Designing a neurofeedback study

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Overview

1. Defining neurofeedback target(s)
2. Feedback presentation
3. Participant involvement
4. Session setup
5. Control condition(s)

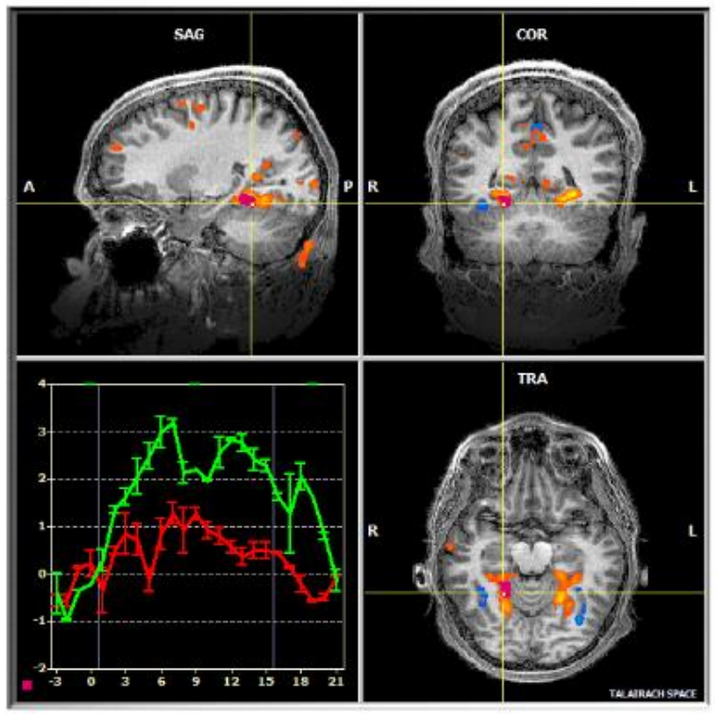
1.
Definition of neurofeedback target(s)

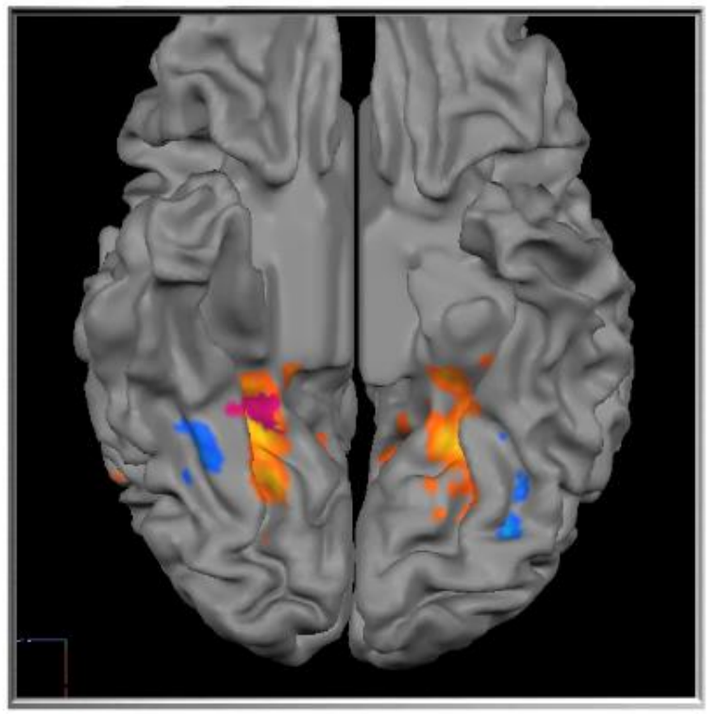
How to select target region?

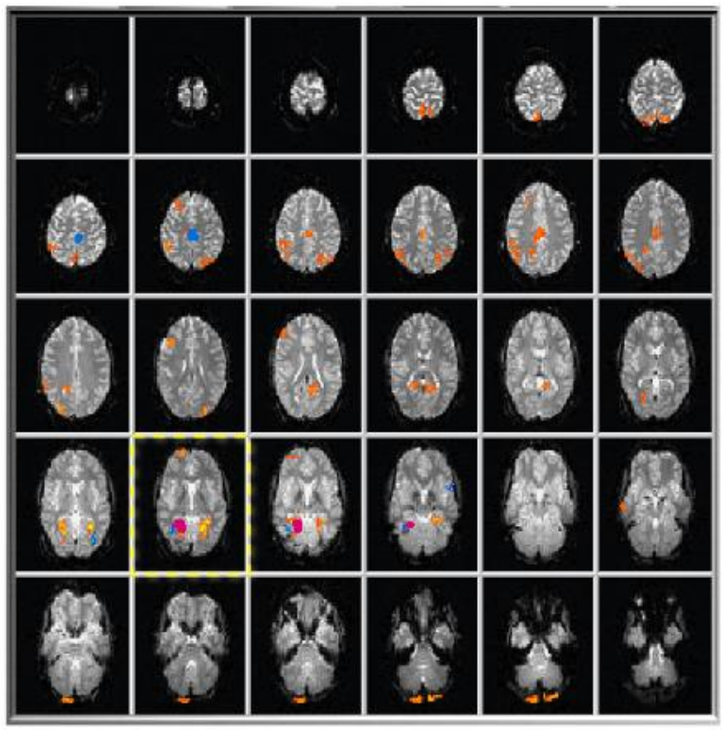
1. <u>Anatomically</u>
   - Peak coordinates from an atlas
   - Templates from brain parcellations

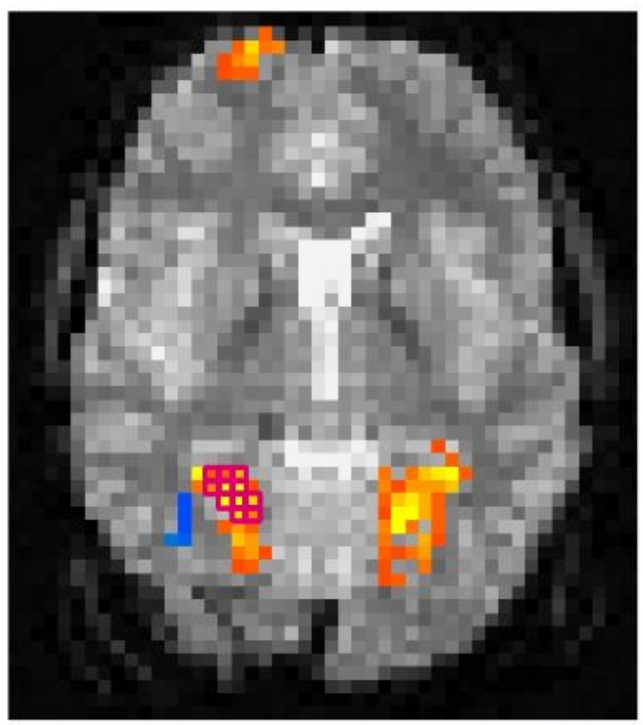
2. <u>Functionally</u>
   - Peak coordinates from literature (e.g. Neurosynth)
   - Templates from previous studies
   - **Functional localiser**

Real-time region-of-interest (ROI) signal extraction









Caroline Benjamins

Target region selection from localiser results

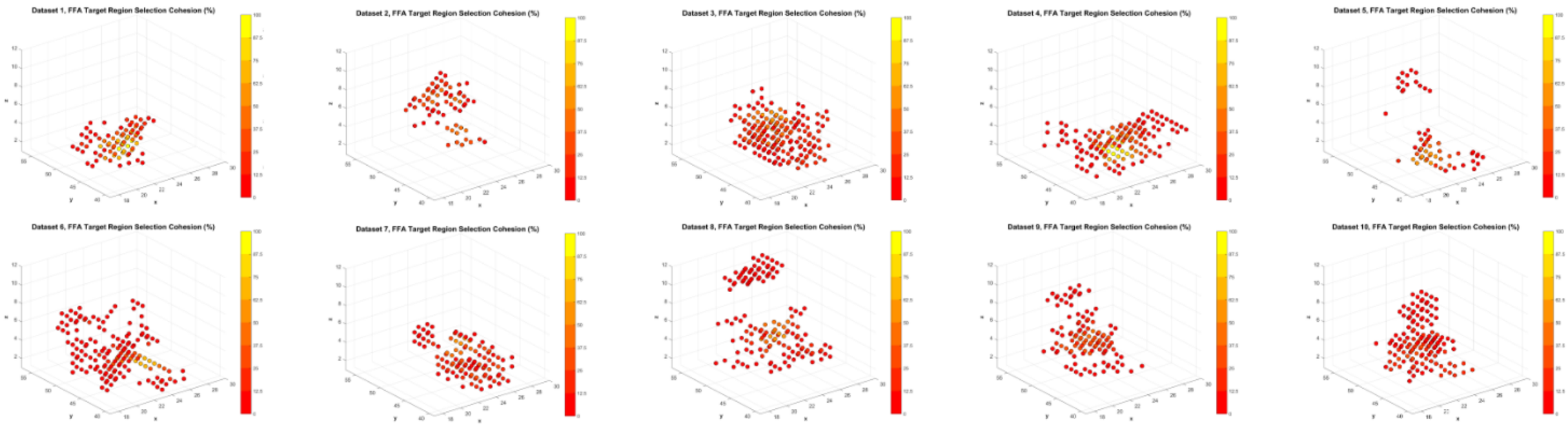


Figure 1. *Coordinates (in native space) of all voxels included in FFA Target Region Selection across all participants, for each data set. Colour of voxels indicates percentage coherence between participants.*

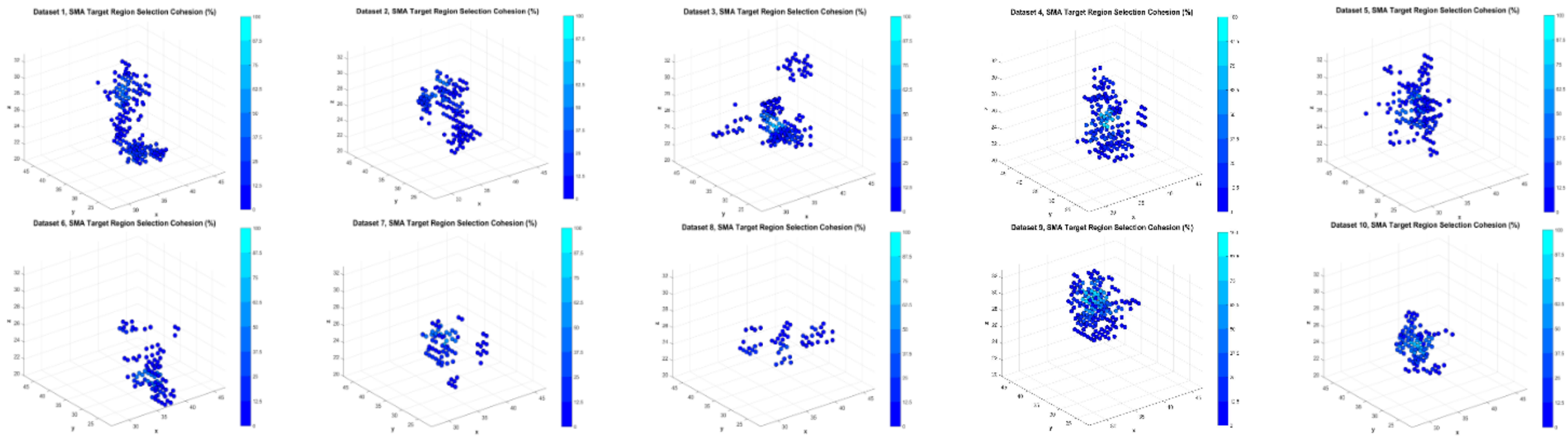
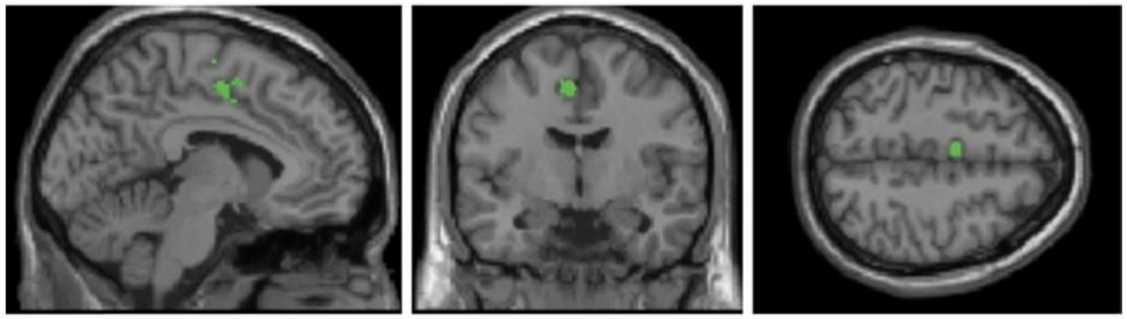


Figure 2. *Coordinates (in native space) of all voxels included in SMA Target Region Selection across all participants, for each data set. Colour of voxels indicates percentage coherence between participants.*

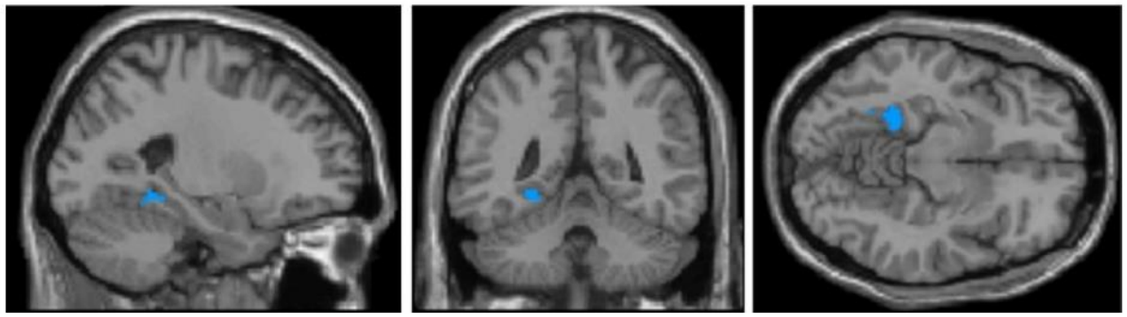
Krause et al., unpublished

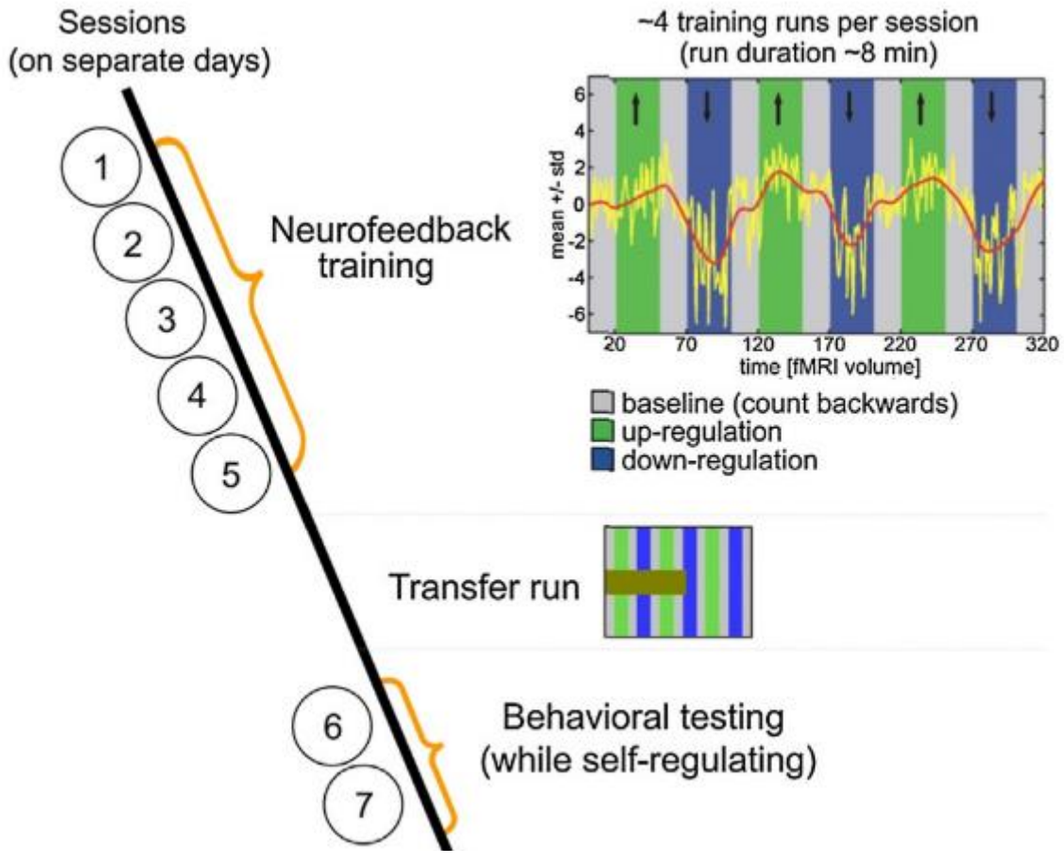
Activation of multiple regions

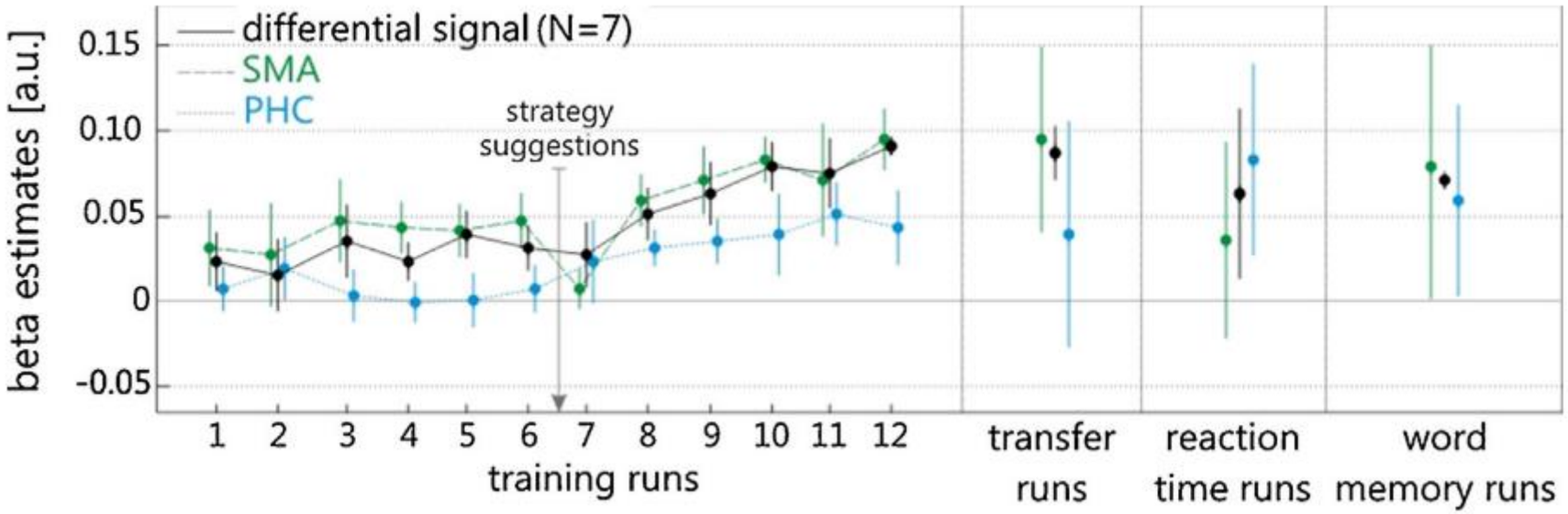
A) Supplementary motor ROI



B) Parahippocampal ROI



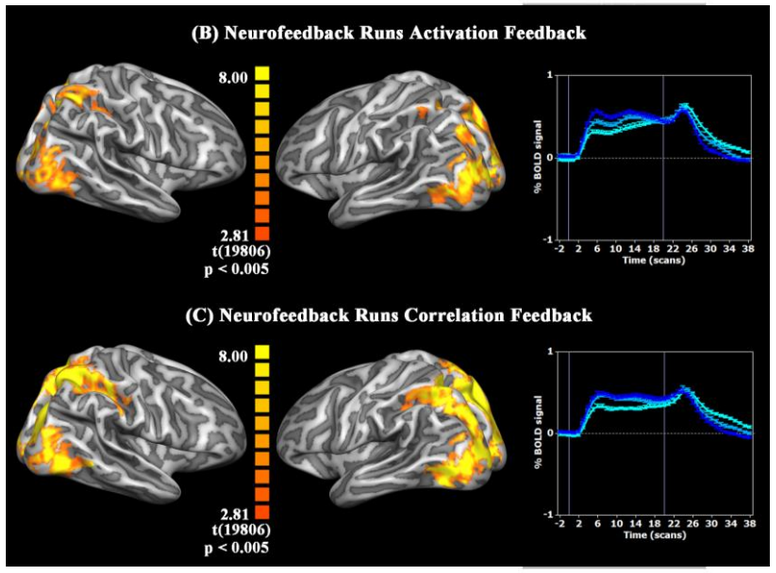


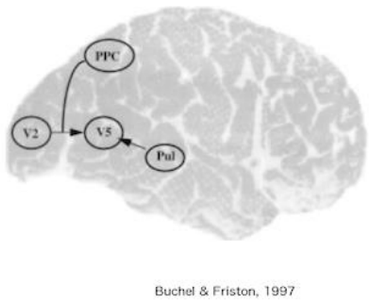


Scharnowski et al., 2015

Functional connectivity-based neurofeedback (FcNef)

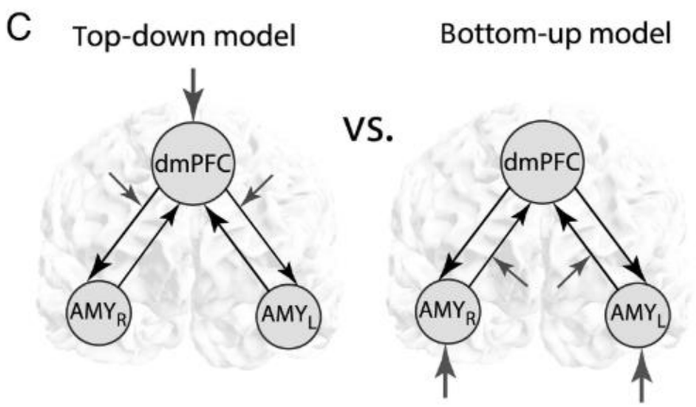
(Partial) correlation (e.g. Krause et al., unpublished)

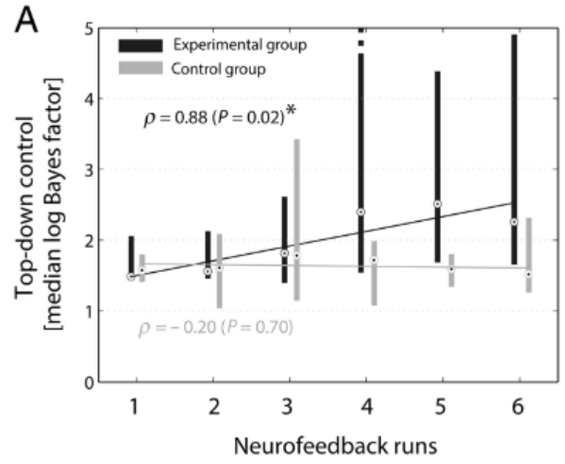




Buchel & Friston, 1997

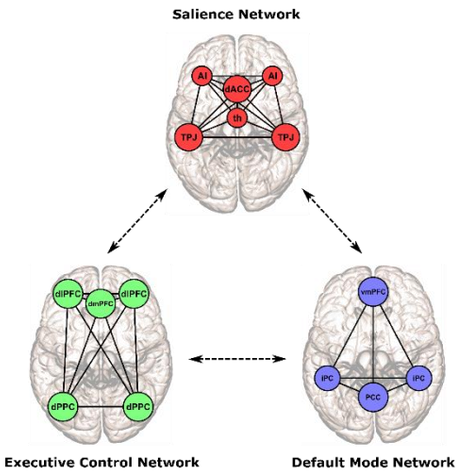
Dynamic Causal Modelling (e.g. Koush et al., 2017)

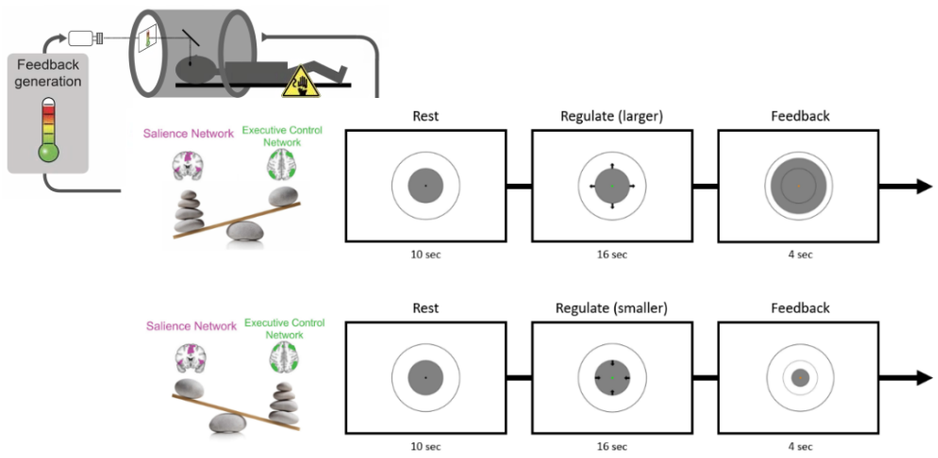




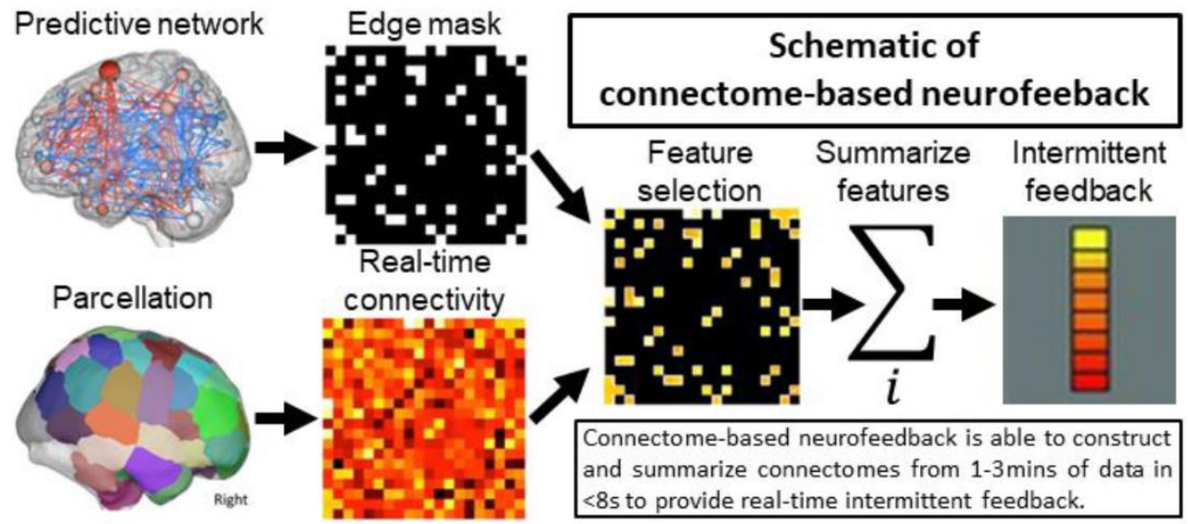
Network-based neurofeedback (NetNef)

Large-scale brain networks (Krause et al., 2021)

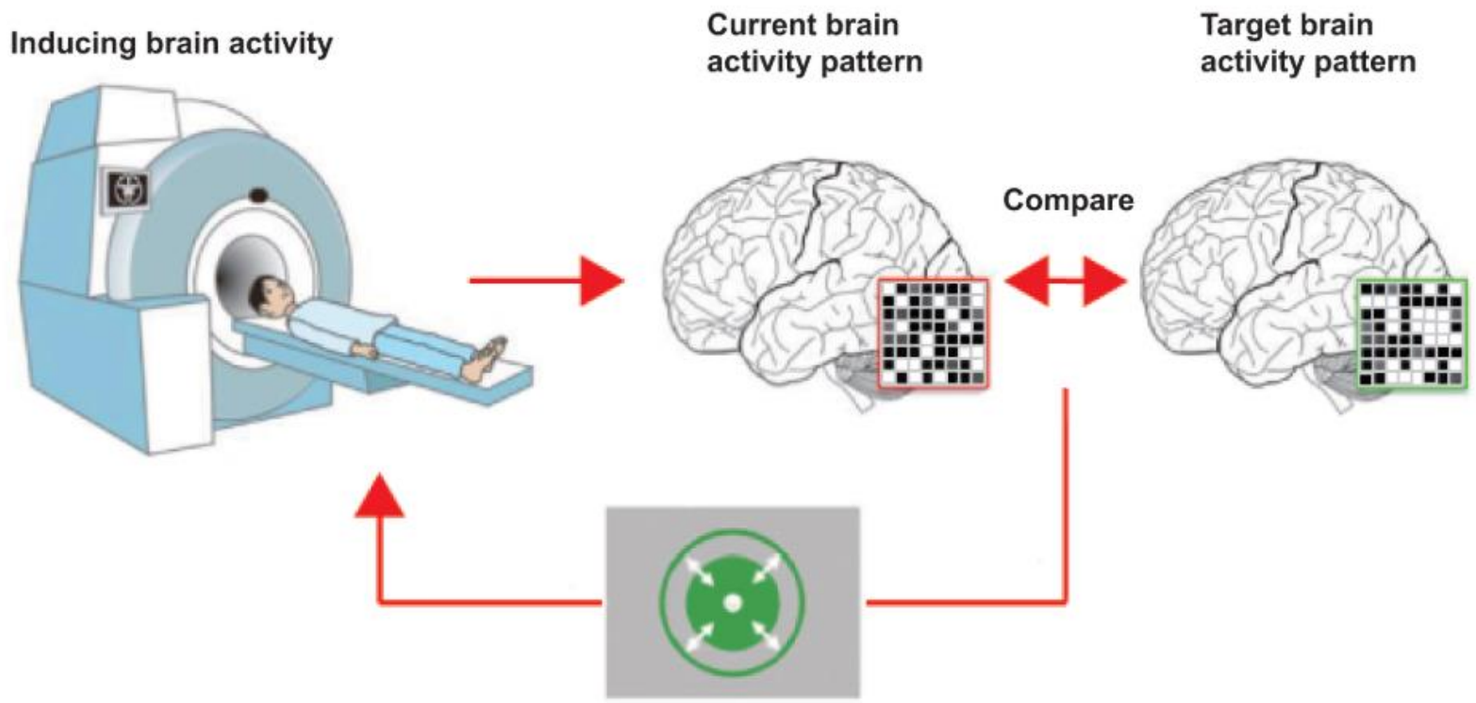




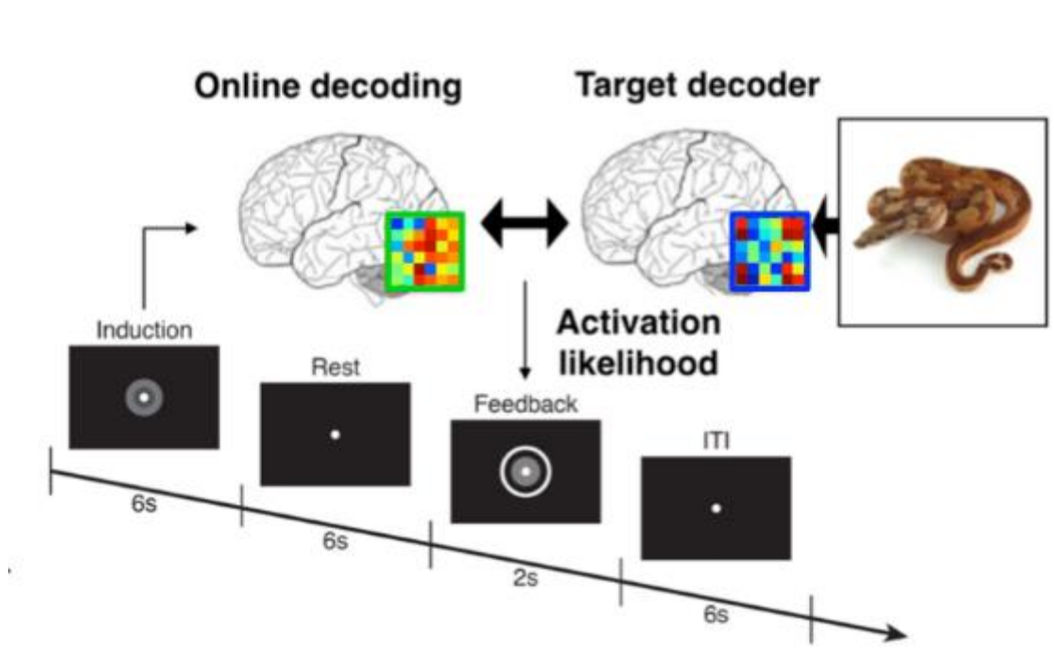
Entire connectome (Scheinost et al., 2020)

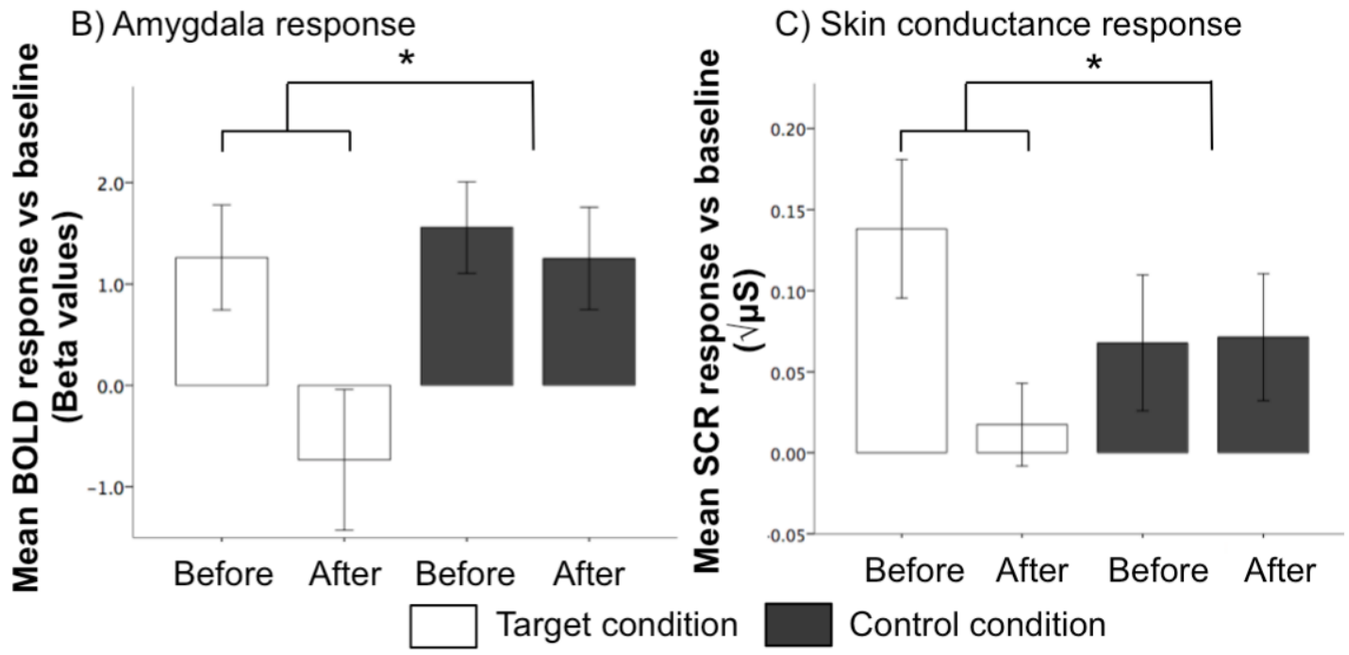


Decoded neurofeedback (DecNef)



Unconscious neurotherapy for common fears (Taschereau-Dumouchel et al., 2017)

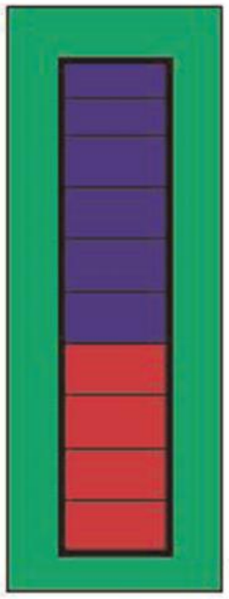


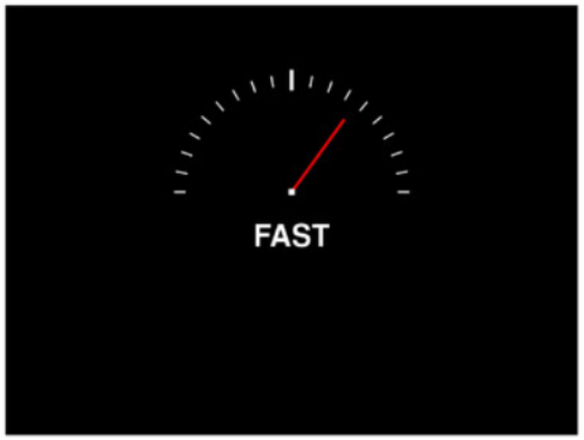


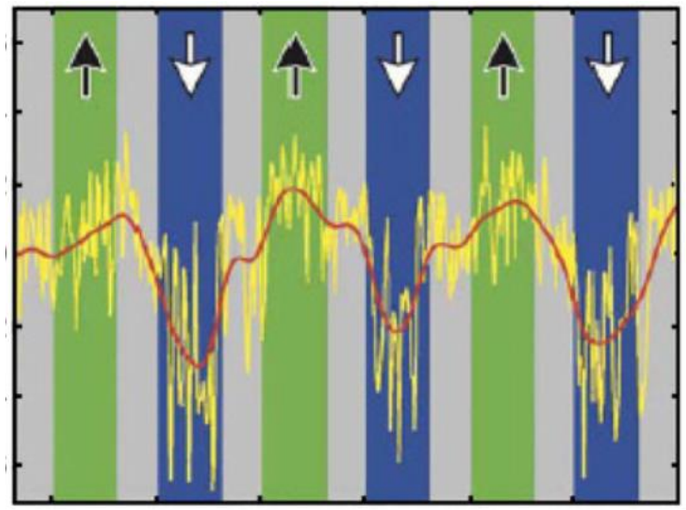
2.

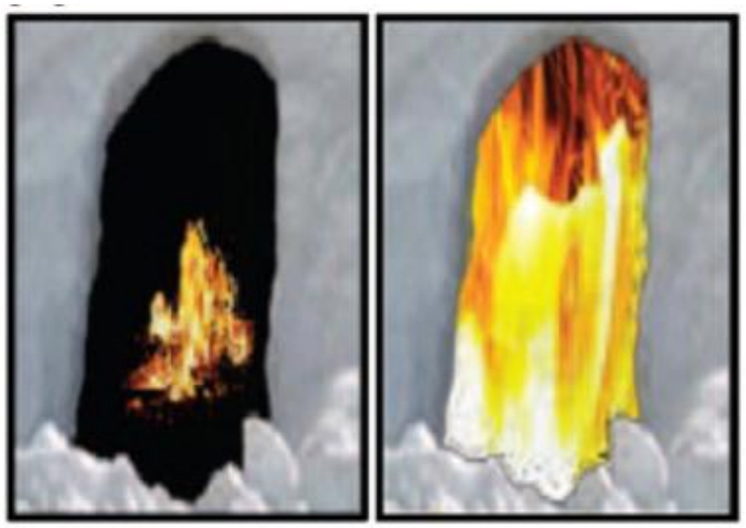
Feedback presentation

Many options



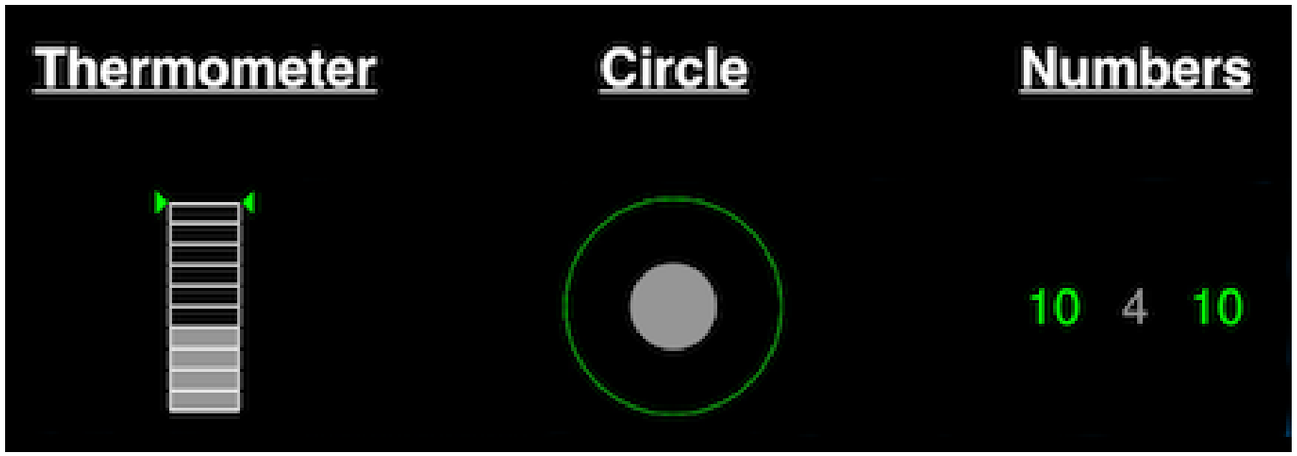


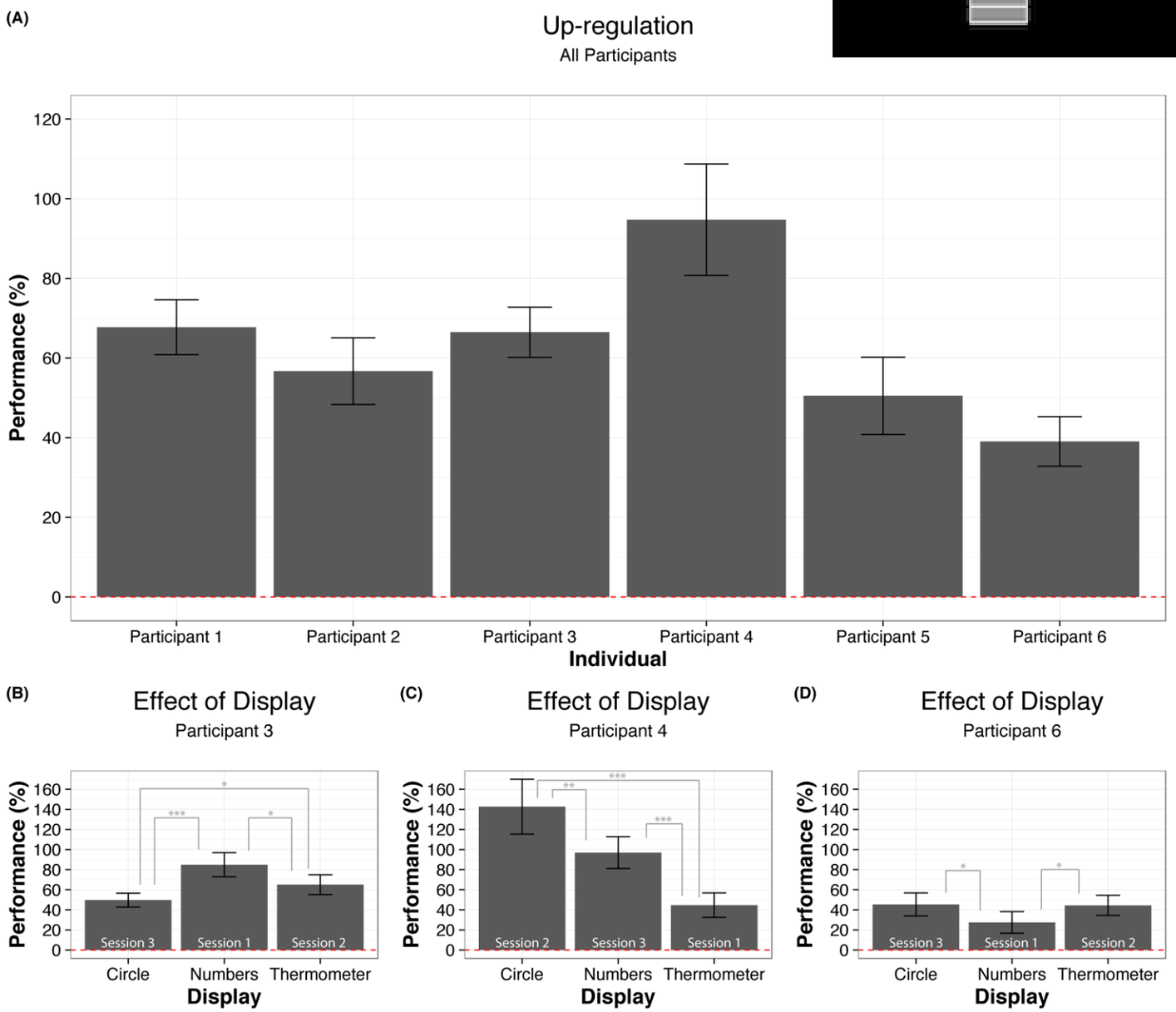




Does it matter?

- Probably not, however…





Krause et al., 2017

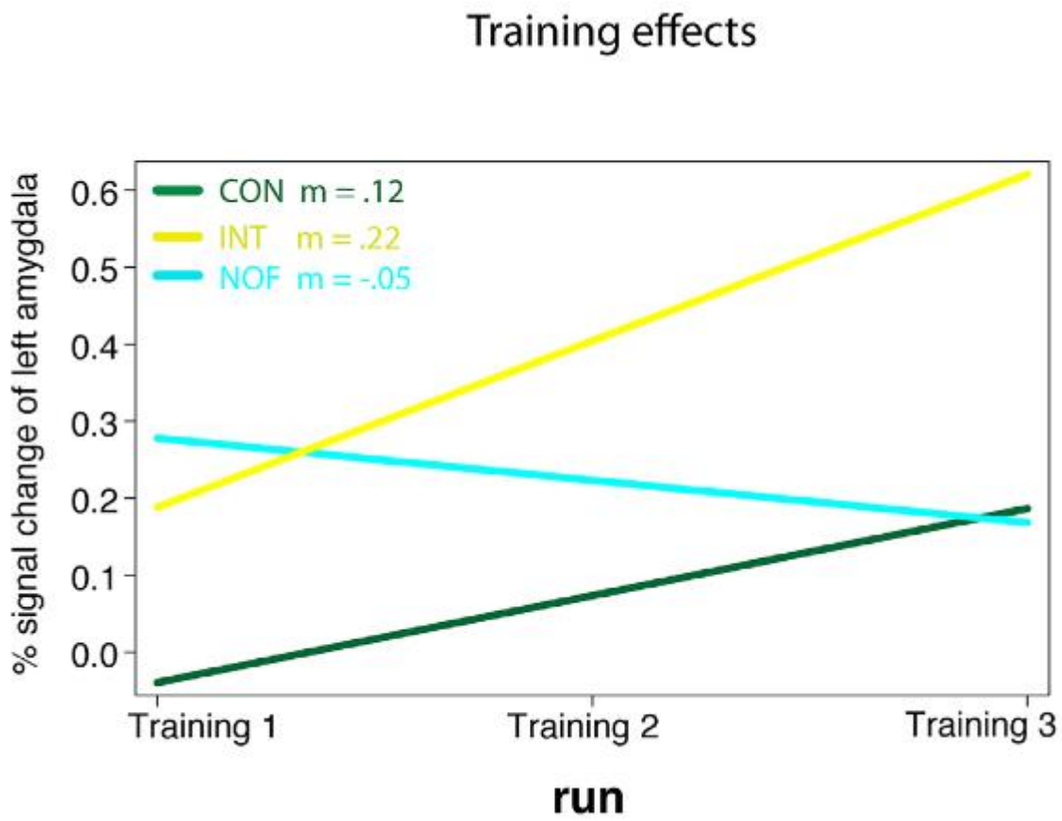
Continuous vs. intermittent feedback

- Continuous:
  - Give feedback as soon as it is available
  - During regulation attempts
  - More common in EEG NF (fMRI is always a bit behind)
  - "Dual task" problem: Feedback processing vs. regulation

- Intermittent:
  - Give feedback only after regulation attempts
  - Decouples feedback processing from regulation

Intermittent feedback has been shown to be superior

- (at least for studies with explicit regulation strategies)



Heilrung et al., 2018

3.
Participant involvement

Explicit vs. implicit neurofeedback

- Explicit:
  - Participant is aware of the purpose of the training
  - Knows the involved regions and their functions
  - Knows what the feedback signal is

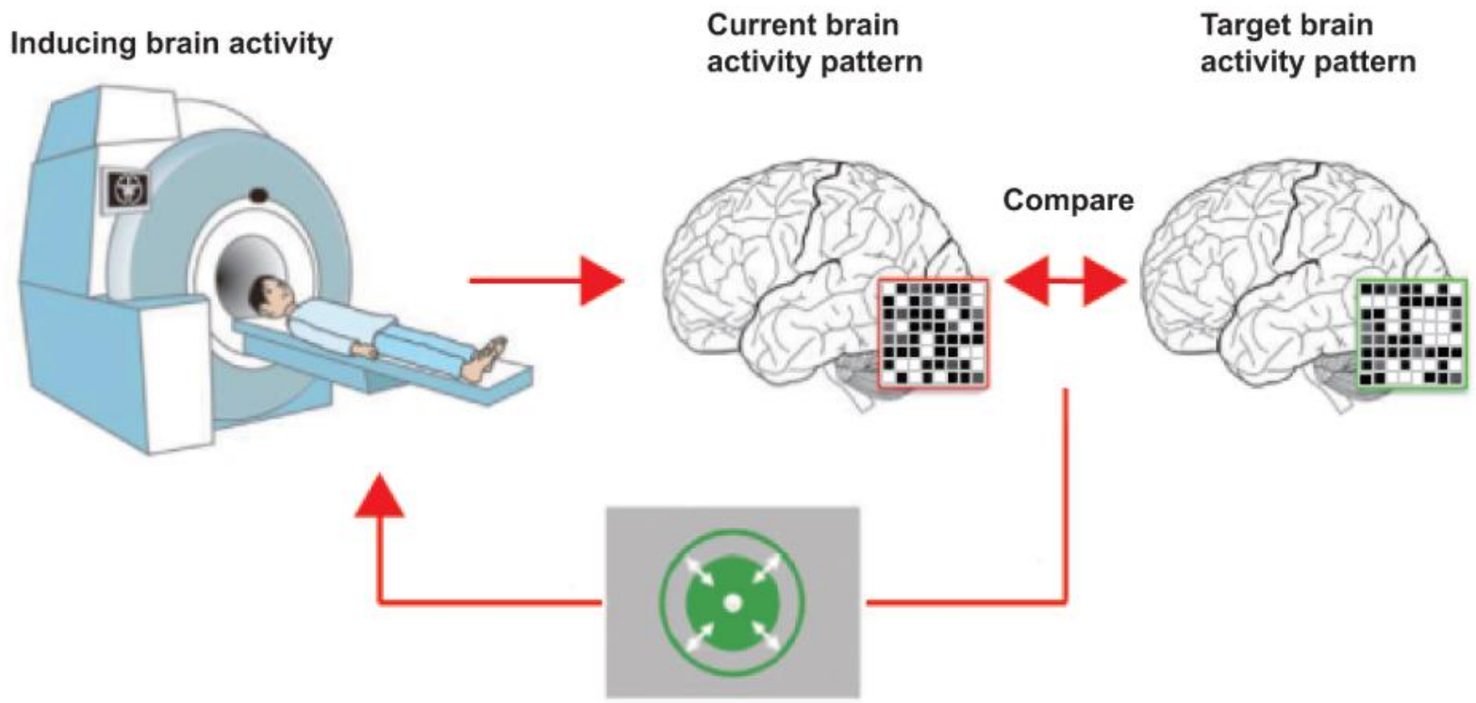
- Implicit:
  - Participant is not informed about the purpose of the training
  - Does not know details about involved regions or the feedback signal

Conscious vs. unconscious neurofeedback

- Conscious:
  - Participant is aware of the fact that there is feedback
  - Asked to actively incorporate and learn from the feedback

- Unconscious:
  - Participant is not informed about the fact that there is feedback
  - Does not know that they are in control

Decoded neurofeedback (DecNef)



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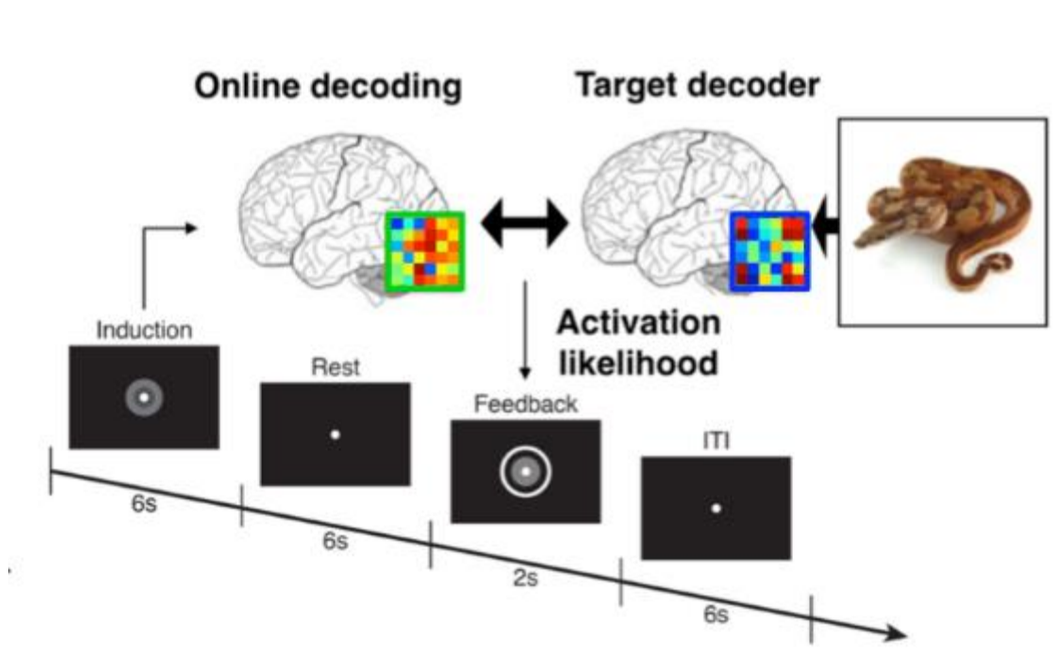
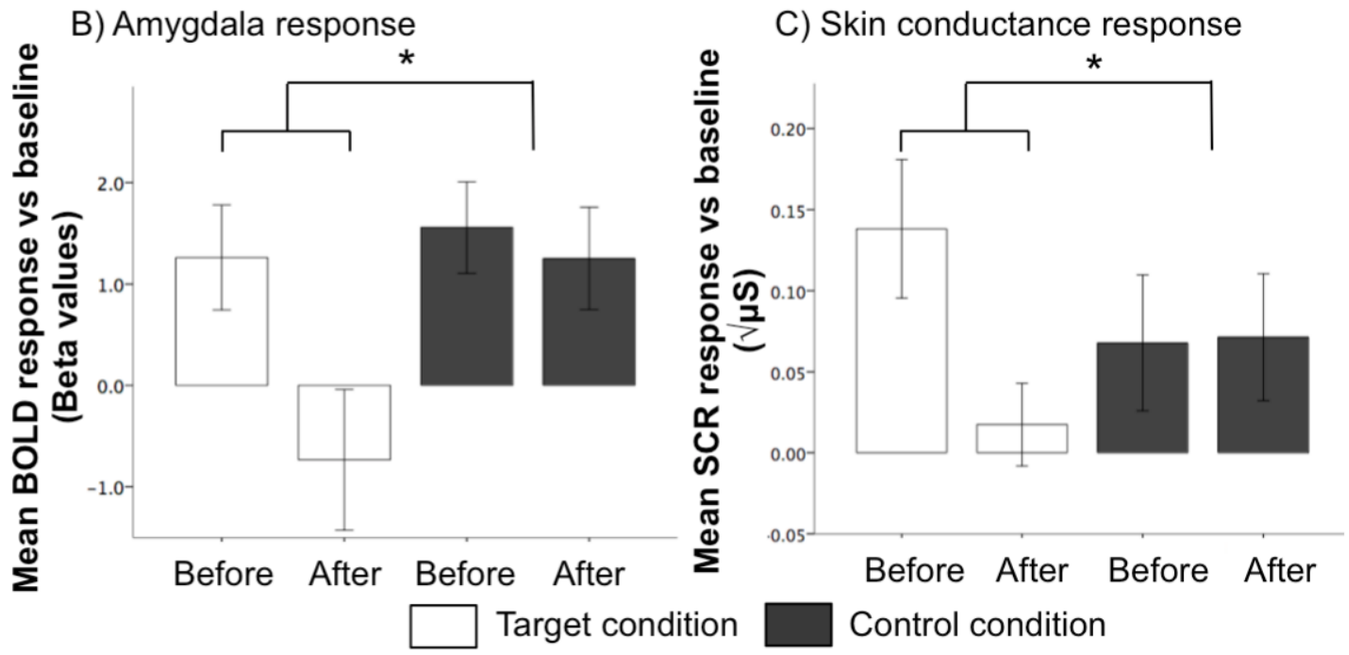




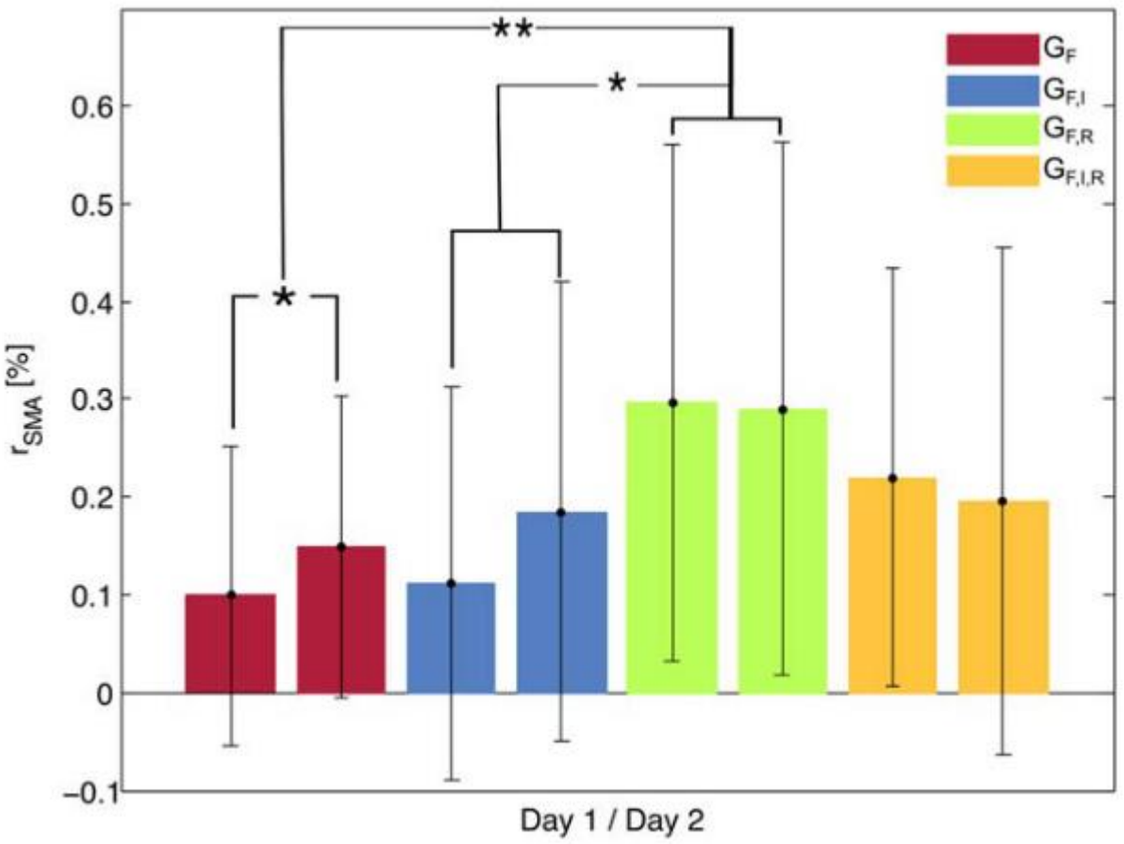
Explicit regulation strategies?

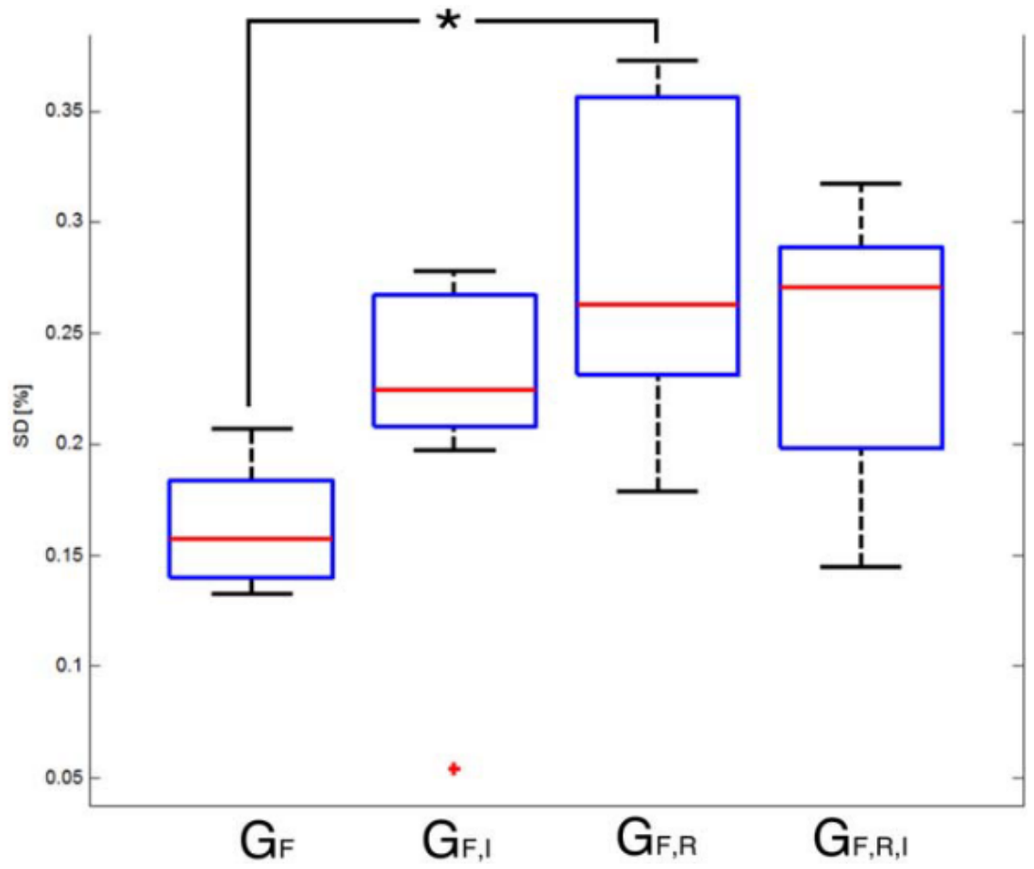
- Pro:
  - Clearer instruction for the participant
  - More comparable across participants

- Con:
  - Doesn't consider inter-individual differences in working strategies
  - Changes the task from "learning a new skill" to "refining an already present skill"

Doesn’t seem to affect regulation performance

- (at least not for SMA)





Sepulveda et al., 2016

4.

Session setup

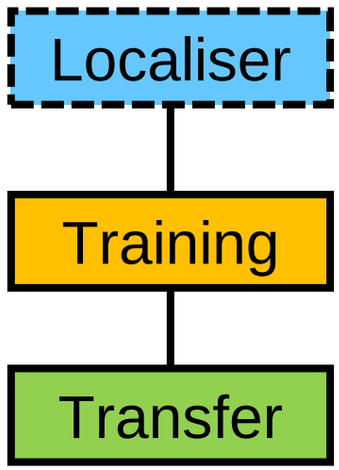
Basic building blocks

Localiser **Functional localiser run to define region(s) of interest (optional)**

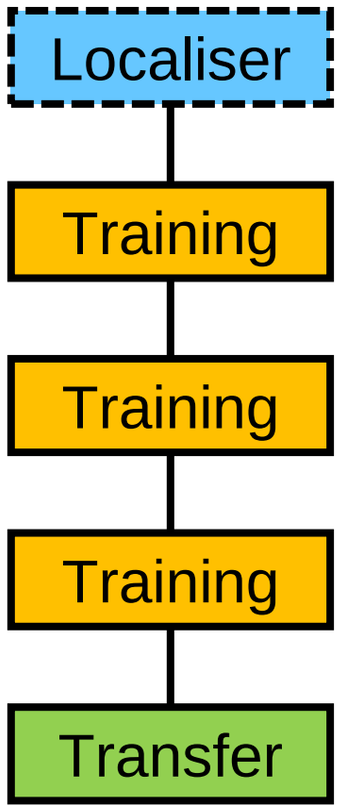
Training **Neurofeedback training run(s) to learn the brain regulation**

Transfer **Transfer run to test brain regulation (without feedback)**

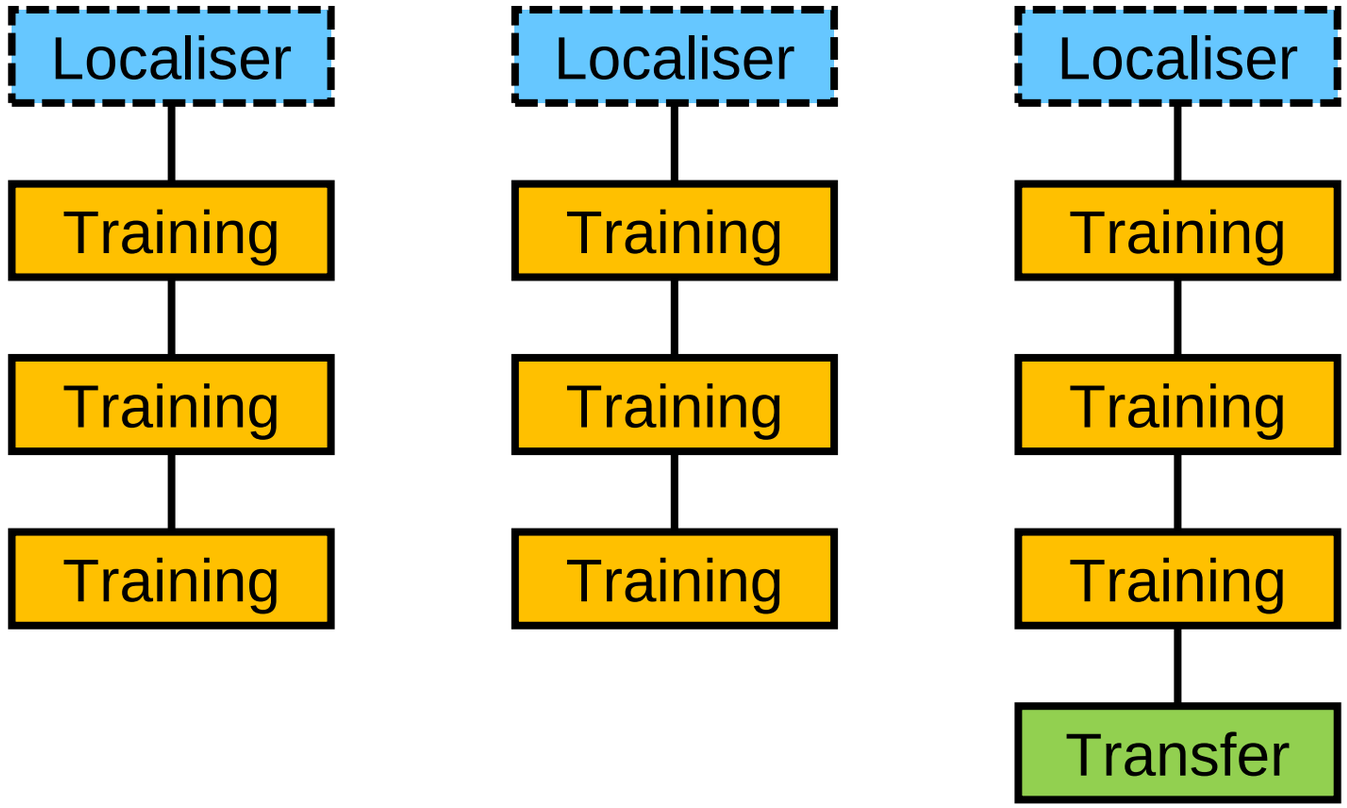
Simplest design (probably not very effective)



Design with multiple training runs



Design with multiple training sessions



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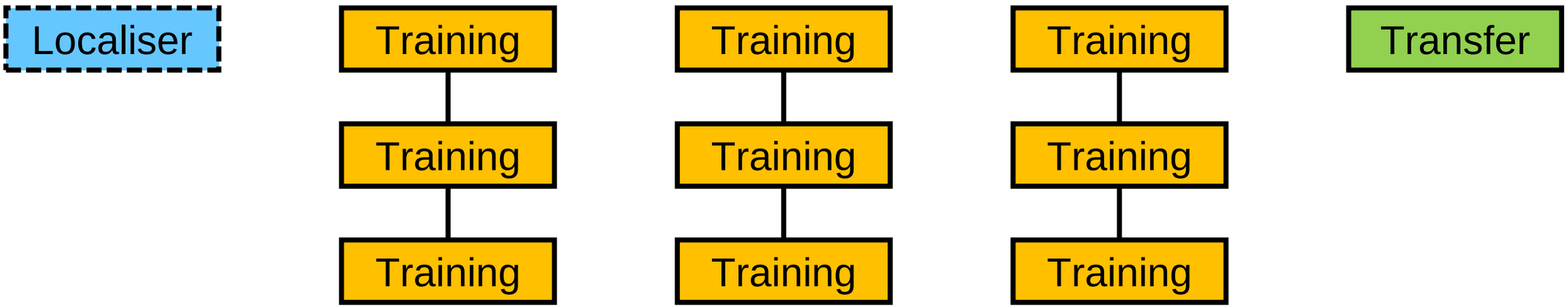


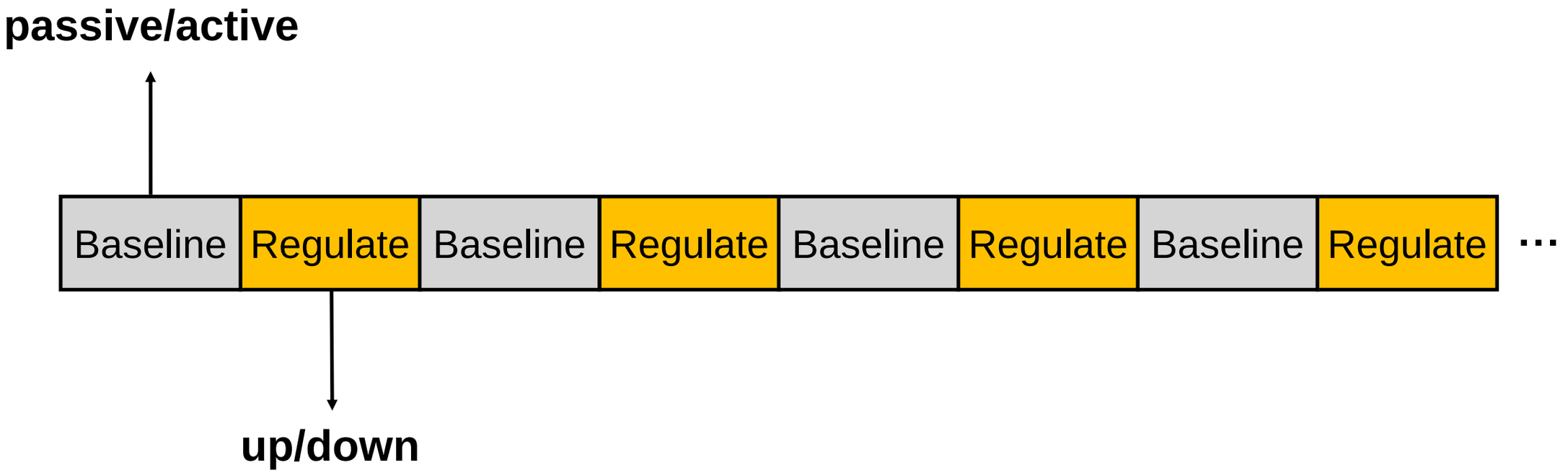
How long to train participants?

- **As long as you can!**

- Currently an open question
- Probably depends on many different things
- In literature: 1-5 training sessions

- Consider adaptive designs
  - Start with N session
  - After N sessions, analyse data
  - If not learned yet, offer N+1 session

“Classic” neurofeedback training run



Passive vs. active baseline

- Passive baseline:
  - "Rest"
  - "Letting the mind wander"

- Active baseline:
  - Some other task that is unrelated to what you want people to regulate
  - "Counting (backwards)" is a common choice

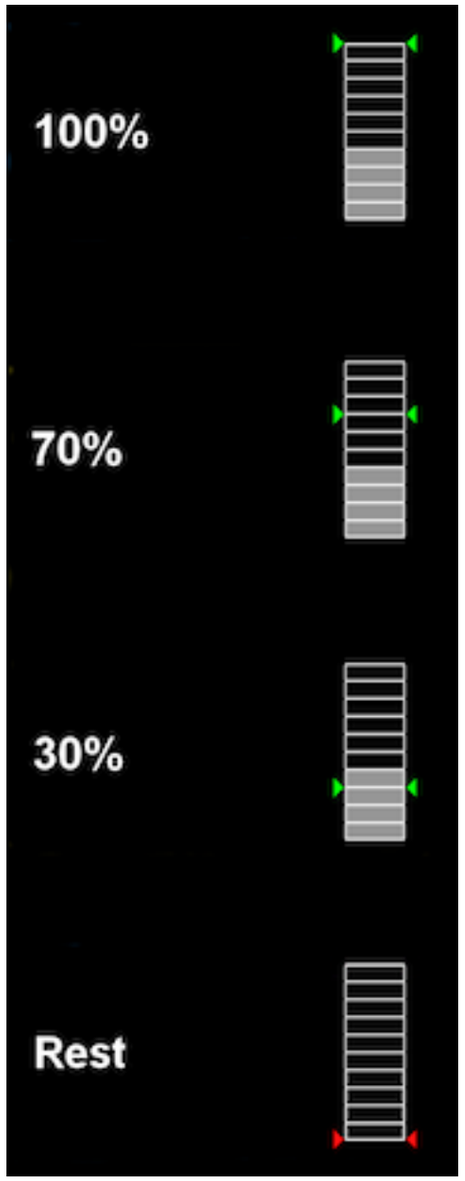
Up or down, binary or gradual regulation?

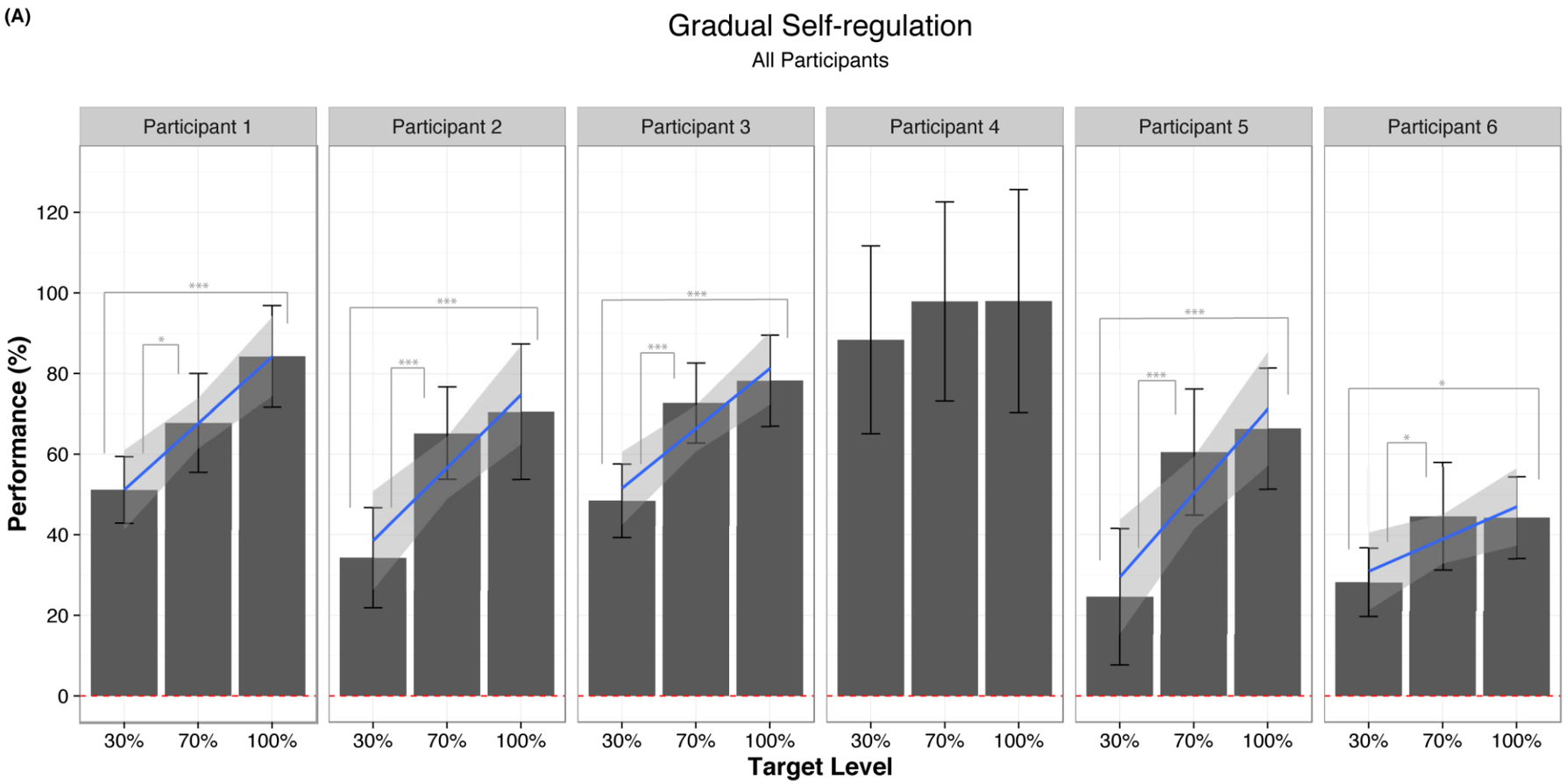
- Train to upregulate or downregulate targeted brain signal
- Or both! (i.e. train bidirectional control)

- <u>Binary (on/off) regulation:</u>
  - Ask participants to increase/decrease signal as much as they can

- <u>Gradual (fine-grained) regulation:</u>
  - Ask participants to regulate to specific indicated level

Gradual feedback





Krause et al., 2017

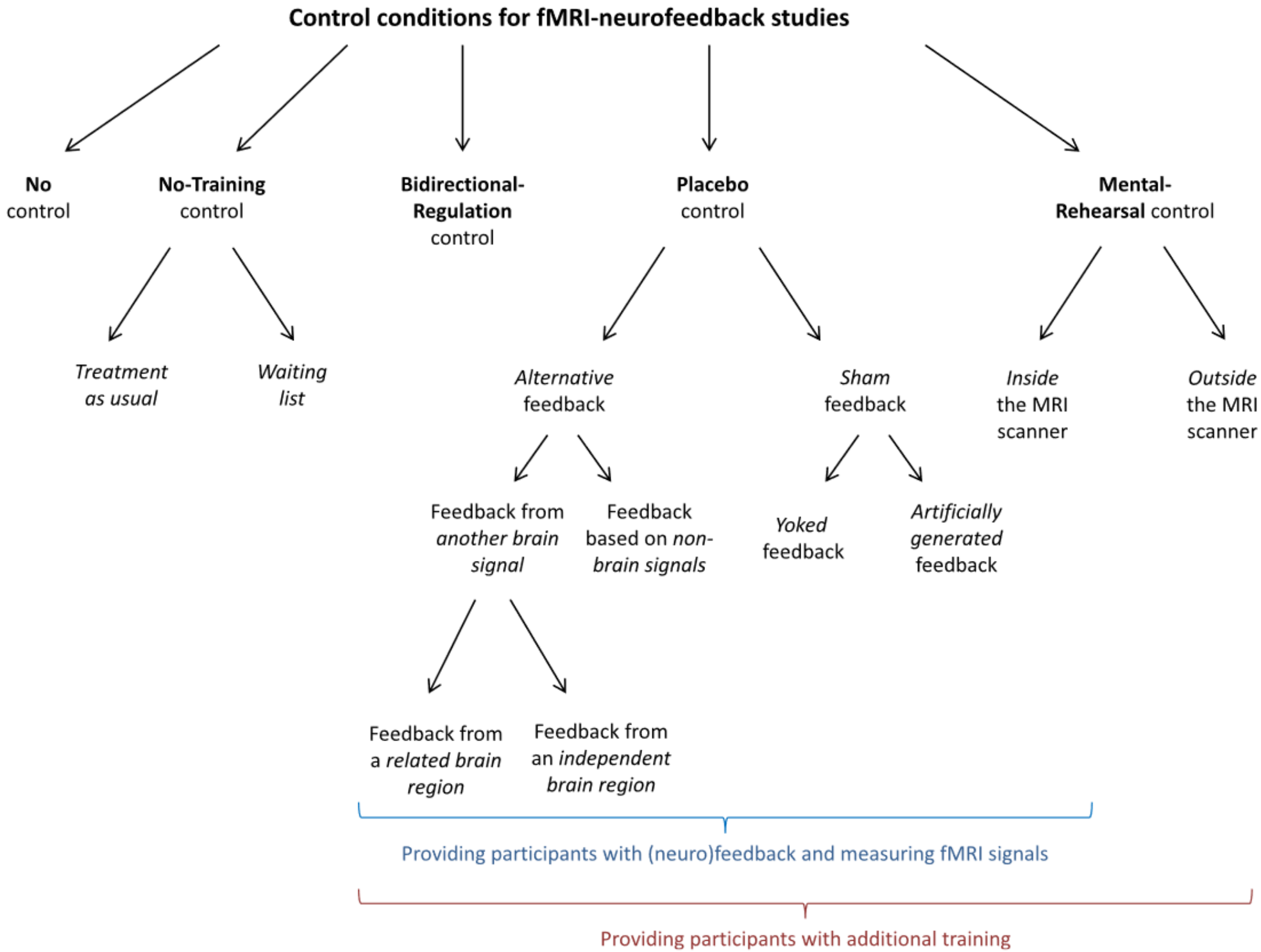
5.

Control condition(s)

What to control for?

- Participant motivation/perception of success
- Neurophysiological specificity
- Placebo/expectation effects/participant bias
- Non-specific effects
- Behavioural effects

So many options…



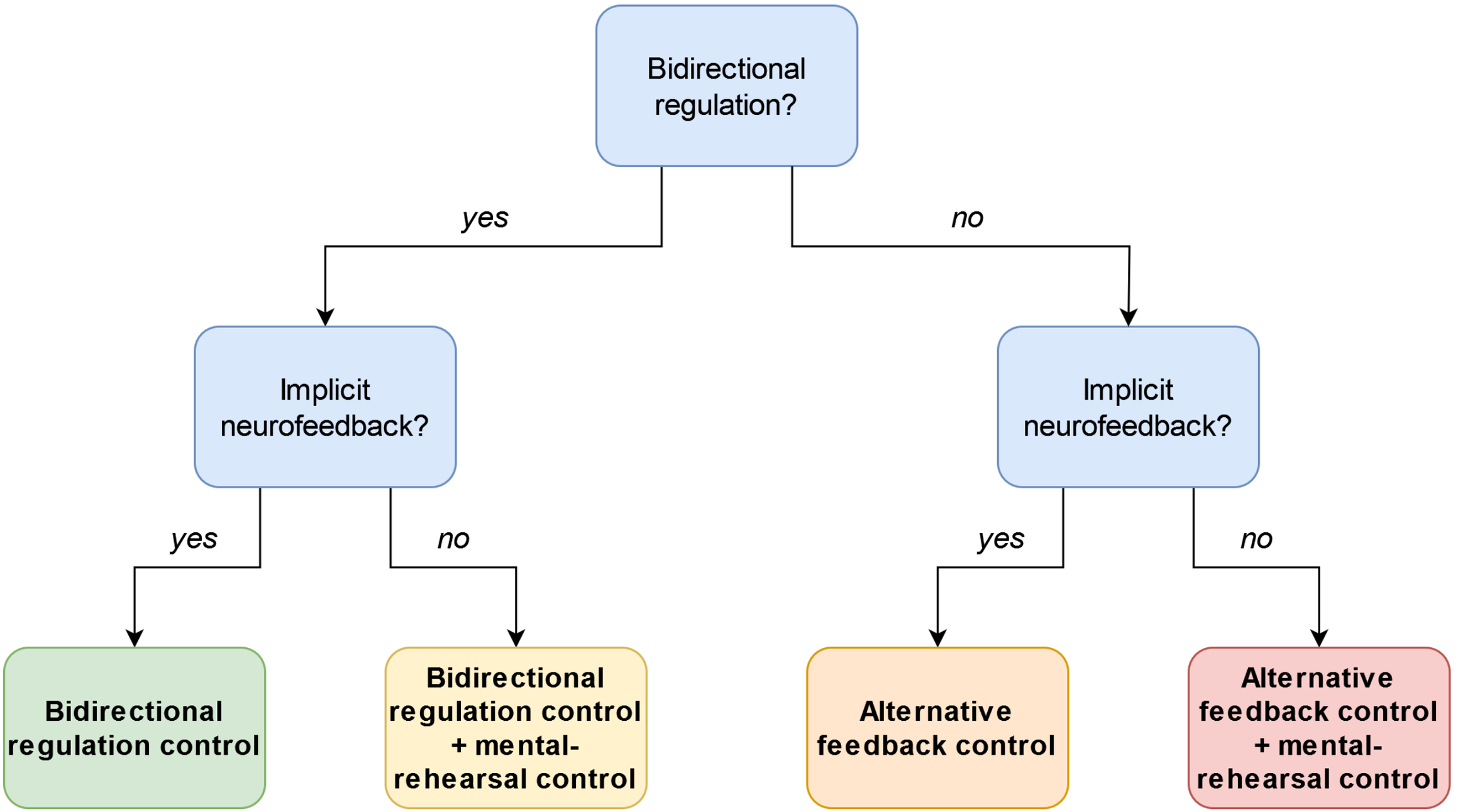
Sorger et al., 2019

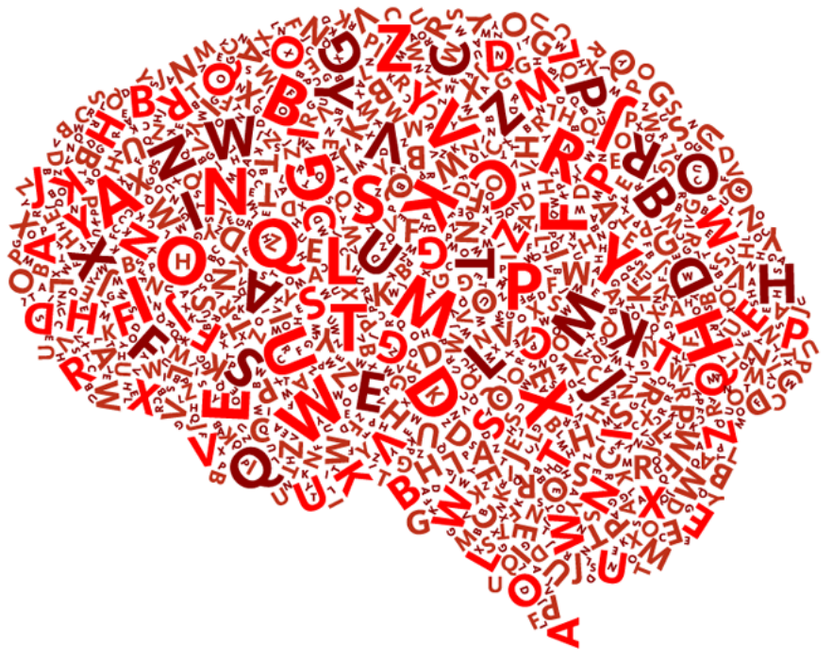
What to pick?

Factors to be controlled for to establish causality	No control	No-training Control		Bidirectional-Regulation Control	Placebo Control				Mental-Rehearsal Control	
		Treatment as usual+	List of matched participants/ Waitlist+		Alternative feedback		Sham feedback		Inside the MRI scanner	Outside the MRI scanner
					Feedback from an **Alternative Brain Signal**	**Feedback** based on **non-brain signals**	**'Yoked' feedback**	**Artificially generated feedback**		
Equal **Motivation/ Perception of Success**	✗	✗	✗	✓	✓ * @	✓ *@	✓ ^	✓ ^	✗	✗
Demonstrate neuro**physiological specificity**	✗	✗	✗	✓	✓	✗	✗	✗	✗	✗
Exclude **placebo effects**	✗	✗	✗	✓	✓ *@	✓ *@	✓ ^	✓ ^	✗	✗
Exclude **global (spatially non-specific) effects**	✗	✗	✗	✓	✓	✓	✓	✓	✓	✗
Exclude **Behavioral effects**	✗	✗	✗	✗	✗	✗	✗	✗	✓	✓
Remarks	Extremely economical	Economical Crucial (and fairest) control group in clinical context	Very economical	Up- and downregulation of the same region might not always be possible Not always ethically justifiable+	Regions' signal properties should be matched across groups Might be too conservative (critical region might be trained via functional connectivity) Risk of unblinding participants	Risk of unblinding participants	Risk of unblinding participants	Should be generated considering properties of the hemodynamic response Risk of unblinding participants	Not always possible (implicit neurofeedback) Control participants should not be aware of the existence of the neurofeedback group	Not always possible (implicit neurofeedback) Can considerably minimize scanning costs Control participants should not be aware of the existence of the neurofeedback group

Sorger et al., 2019

My (personal) advice





Questions?