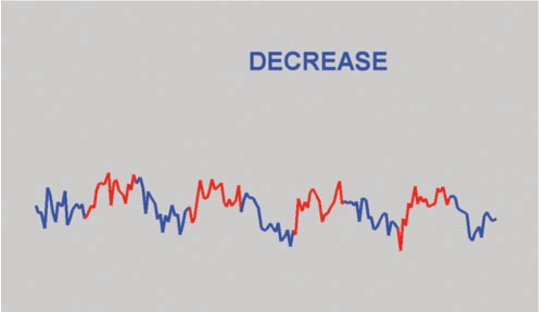
Modulation of functionally localized right insular cortex activity using real-time fMRI-based neurofeedback



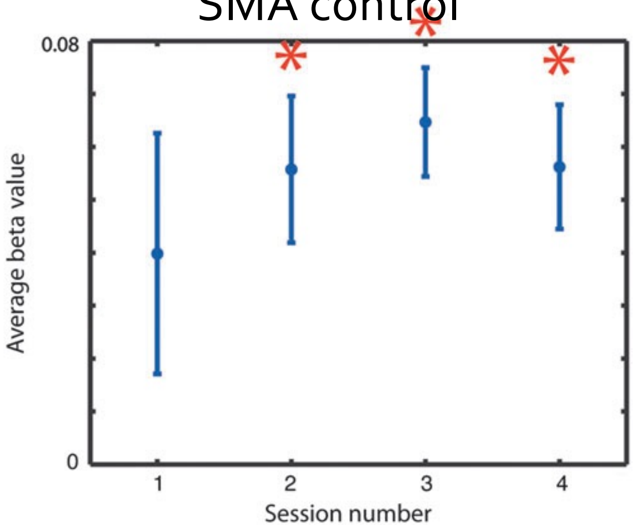
Berman, Horovitz ,Hallett Frontiers in Human Nsci 2013

Biofeedback of Real-Time Functional Magnetic Resonance Imaging Data from the Supplementary Motor Area Reduces Functional Connectivity to Subcortical Regions

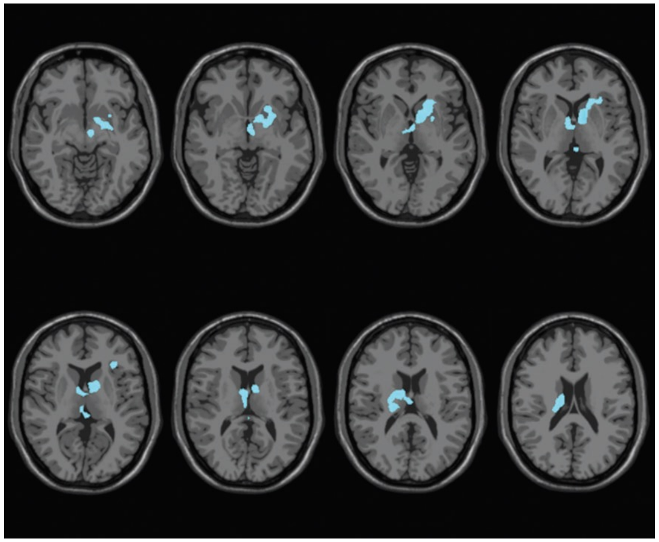
Hampson et al. BRAIN CONNECTIVITY
Volume 1, Number 1, 2011



SMA control

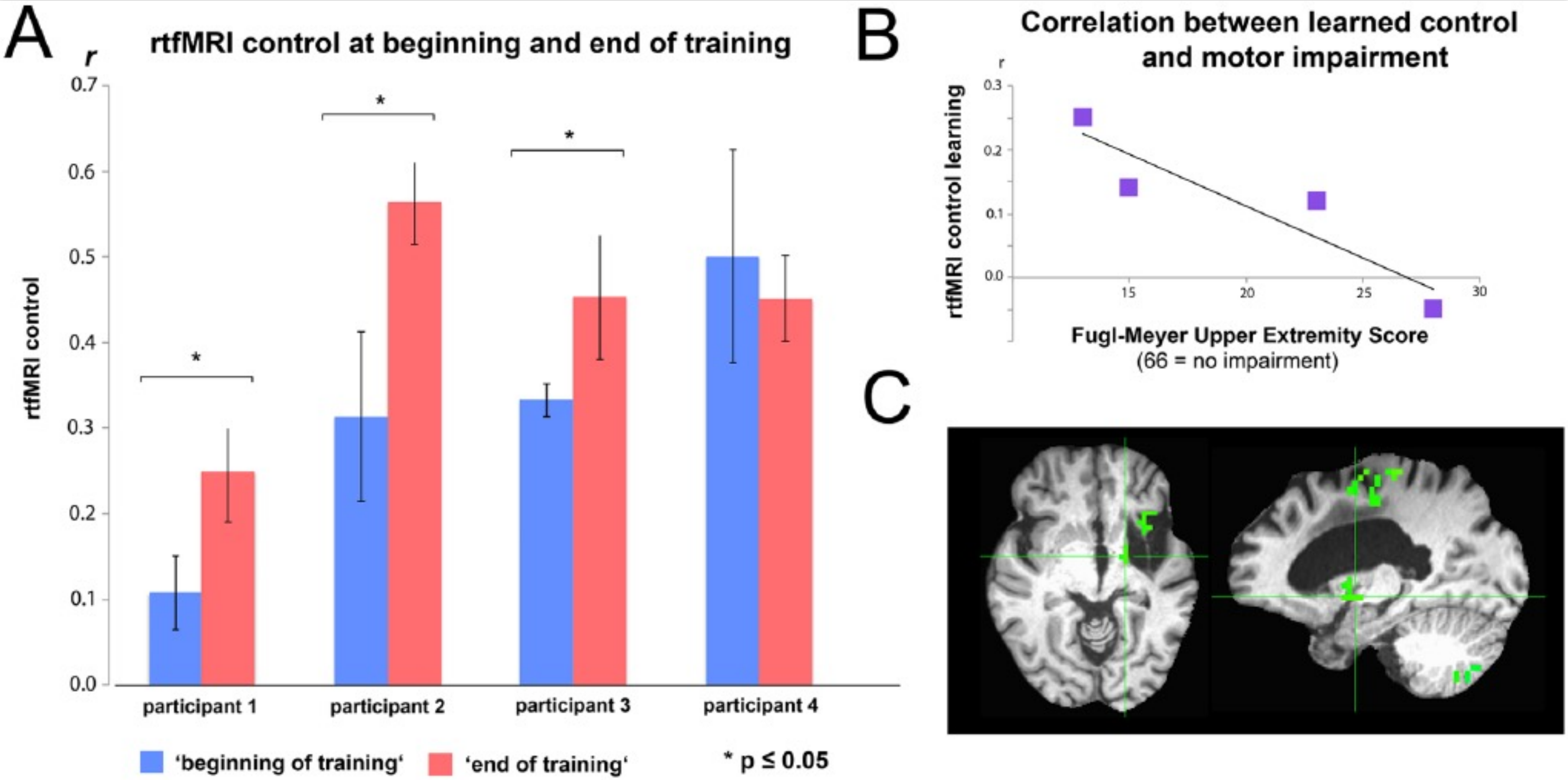


post-hoc SMA connectivity



A decrease in resting state connectivity between the SMA and subcortical regions was found after biofeedback of SMA activity level.
This suggests that a similar biofeedback paradigm may yield clinical improvement in TS patients.
Controlled studies in the patient group are needed to determine the efficacy of this novel treatment approach for TS.

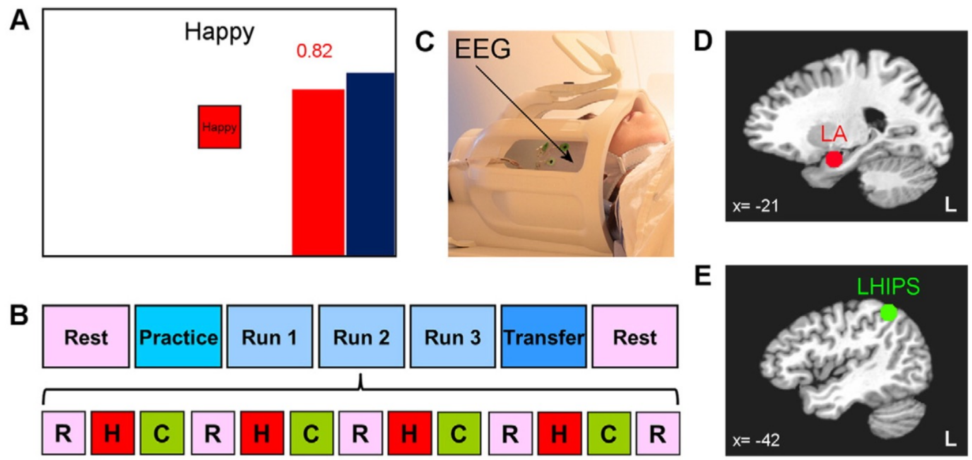
Neurofeedback fMRI connectivity rehabilitation STROKE patients

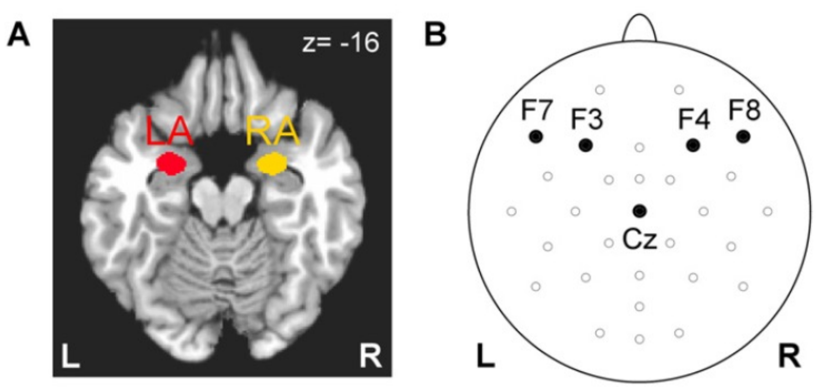


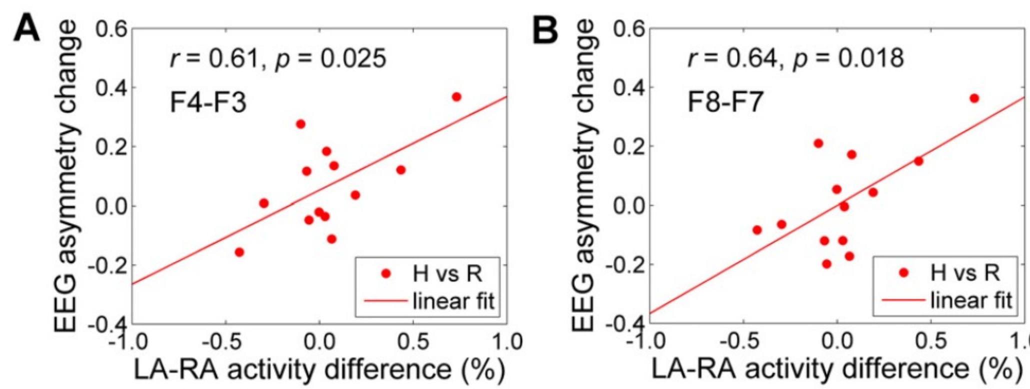
Liew et at. Neurorehabilitation and Neural Repair 2016, Vol. 30(7) 671– 675

Use EEG to understand fMRI neurofeedback

Zotev et al. NeuroImage: Clinical 11 (2016) 224–238





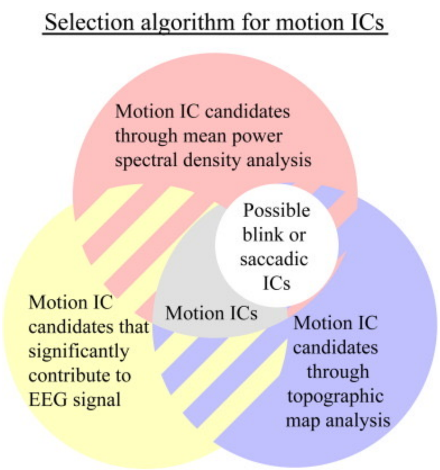


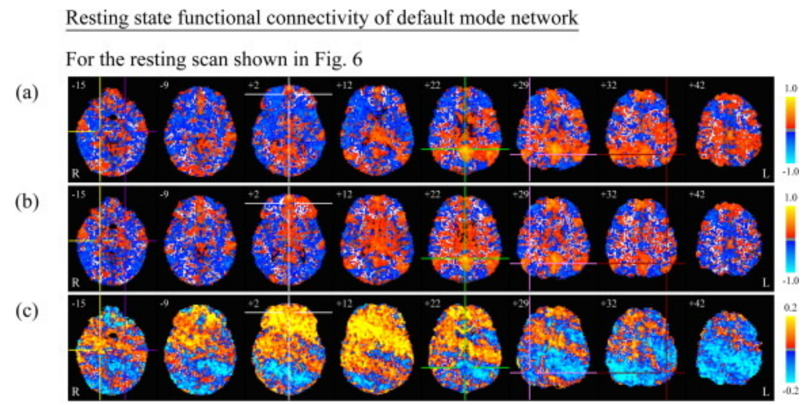
Automatic EEG-assisted retrospective motion correction for fMRI (aE-REMCOR).

Chung-Ki Wong, Vadim Zotev, Masaya Misaki, Raquel Phillips, Qingfei Luo, Jerzy Bodurka. Neuroimage 2016

Highlights

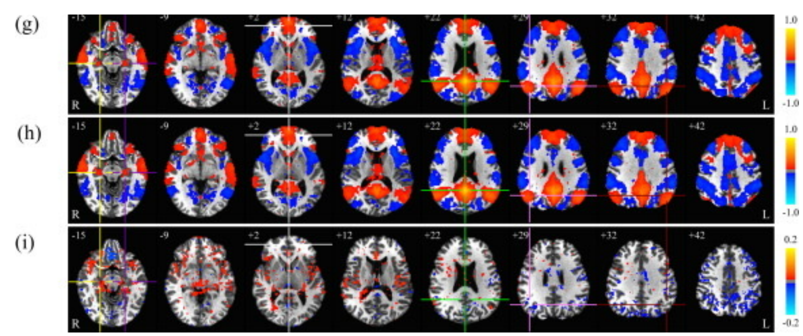
- aE-REMCOR is capable to automatically detect rapid head and cardioballistic motions.
- Motion effects can be corrected by aE-REMCOR on slice-by-slice basis in fMRI data.
- improve accuracy of the rs-fMRI connectivity analysis.
- aE-REMCOR provides incentive for conducting simultaneous EEG & fMRI.





Resting state connectivity of the default mode network (DMN).
Top: Individual subject. (a)–(b): Correlation map without and with aE-REMCOR for the scan with significant rapid head movements (c) difference.

(g-h-i) Group results



Prerequisites of a good neurofeedback study

Construct validity of the feature

- The feature (e.g., the relative power of an oscillation), which is indented to be modulated by neurofeedback, should be selected **hypothesis-driven,** thus based on current knowledge of cognitive neuroscience and should guide the implementation of the online-feature-extraction, such as the electrode placement for feedback.

Trainability of the feature

- The modulated feature should show **positive learning indices** in contrast to untrained features.
- The learning indices should be evaluated regarding their effect strength by **calculating effect sizes**.

Transfer to performance

- According to the construct validity, the neurofeedback training is expected to result in **behavioral (performance) changes**.

Usage of an active control group

- The usage of a **credible sham-/pseudo neurofeedback control group** strongly recommended..
- An **ABA design** can be used alternatively when the implementation of an active control group is not possible.
- The usage of control groups helps to distinguish between **true enhancements, repetition-related** and **non-specific effects**. A passive control group controls for repetition-related effects, whereas an active control group controls for repetition-related and unspecific-effects arising for instance from the contact with the training instructor, from regular lab visits, training induced-management etc.

Random assignment of participants

- **Effects not related to the intervention are prevented** such as selection effects, expectancy effects, effects due to events between pre-and post measurements (maturation, developmental effects), regression to the mean
- Alternatively, the usage of a (pseudo) randomized approach can be performed.

Enriquez-Geppert et al. Front. Hum. Neurosci., Feb 2017 doi.org/10.3389/fnhum.2017.00051

Open questions for clinical applications

- In which neurological diseases is rtfMRI neurofeedback appropriate, and under what conditions is it inappropriate?
- Under which conditions is rtfMRI neurofeedback more advantageous than other interventions?
- To what extent is the behavior of healthy participants a model for patients?
- Can self-regulation be repeated outside the clinic?
- How effective is the treatment, and how long does the effect last?
- What are the side-effects?
- Is there a maximum dosage a patient can provide oneself?

Real-time **fMRI neurofeedback**: Progress and challenges
J. Sulzer, et al. Neuroimage. 2013 Aug 1; 76
doi: 10.1016/j.neuroimage.2013.03.033