

Real-time fMRI: challenges and uses

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A Critical Examination of Real-Time fMRI Neurofeedback



March 28-29 2019 | NIH Campus, Bethesda, MD, Natcher Building 45

What is neurofeedback?

How can we provide feedback with fMRI?

Neurofeedback

- Translating signals from the brain to a signal subjects can perceive (visual, auditory)
- Various recording techniques:
 - EEG
 - Invasive methods
 - Real time fMRI

Real-time fMRI

- Usually, fMRI data is processed post acquisition



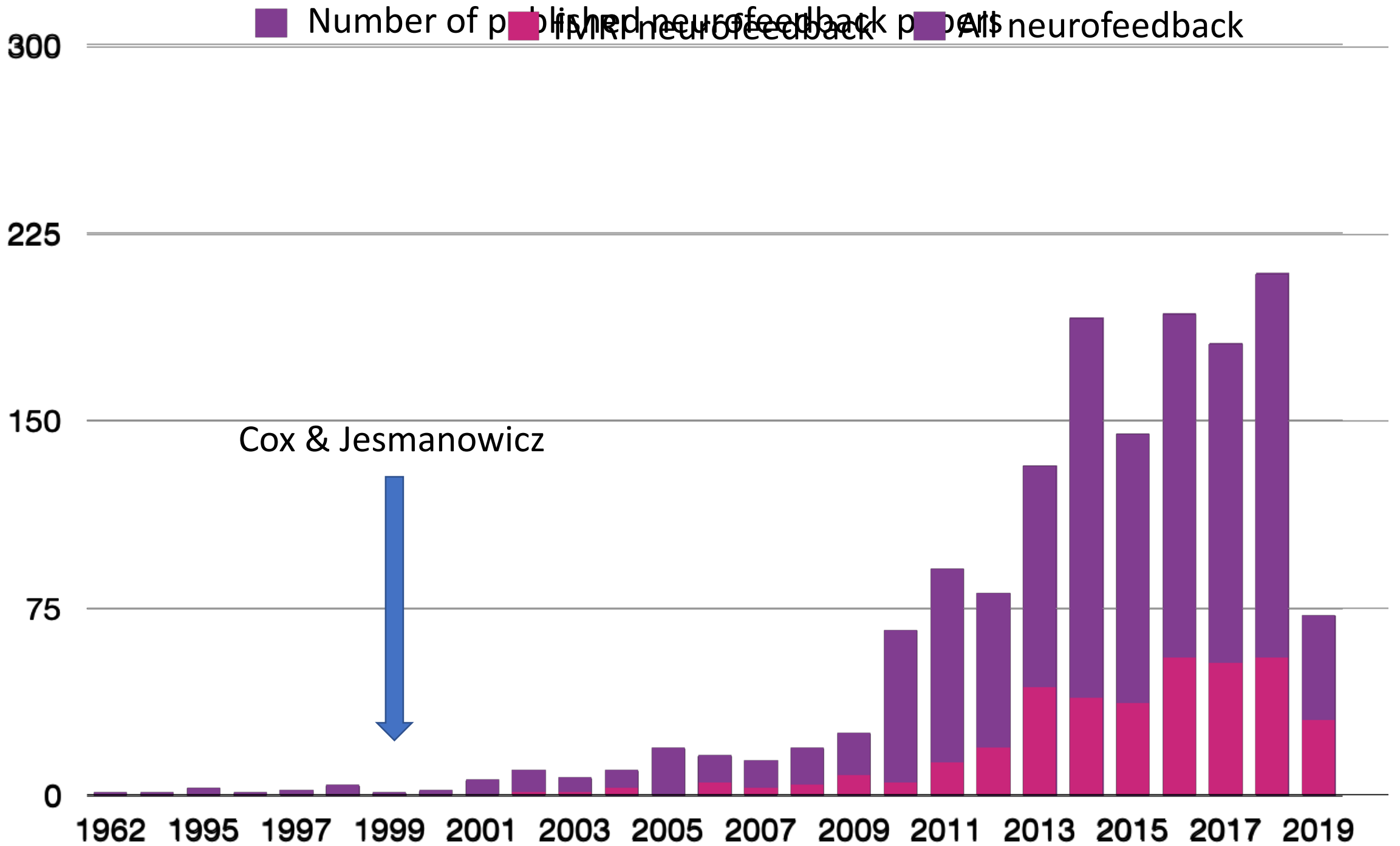
Article |  Full Access

Real-Time Functional Magnetic Resonance Imaging

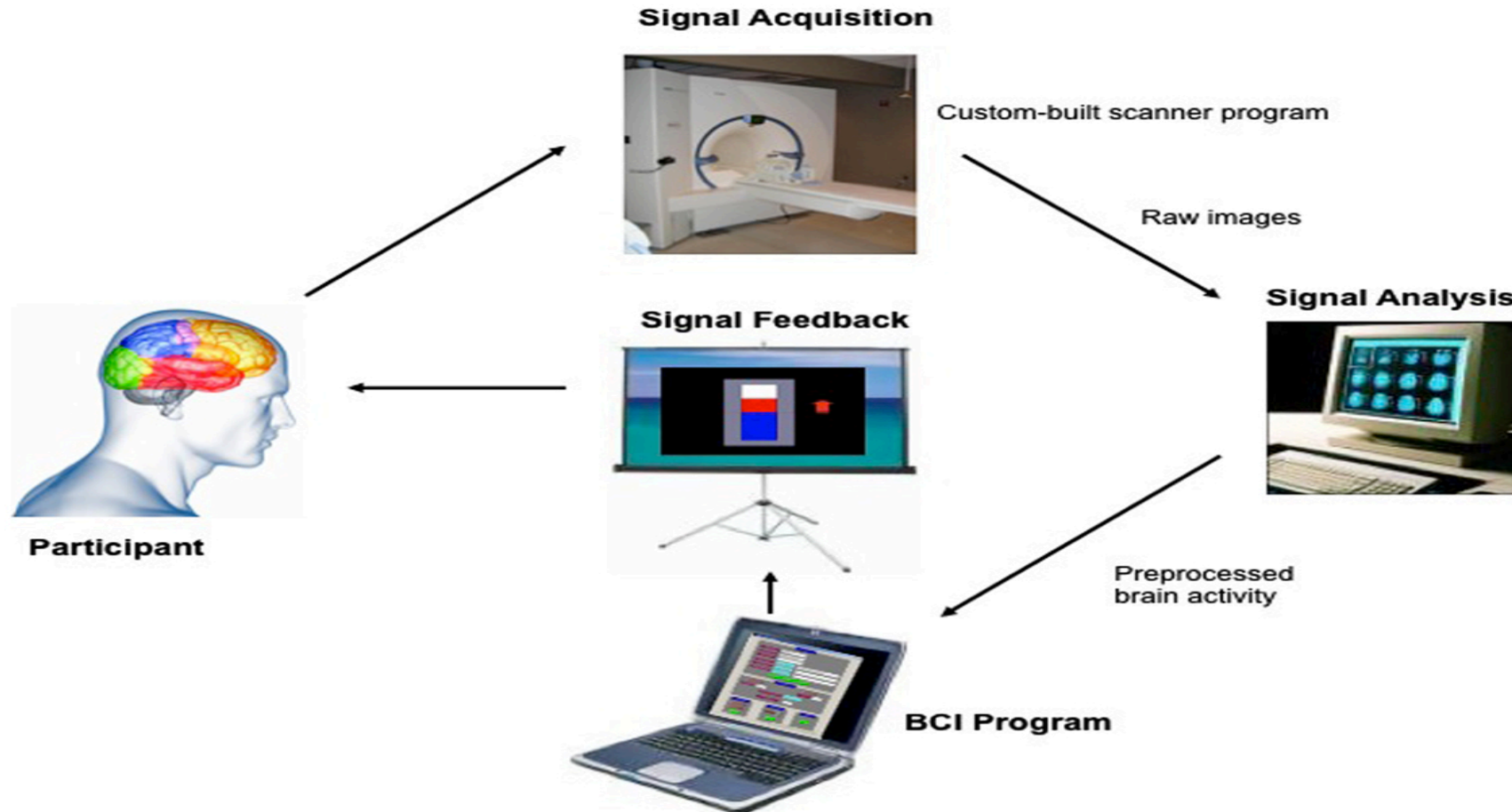
Robert W. Cox PhD, Andrzej Jesmanowicz, James S. Hyde

First published: February 1995 | <https://doi.org/10.1002/mrm.1910330213> | Cited by: 167

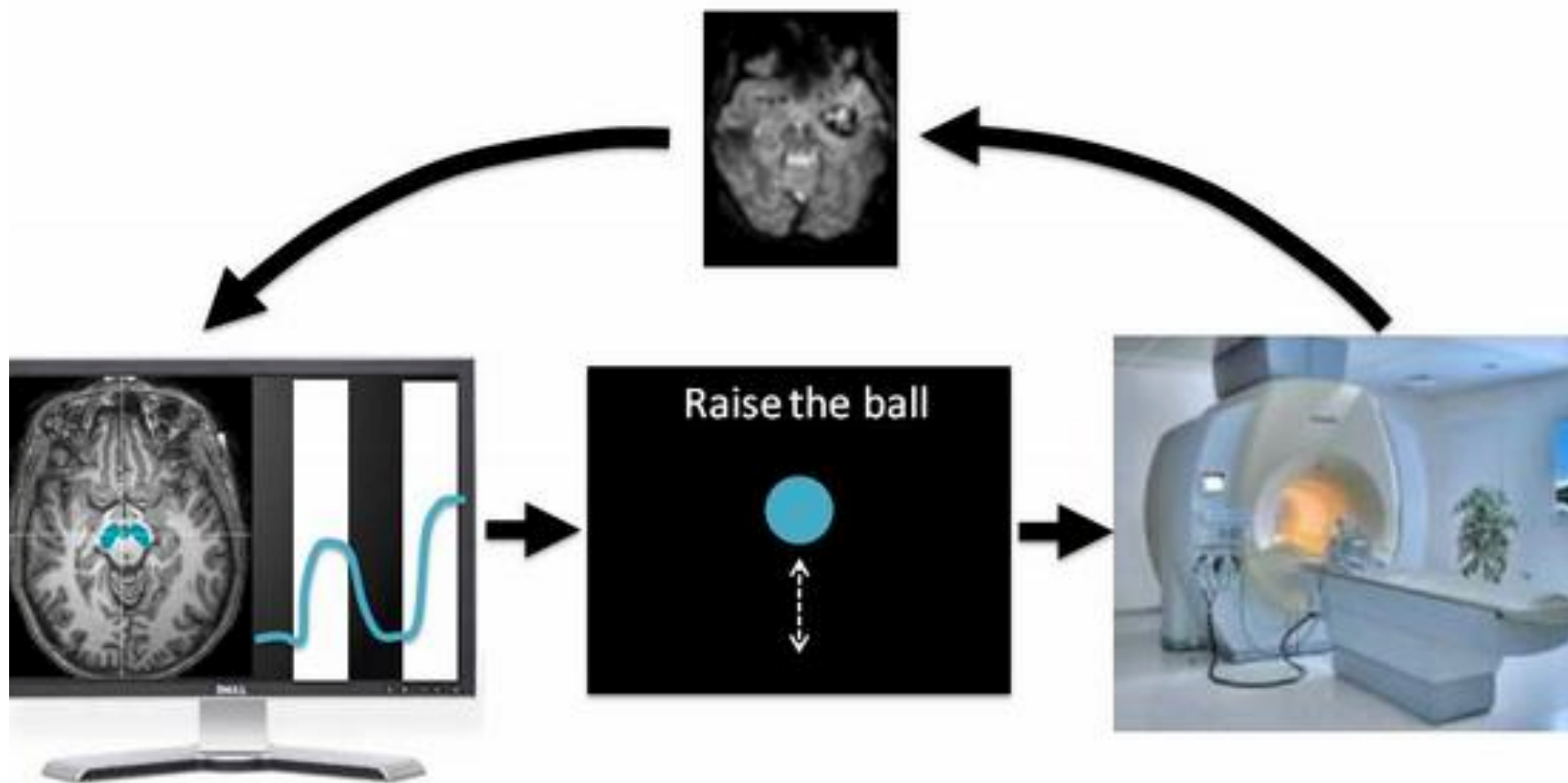
- Real-time fMRI allows us to look at fMRI data online, during the scan



Neurofeedback



Neurofeedback



AFNI Plugin: Set Real-Time Acquisition Options

Quit

Set+Keep

Set+Close

Help

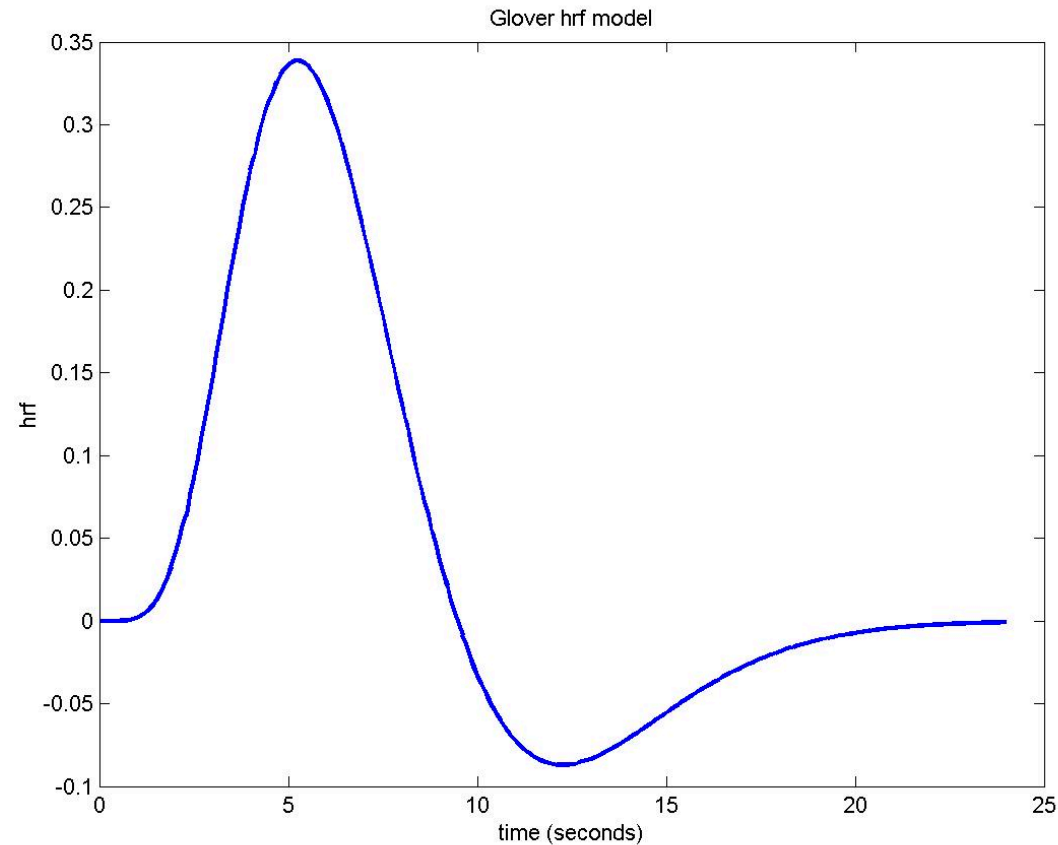
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Preprocessing

- Register everything to a common space (anatomical and functional data, pre-defined regions of interest)
- Motion correction
- Physiological noise regression
- Detrending
- Optimally combined echoes

Limitations of the signal

- Processing can be fast, but the fMRI signal is slow
 - Slow acquisition
 - BOLD is slow



Limitations of the signal

- fMRI data is noisy!
- Global signal artifacts / real global signal



Methods to detect, characterize, and remove motion artifact in resting state fMRI



Jonathan D. Power^{a,*}, Anish Mitra^a, Timothy O. Laumann^a, Abraham Z. Snyder^{a,b},
Bradley L. Schlaggar^{a,b,c,d}, Steven E. Petersen^{a,b,d,e,f,g}

What can we feedback?

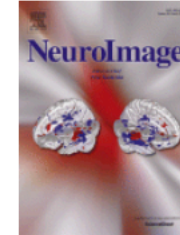
- Single re



Research Article

NeuroImage

Volume 88, March 2014, Pages 113-124






**Self-regul
The righ**

Self-regulation of the anterior insula: Reinforcement

**Self-Regulation of Amygdala Activation Using Real-Time fMRI
Neurofeedback**

Giuseppina R
Niels Birbaur

Vadim Zotev , Frank Krueger , Raquel Phillips, Ruben P. Alvarez, W. Kyle Simmons, Patrick Bellgowan, Wayne C. Drevets,
Jerzy Bodurka 

Published: September 8, 2011 • <https://doi.org/10.1371/journal.pone.0024522>



What can we feedback?

- Classifier output

Trends in Cognitive Sciences

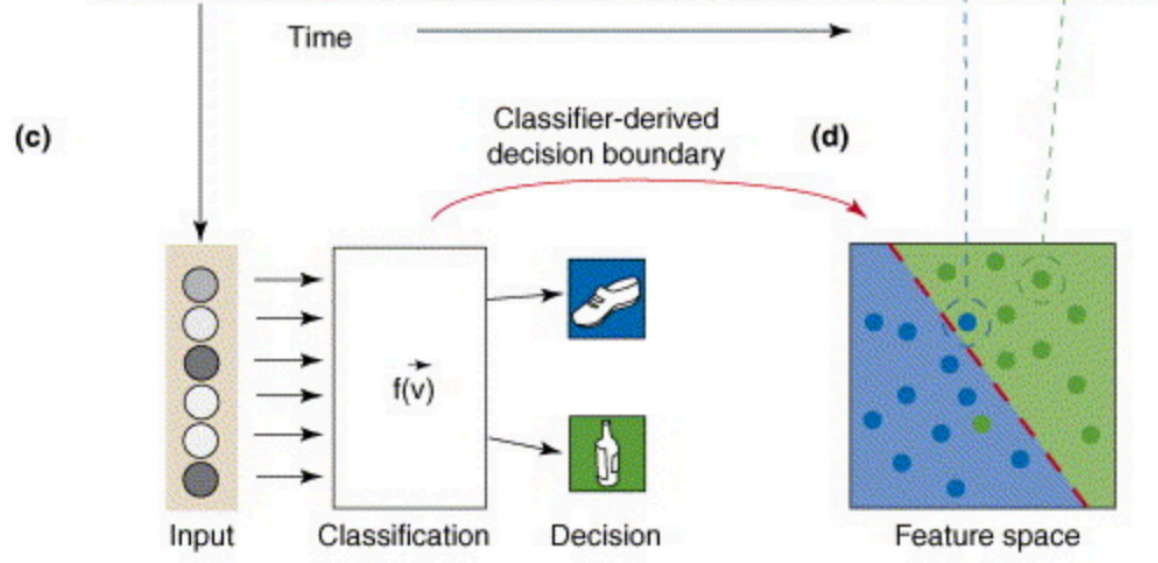
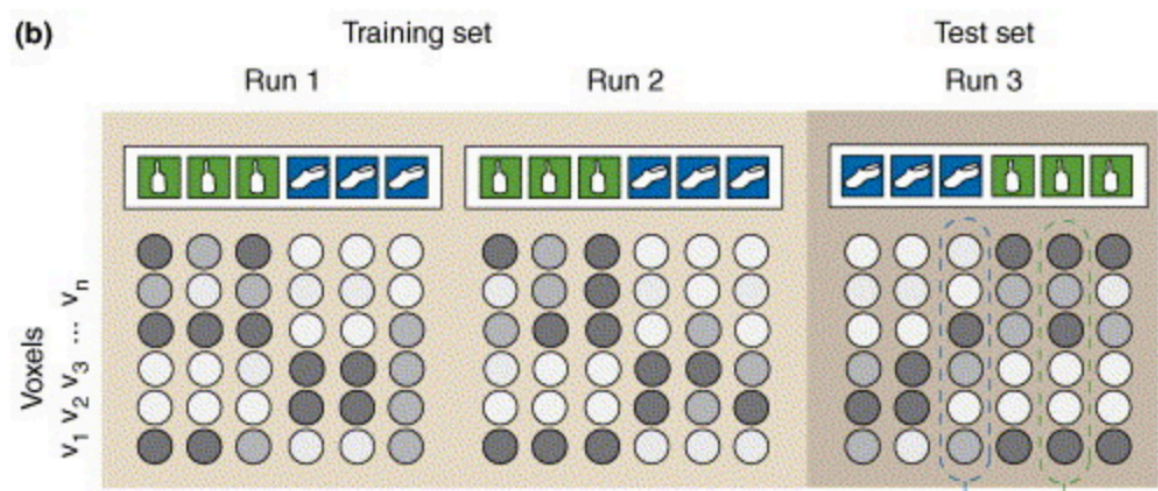
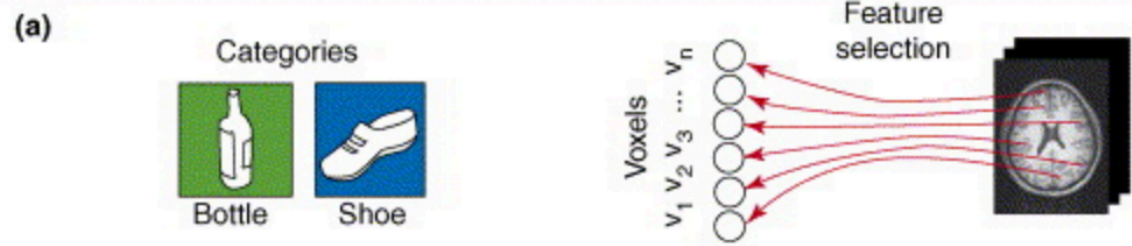
Volume 10, Issue 9, September 2006, Pages 424-430



Review

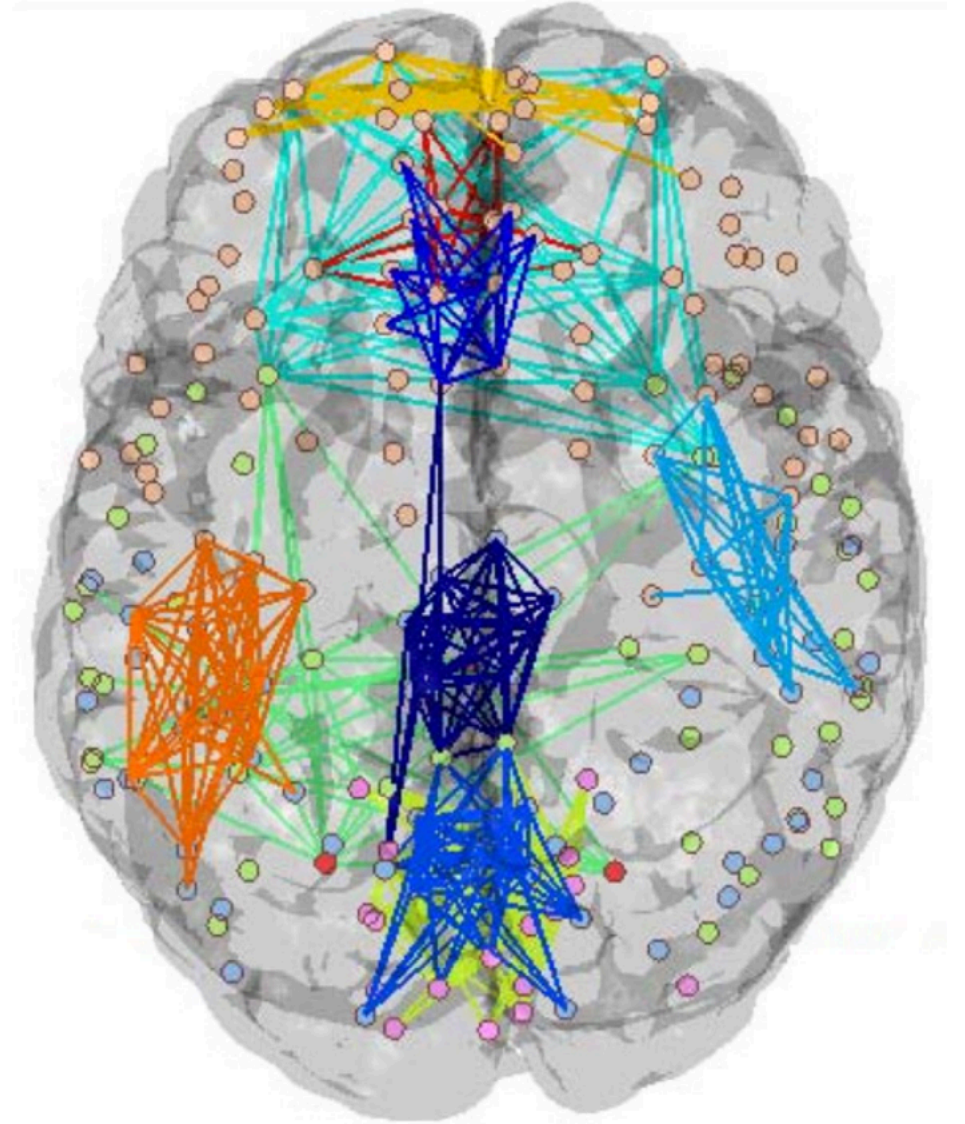
Beyond mind-reading: multi-voxel pattern analysis of fMRI data

Kenneth A. Norman ¹ ✉, Sean M. Polyn ², Greg J. Detre ¹, James V. Haxby ¹



What can we feedback?

- Correlations between regions
- Not trivial – calculating correlations takes time



Why should we do neurofeedback?


What can we do with neurofeedback that we can't do with traditional experiments?

Goals of neurofeedback

Regular Article

Addiction Biology

SSA SOCIETY FOR THE
STUDY OF
ADDICTION

HUMAN NEUROIMAGING STUDY |  Full Access |

Real-time functional magnetic resonance imaging neurofeedback can reduce striatal cue-reactivity to alcohol stimuli

Martina Kirsch, Isabella Gruber, Matthias Ruf, Falk Kiefer, Peter Kirsch 

Maastricht, The Netherlands

Goals of neurofeedback

- Clinical applications
- Enhance performance

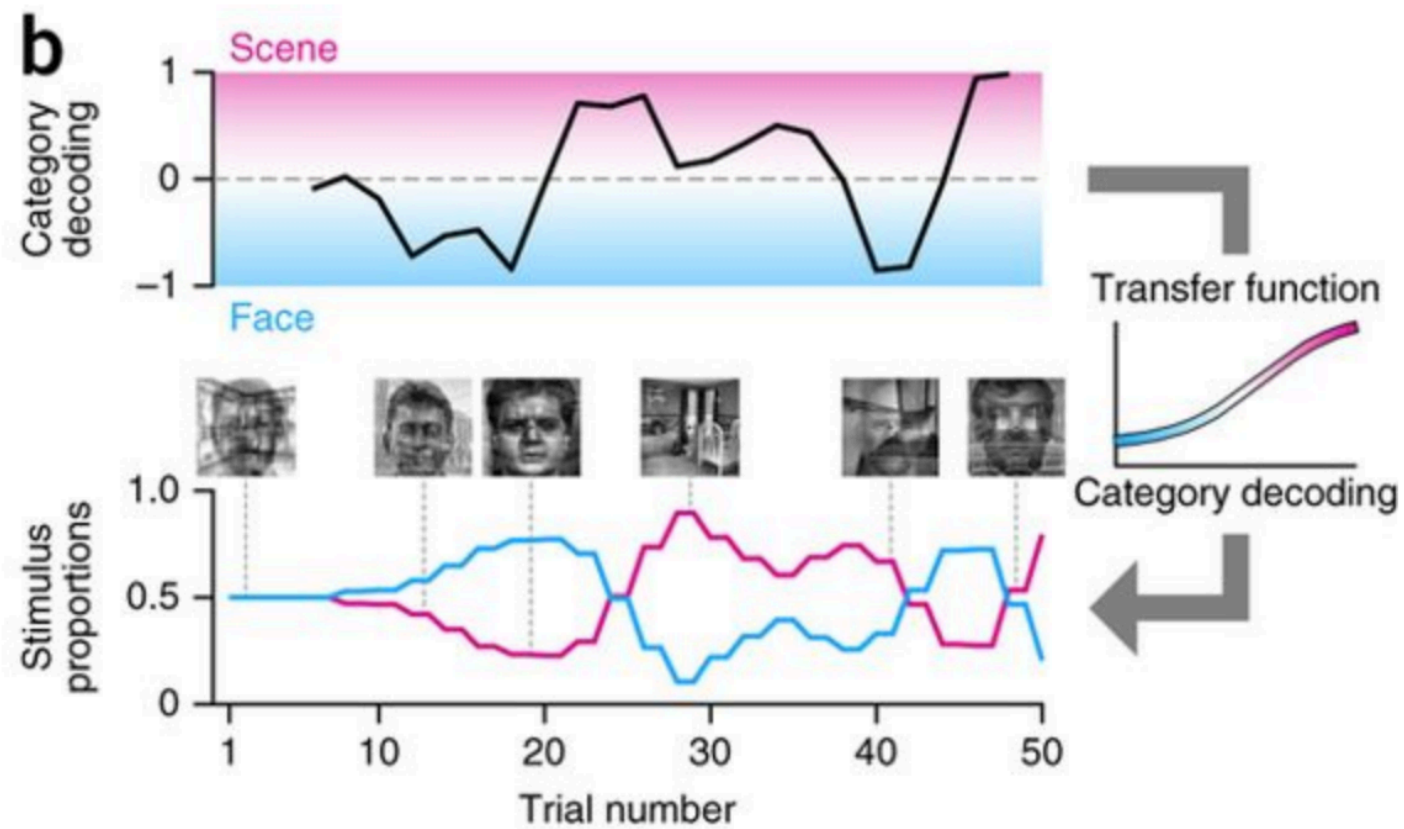
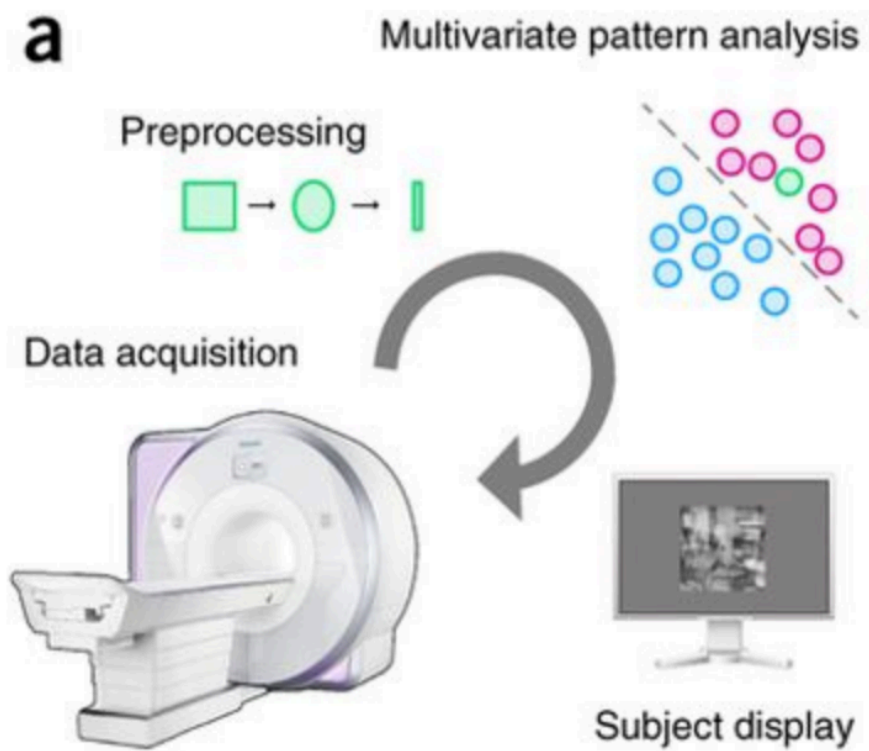
nature
neuroscience

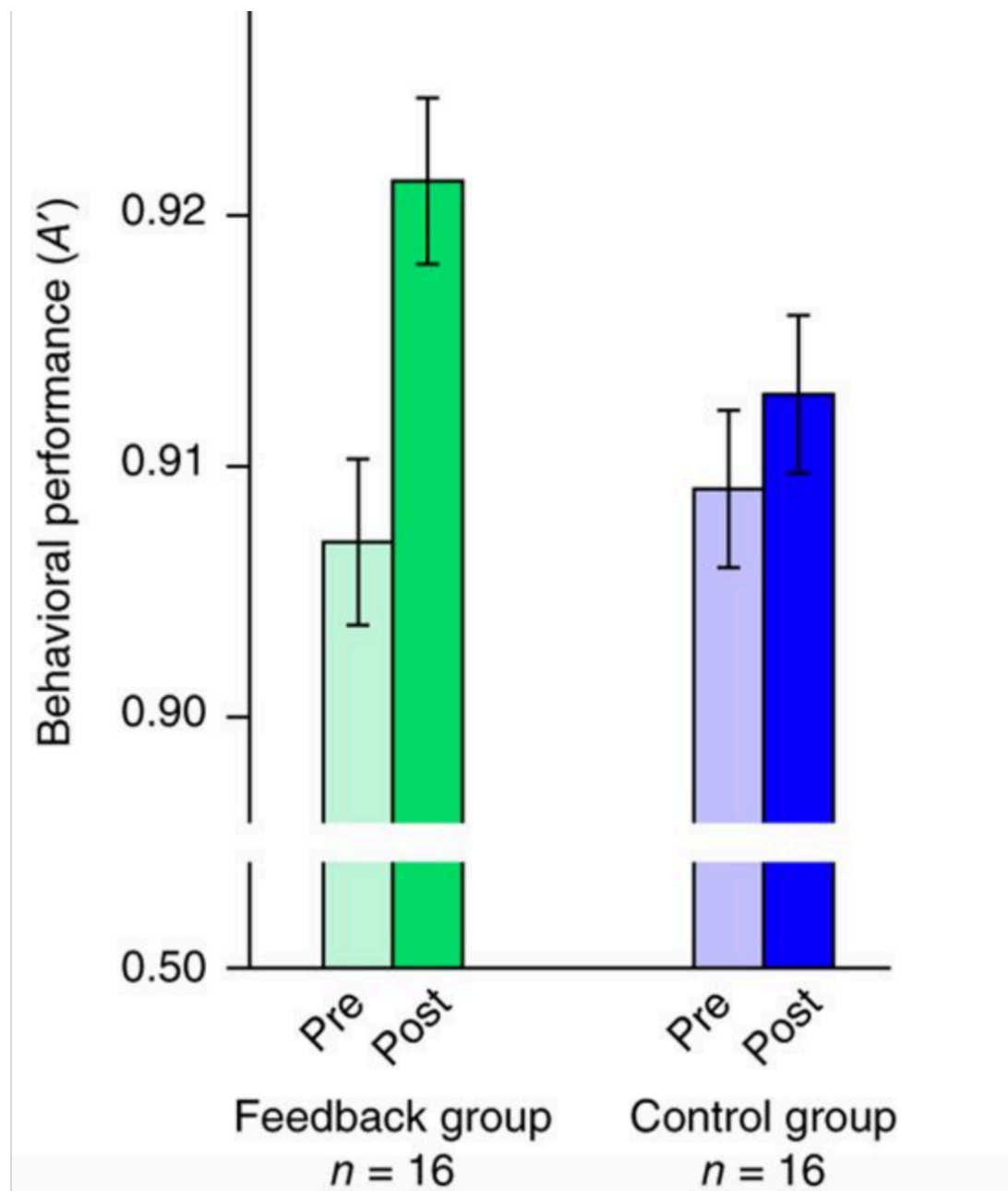
Article | Published: 09 February 2015

Closed-loop training of attention with real-time brain imaging

Megan T deBettencourt, Jonathan D Cohen, Ray F Lee, Kenneth A Norman & Nicholas B Turk-Browne 

Nature Neuroscience **18**, 470–475 (2015) | [Download Citation](#) 





Goals of neurofeedback

- Clinical applications
- Enhance performance
- Investigate causality, understand the relationships between networks and behavior

Explicit/task based vs. implicit/covert neurofeedback

Should we tell participants how to control the feedback?

Caveats of task-based Neurofeedback

- Doesn't bypass behavior, cannot address the question of causality
- Difficult to disentangle the effects of the task from the effects of the neurofeedback
- Limited in scope, inflexible
- Potentially underestimates the extent of plasticity
- Does not necessarily require a piece of equipment as expensive as an MRI machine

Limits of explicit training in aberrant networks

- Mere repetition is akin to strengthening the wrong “muscles”



Implicit training – covert neurofeedback

- What if we don't give subjects a strategy?
- **Extremely flexible**
- Cannot be done with other methods

Background – Visual Perceptual Learning

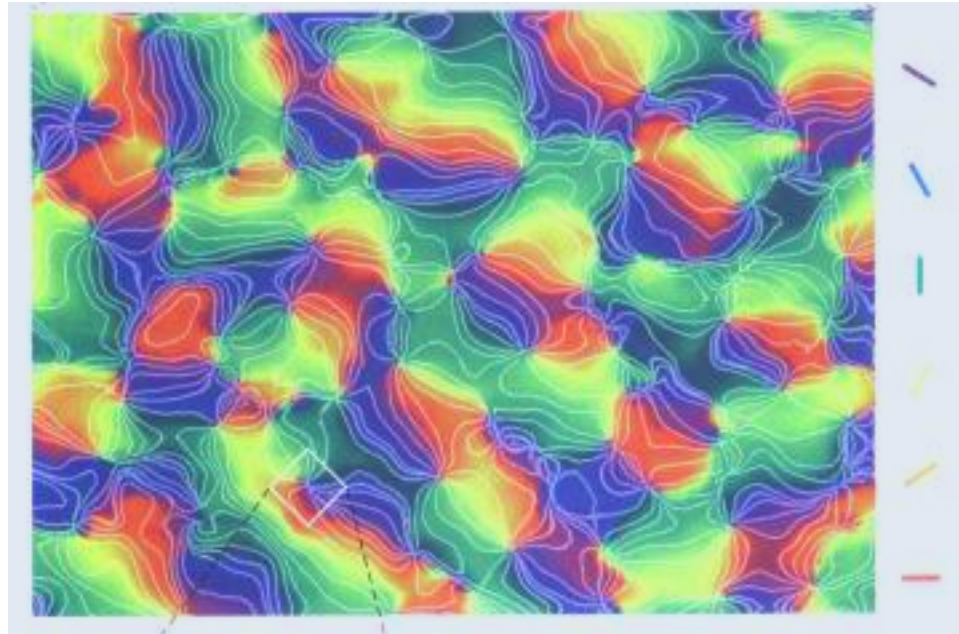
- Practice or training in a particular task often substantially improves perceptual performance. This is known as perceptual learning. Examples:
 - Distinguishing between two musical notes
 - Finding the ripe berries on the bush
 - Reading
 - Finding a tumor on an imaging scan
- Perceptual learning is often restricted to a particular task or stimulus
- Visual perceptual learning (VPL) often correlates with changes in visual areas, but this does not prove causation, and studies have been divided on whether these changes are in early or high order visual cortex

Example

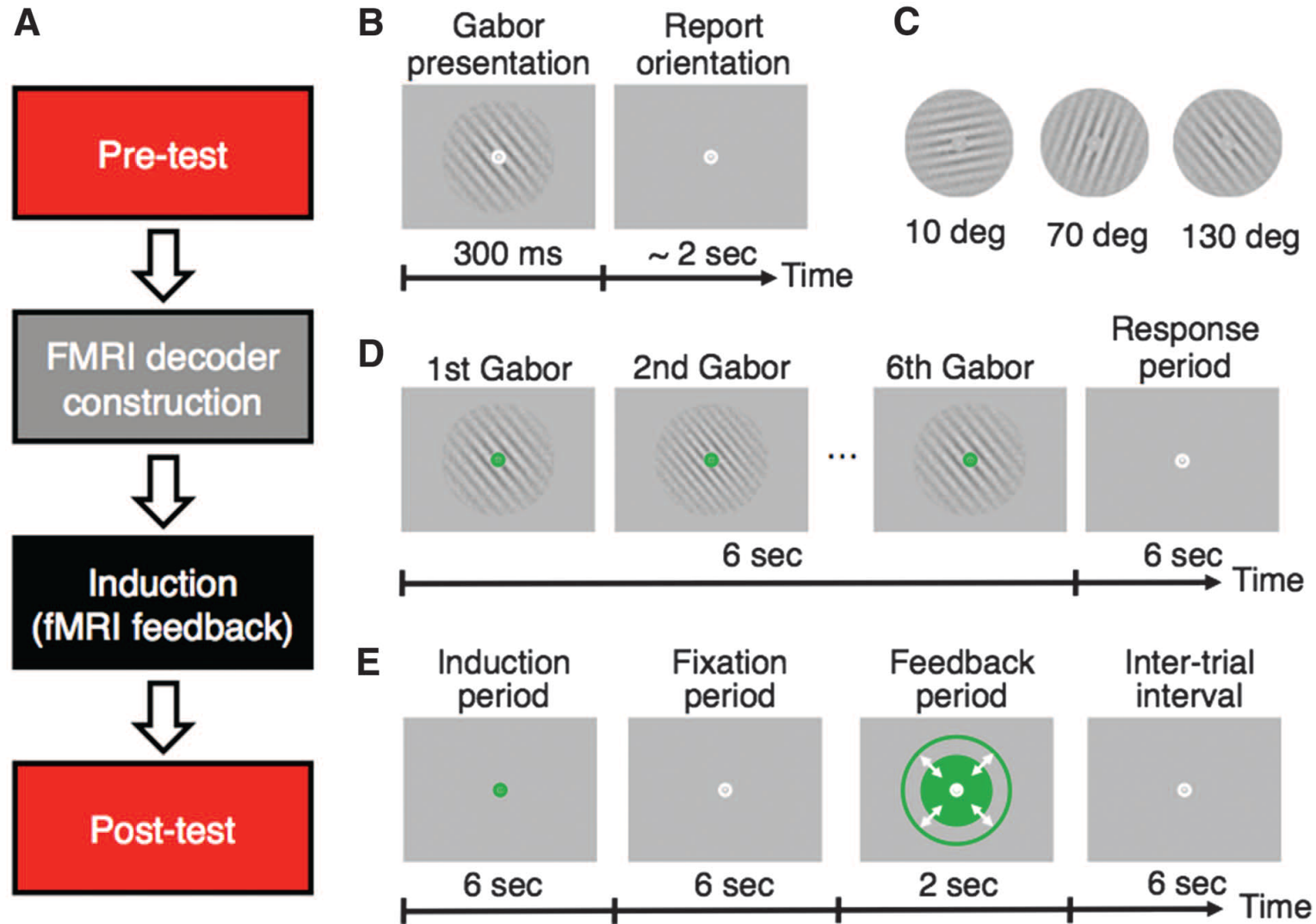


Question

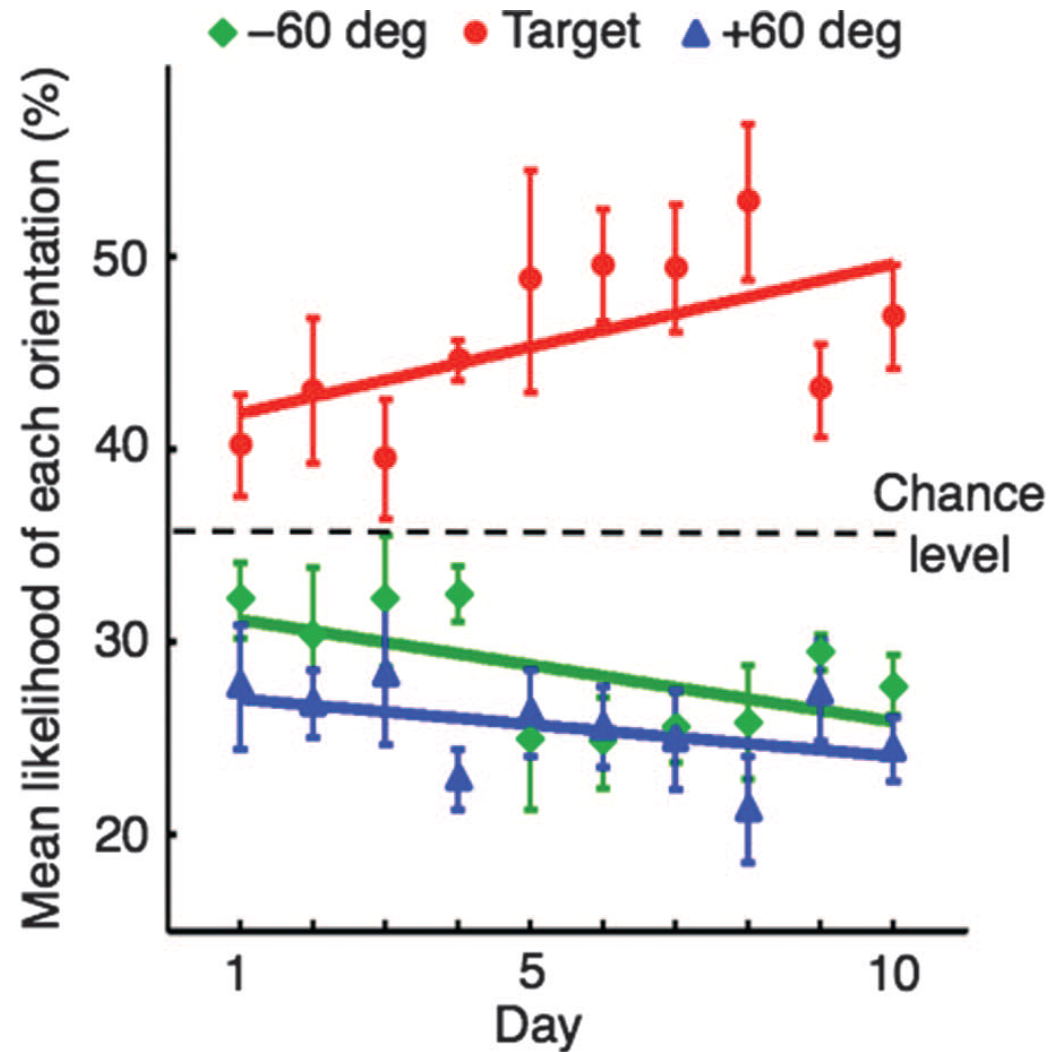
- Is early visual cortex plastic enough to cause VPL?
- Induce change in a very specific manner in early visual cortex, without exposing to the visual stimulus this pattern represents



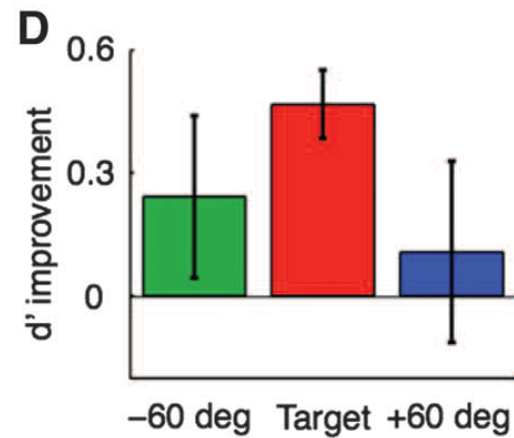
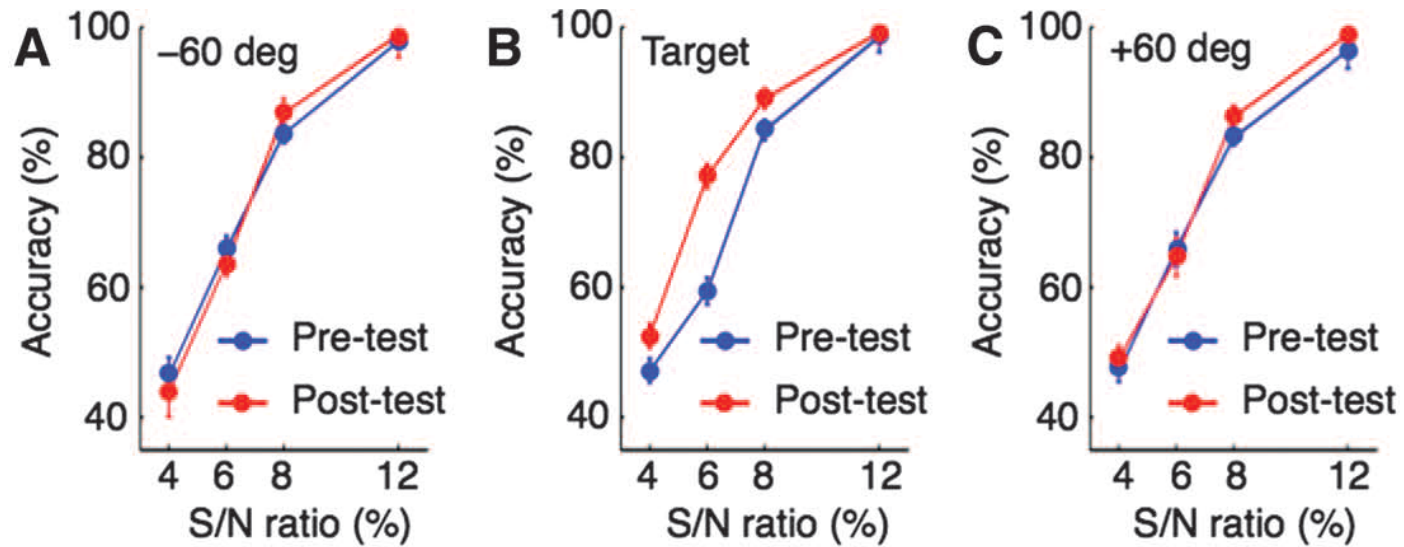
Experimental design



Results – changes in fMRI signal



Perceptual learning



Disentangling task effects from neurofeedback effects

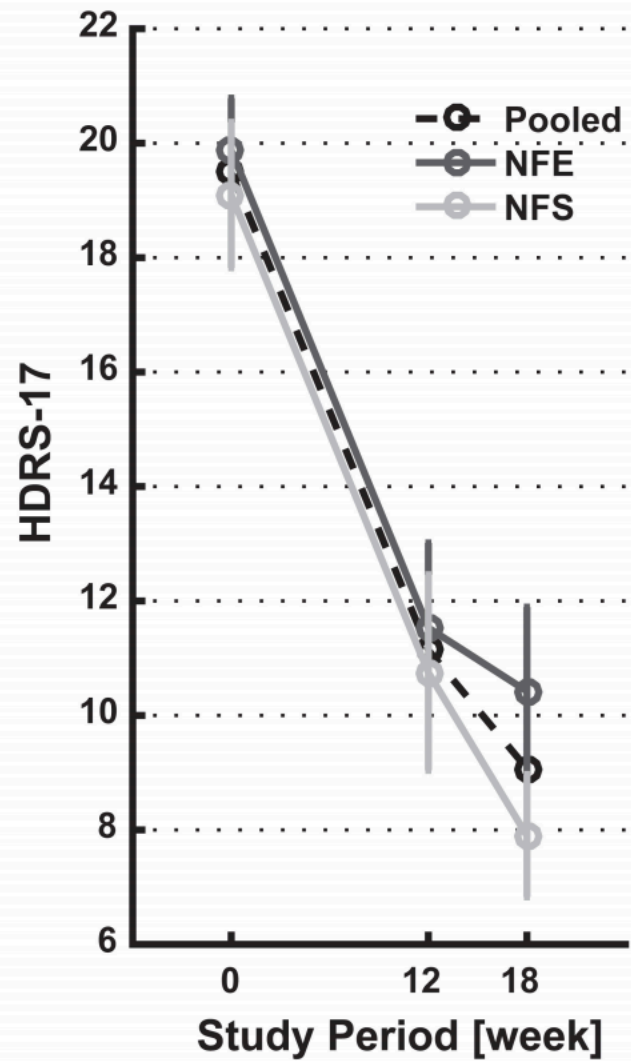
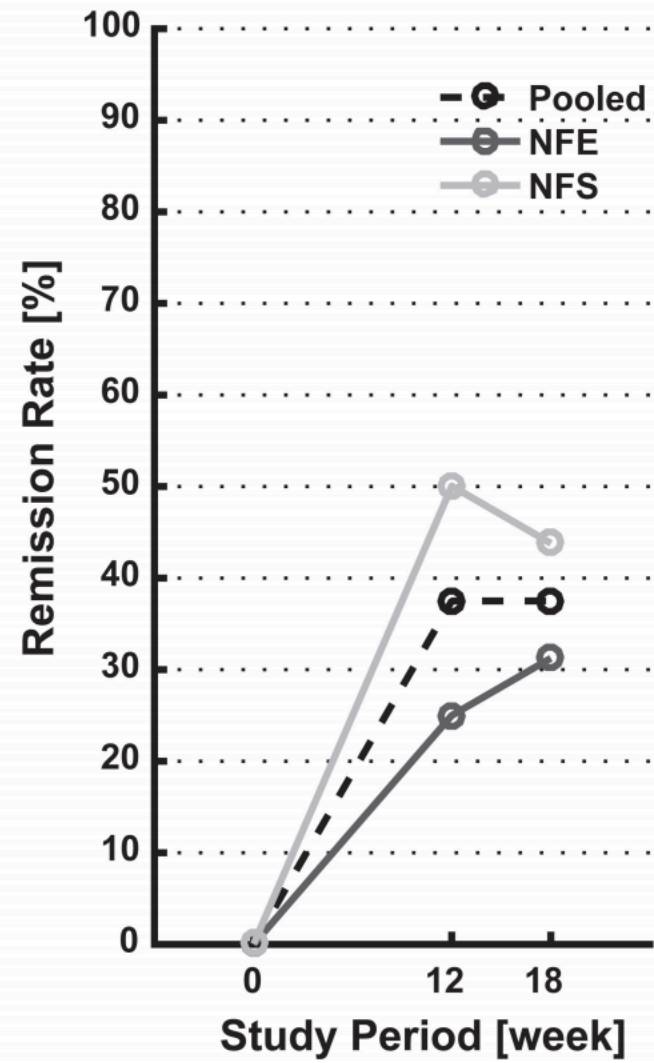
Was it really the neurofeedback driving the change?

Interpreting changes following neurofeedback



Targeting the affective brain - A Randomized Controlled Trial of real-time fMRI neurofeedback in patients with depression

David M. A. Mehler, Moses O. Sokunbi, Isabelle Habes, Kali Barawi, Leena Subramanian, Maxence Range, John Evans, Kerenza Hood, Michael Lührs, Paul Keedwell, Rainer Goebel, David E. J. Linden

A**B**

Caution

- Placebo effects are very strong in many of the conditions targeted by neurofeedback
- If participants are given an explicit strategy, or the feedback is not orthogonal to the network being trained, it is impossible to decouple task effects from feedback effects
- Multiple control groups may be necessary in such a case
- It is important to know what aspect of the training is working

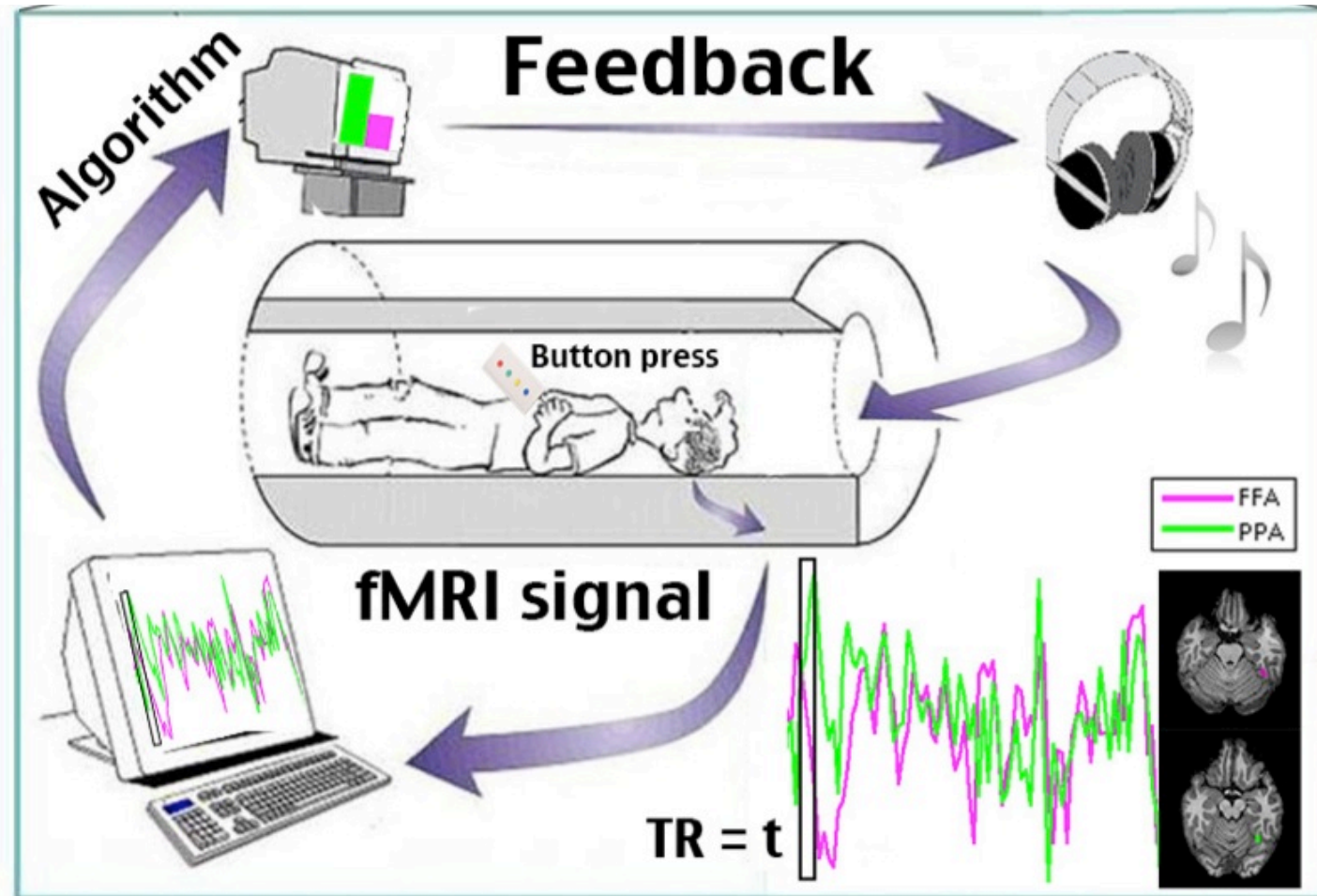
What do we know about what we
can do with neurofeedback?

And what are we still working on?

What we know

- Implicit learning works
- In fact, it doesn't even have to be consciously directed

Does learning have to be conscious?



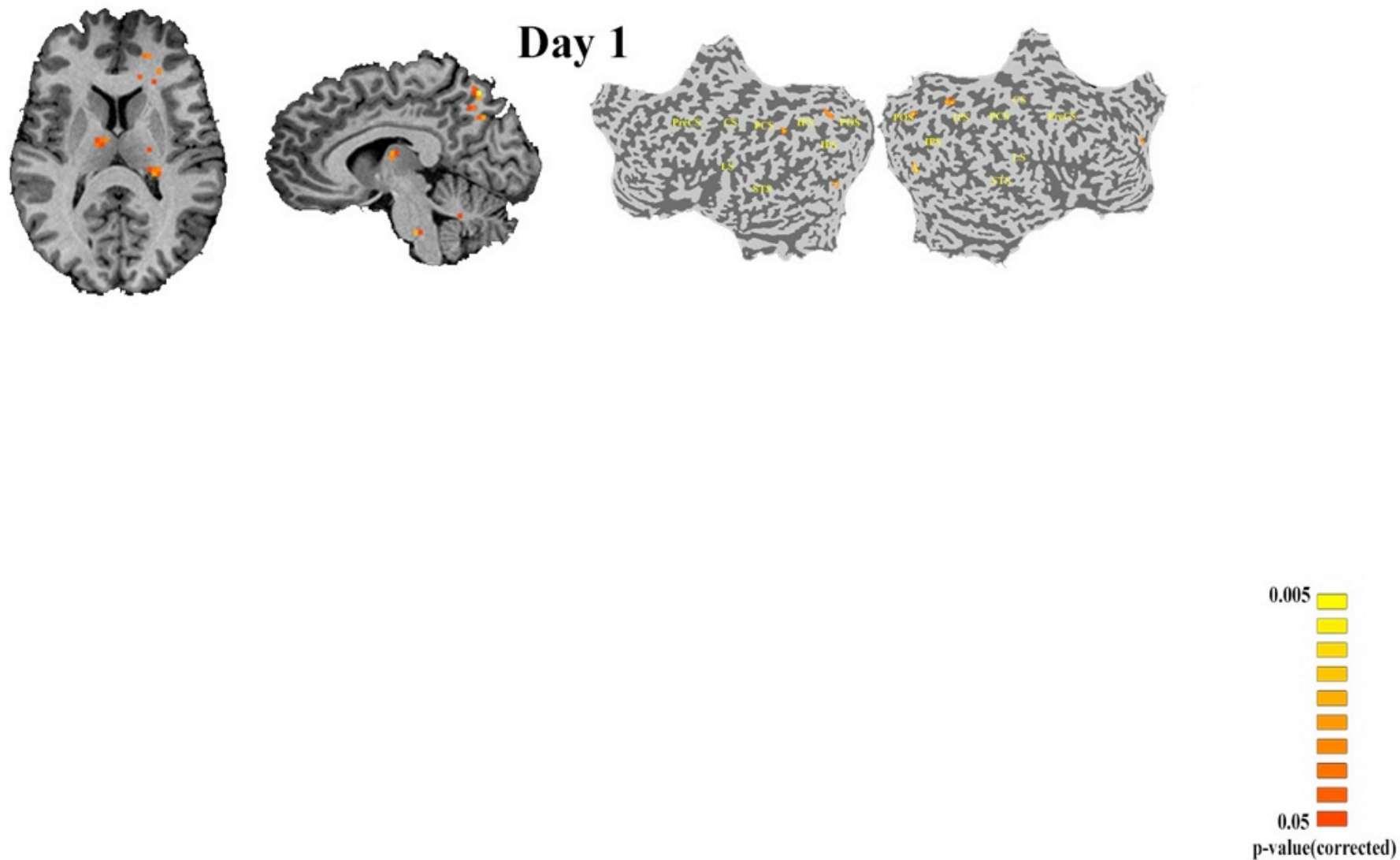
Good



Bad



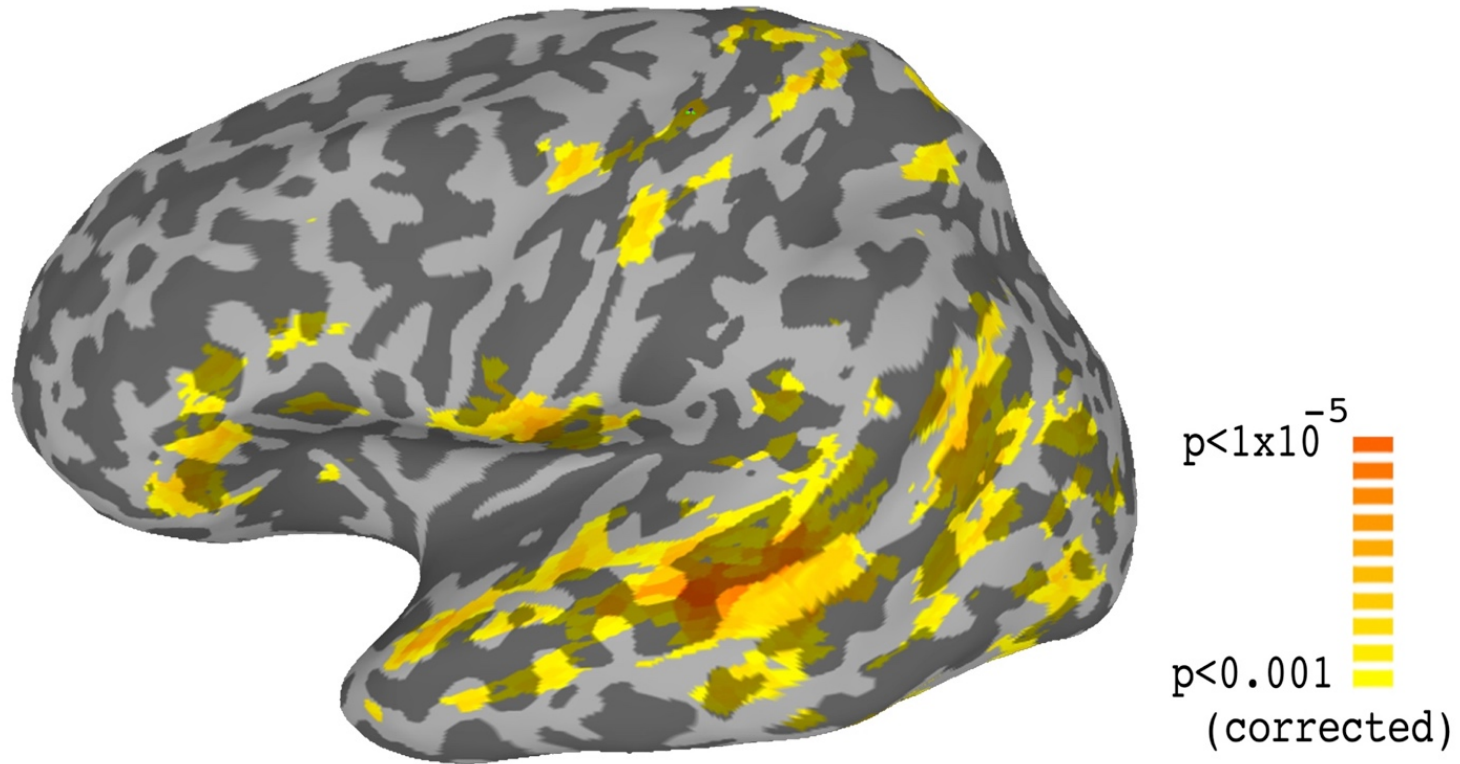
Voxels significantly more correlated to good>bad ROI, during NF



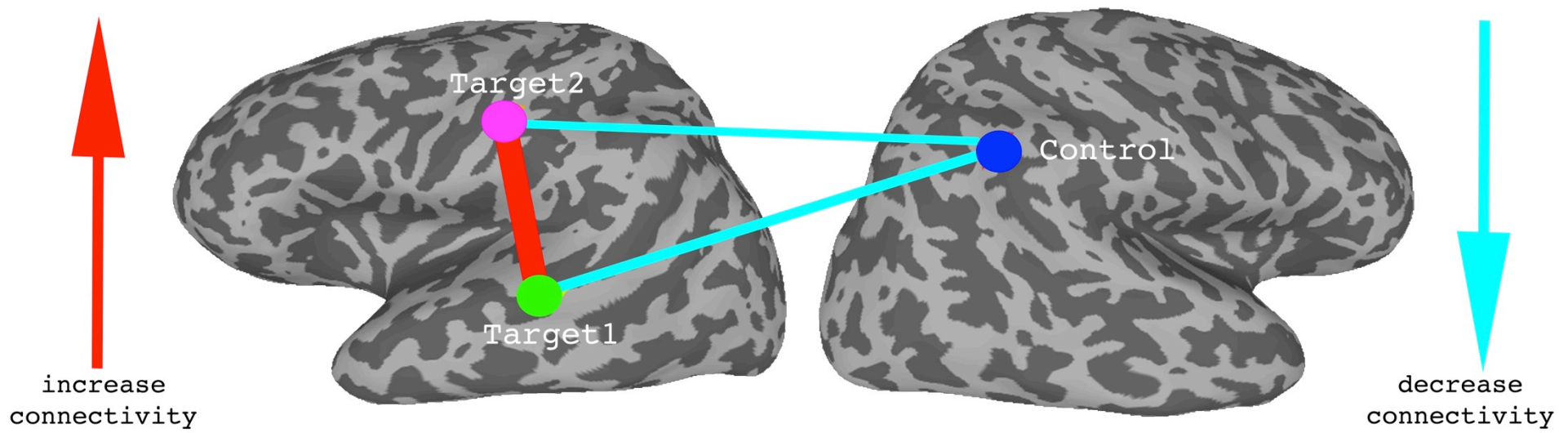
What we know

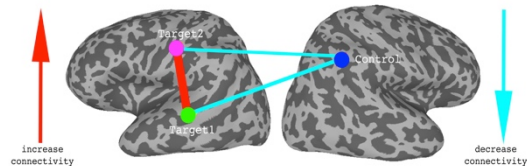
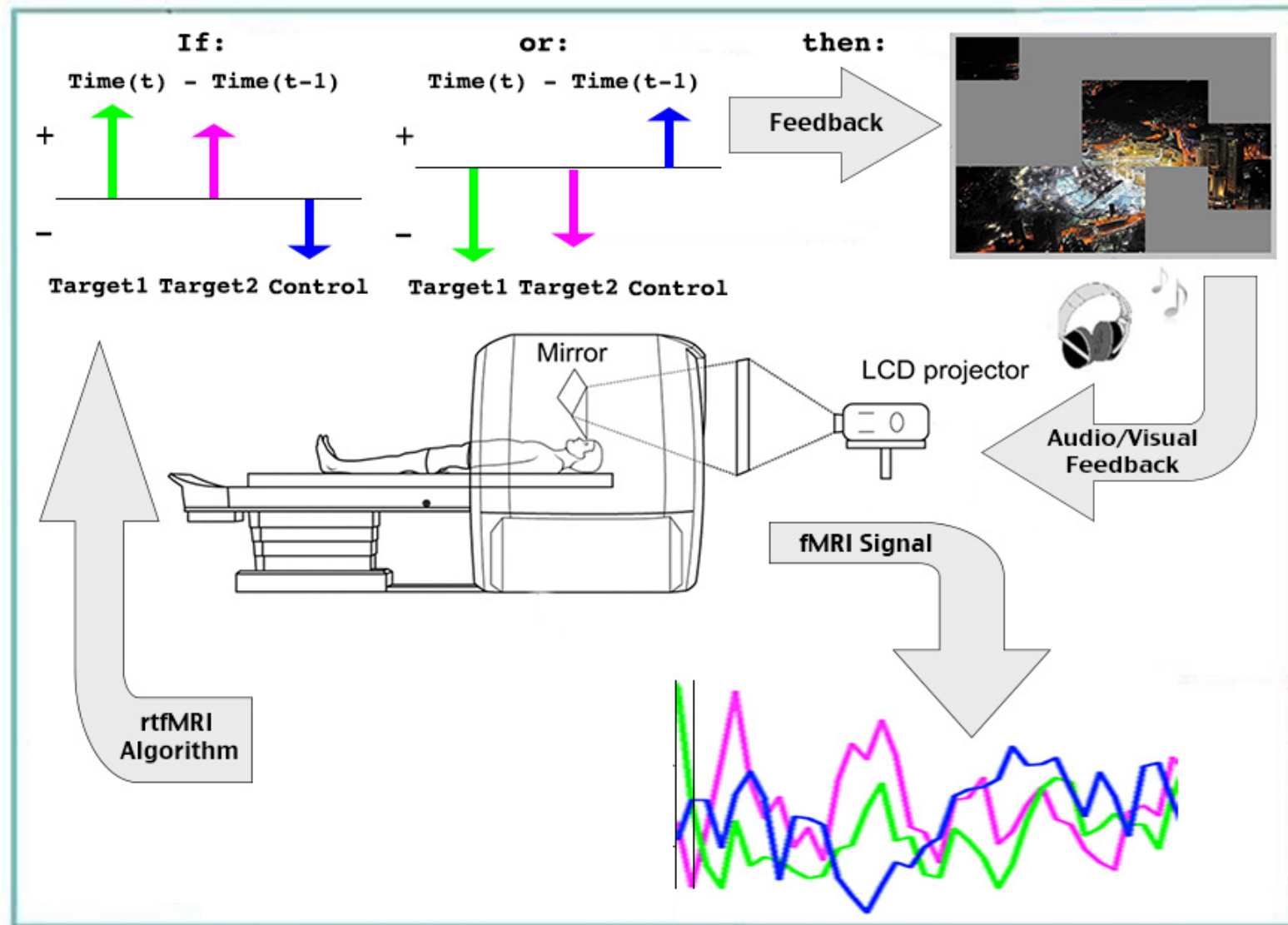
- Implicit learning works
- In fact, it doesn't even have to be consciously directed
- We can robustly change networks through neurofeedback

Aberrant networks in autism



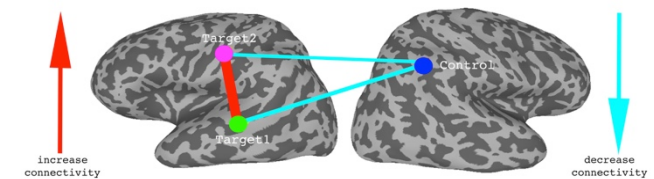
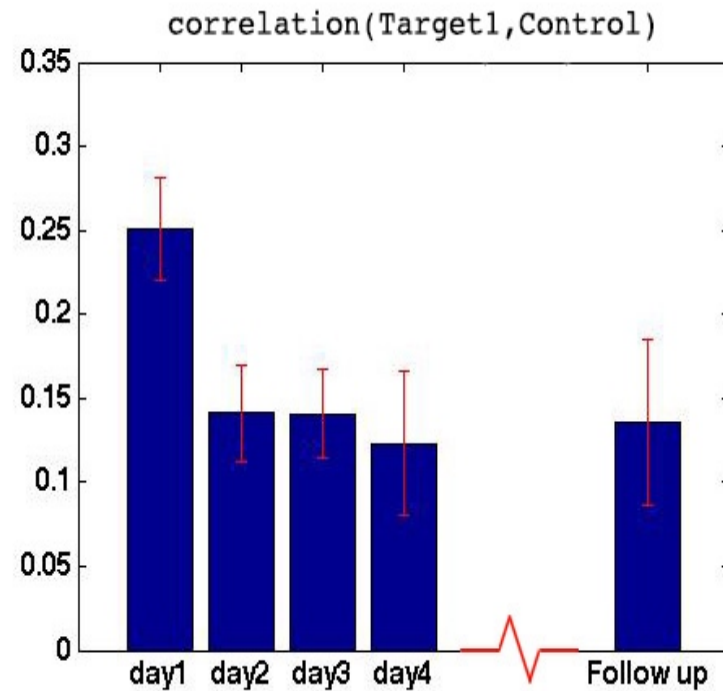
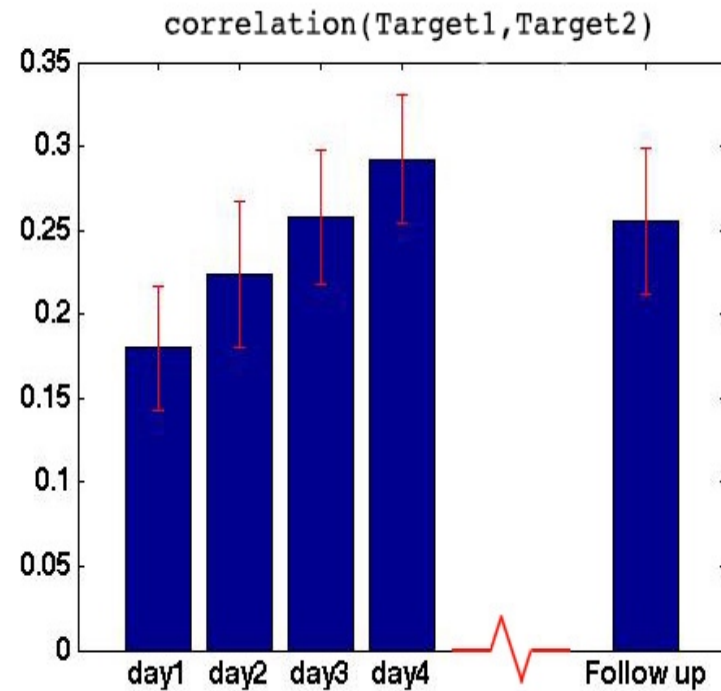
Goal



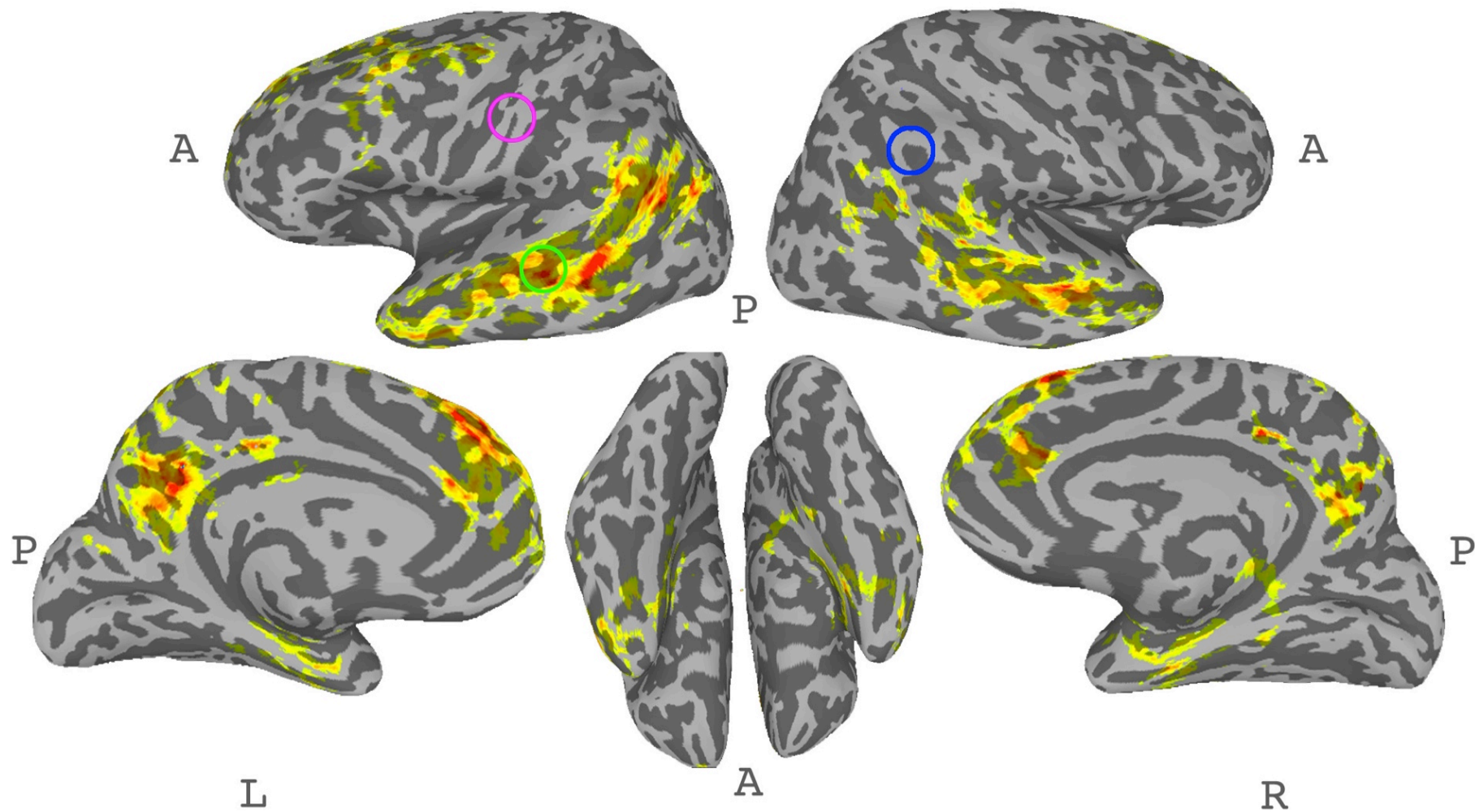




Long term changes



Target 2 minus Control, day 4 minus day 1



Still working on



Conclusions

- Real-time fMRI neurofeedback is a potentially powerful tool
- Neurofeedback can change networks, even when it is implicit
- Caution must be used in the design of neurofeedback studies, and the interpretation of their results
- We need more studies directly testing the link between networks and behavior in an unambiguous manner

Stop!



- Do you need neurofeedback to answer your question?
- Does your planned neurofeedback experiment answer your question?

Open questions

- How does changing the networks change behavior?
- Can you train any network, given the right feedback / enough time?
- What is the mechanism for neurofeedback learning?
- Which factors influence variability between subjects?
- What is the optimal network size / complexity to train?
- What is the optimal network feature to train?
- What is the optimal training technique / level of consciousness?