



# Applications of real-time functional magnetic resonance imaging to alleviation of psychological symptoms

**Neurofeedback, biofeedback and body-contingent approaches to affective and neuropsychiatric symptom management:  
New neuroscience and clinical applications.**

Symposium, Annual Congress, RCPsych 2021

David Linden



## Mental Imagery training in CBT

- Review: “Mental Imagery in Depression: Phenomenology, Potential Mechanisms, and Treatment Implication”



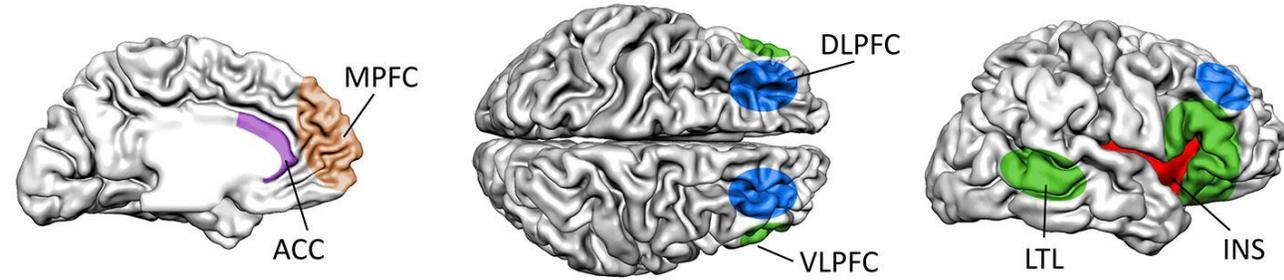
# Relevance of mental imagery for psychotherapy

- Imaginal exposure
- Imagery-based cognitive bias modification
- Imagery rescripting
- Guided imagery
- Targeted use of imagery in neurofeedback



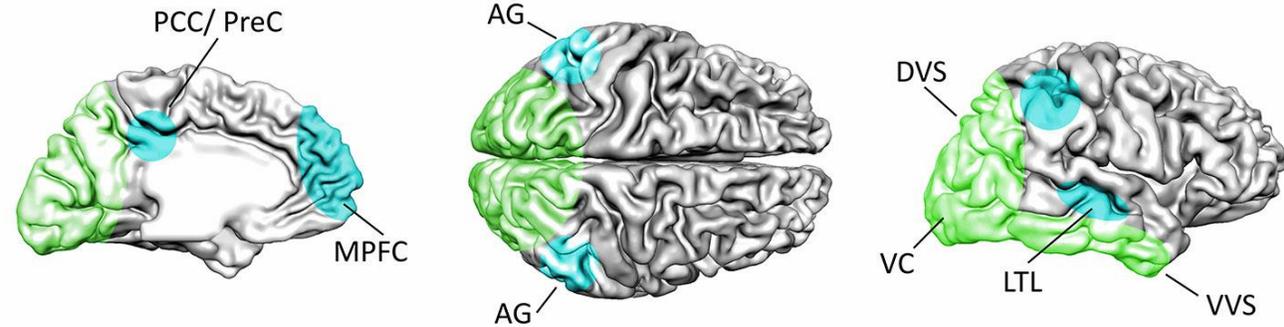
# Neural networks of mental imagery

**A**



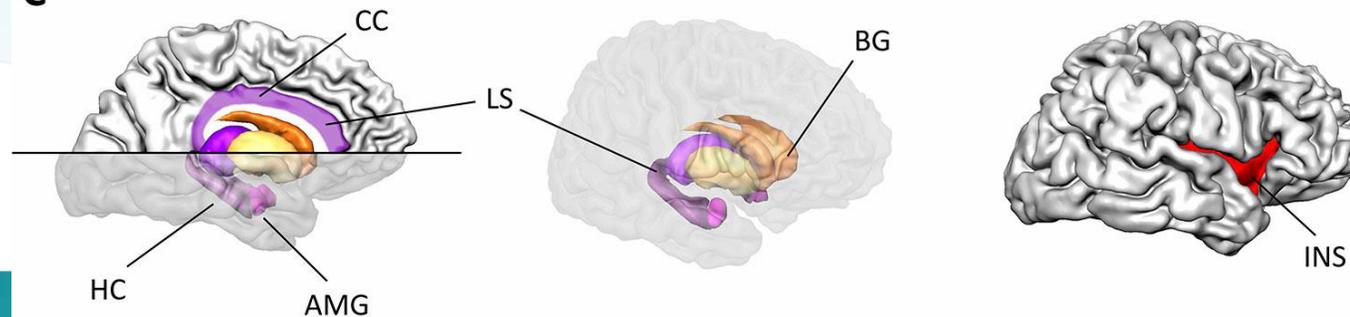
Top-down control

**B**



Endogenous visual experiences

**C**

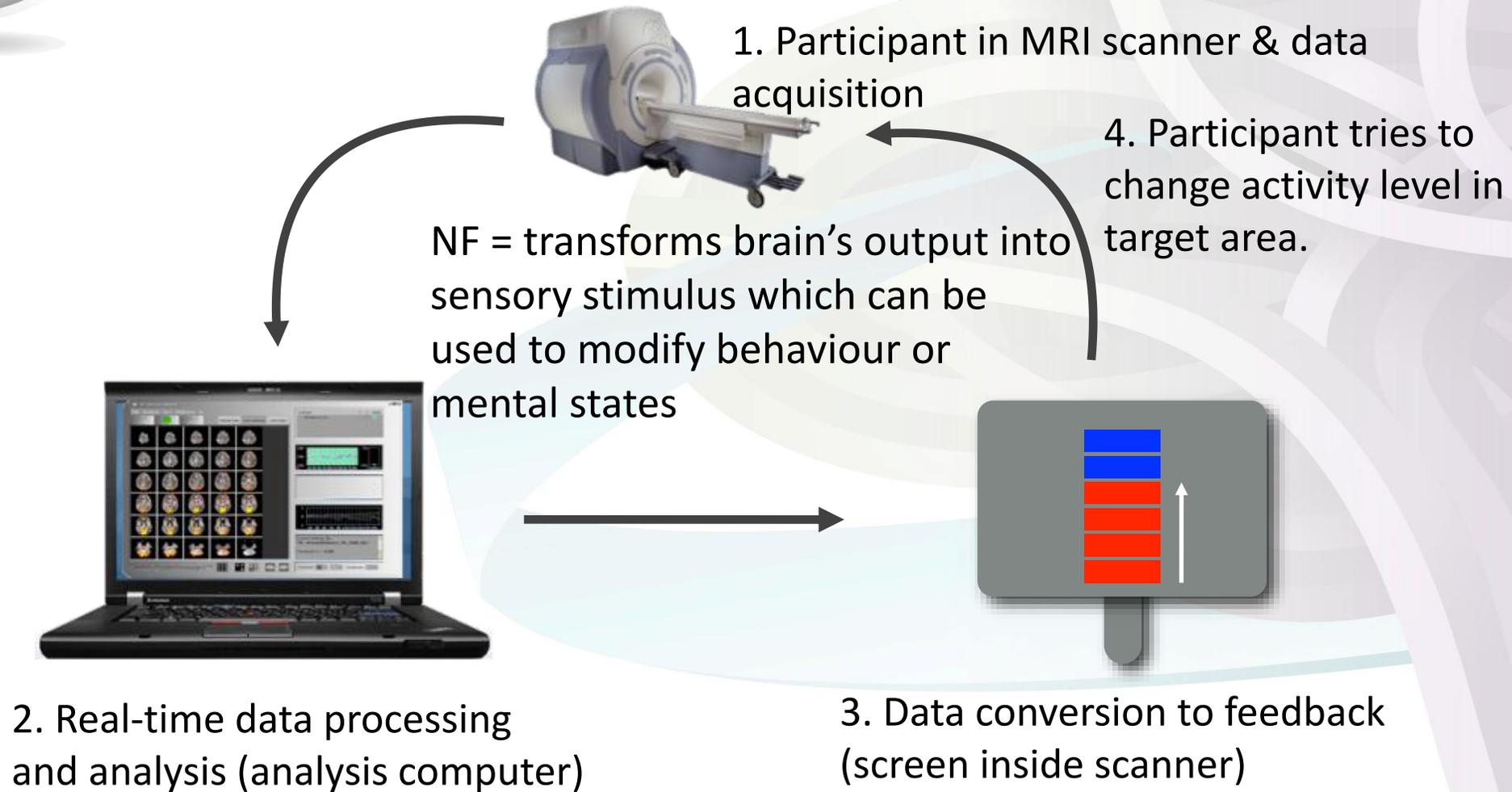


Salience and core affect

Skottnik & Linden,  
<https://www.frontiersin.org/articles/10.3389/fpsy.2019.00779/full>

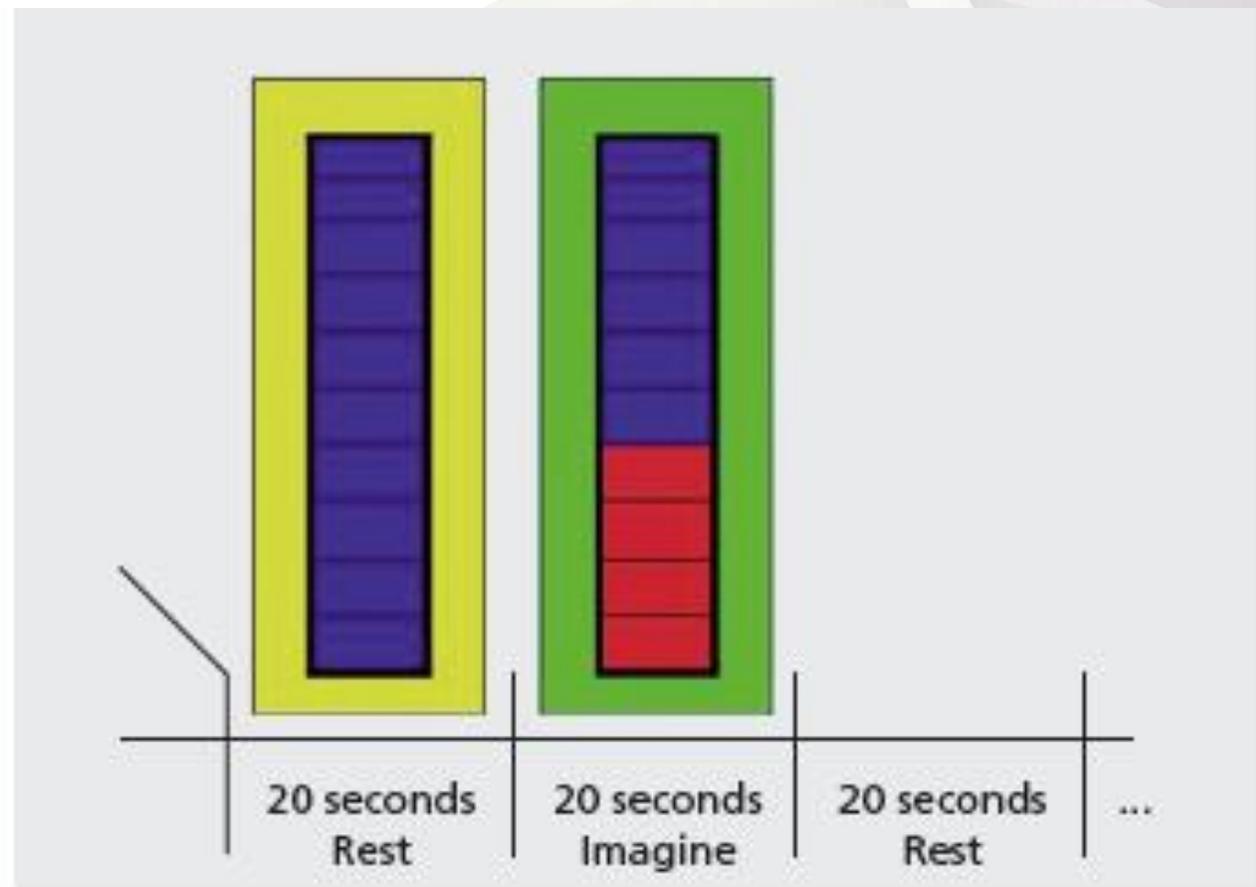


# What is Neurofeedback?





# What the participant sees





## An Alternative Approach – 'Motivational Neurofeedback'

Neurofeedback using picture size variations contingent on target area activation



Repeated size sequence as perceptual control ("mirror run")

Sokunbi, Linden, Habes,  
Johnston, & Ihssen (2014).  
*Frontiers in BN.*

→ Task provides real motivational consequences (approach and avoidance)



# Randomised Controlled Trial of fMRI-NF in depression

- Clinical Outcome: Hamilton Depression Rating Scale (**HDRS**)
- Moderate to severe depression (**HDRS-17: 12-27**) despite psychopharmacological treatment (stable dose >3 months);
- Mean time since first episode ~20 years

Neuropsychopharmacology

[www.nature.com/npp](http://www.nature.com/npp)



**ARTICLE** **OPEN**

Targeting the affective brain—a randomized controlled trial of real-time fMRI neurofeedback in patients with depression

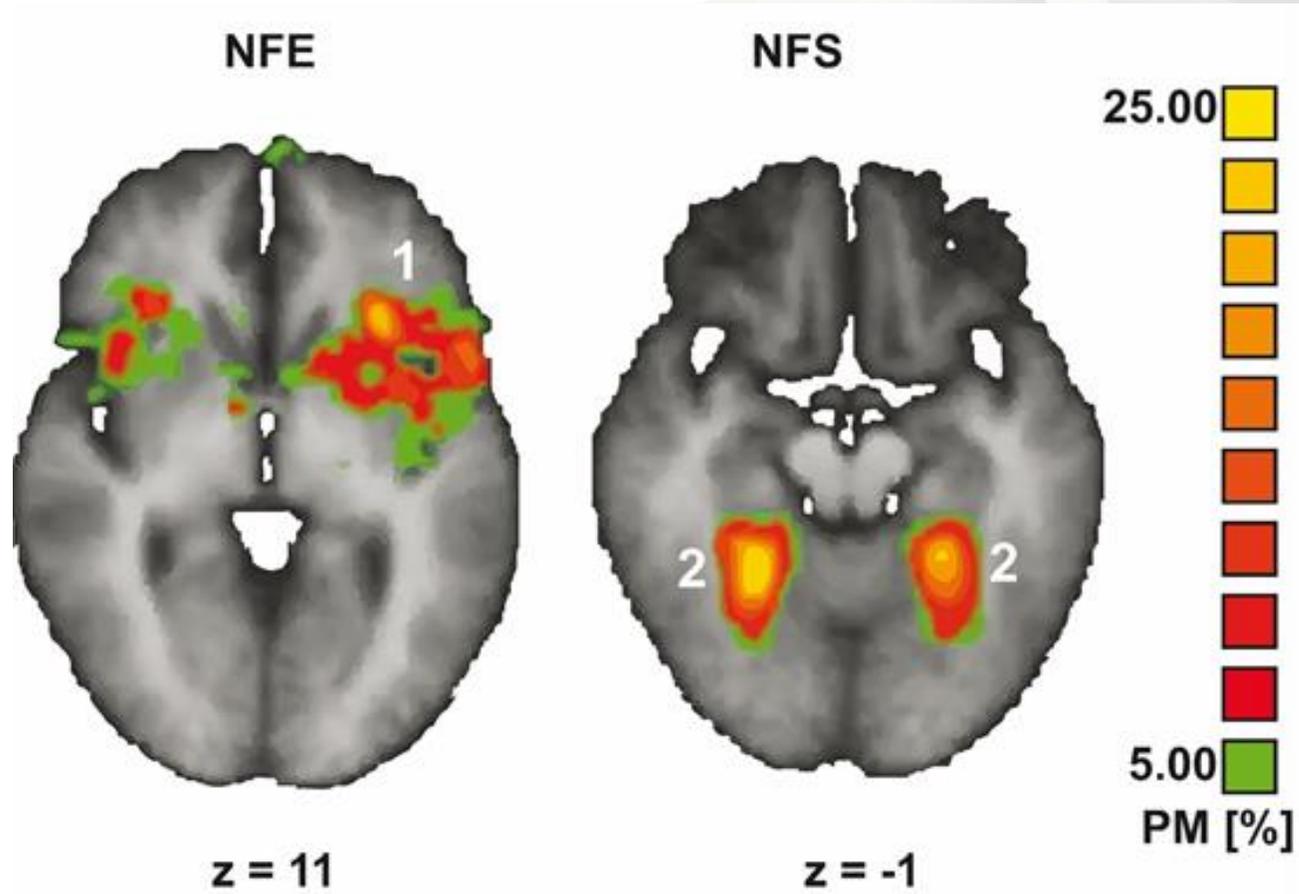
David M. A. Mehler<sup>1,2</sup>, Moses O. Sokunbi<sup>3</sup>, Isabelle Habes<sup>2</sup>, Kali Barawi<sup>1,2</sup>, Leena Subramanian<sup>1,2</sup>, Maxence Range<sup>4</sup>, John Evans<sup>2</sup>, Kerenza Hood<sup>5</sup>, Michael Lührs<sup>6,7</sup>, Paul Keedwell<sup>1,8</sup>, Rainer Goebel<sup>6,7</sup> and David E. J. Linden<sup>1,2,9</sup>



## Randomised Controlled Trial

- 1) NFE group (N=16): mental imagery of positive Emotions (e.g. striatal areas)
  - 2) NFS group (N=16): active control, mental imagery of relaxing Scenes (e.g. parahippocampal place area (PPA))
- Passive viewing localiser (NFE: IAPS; NFS: scenes, faces, animals)

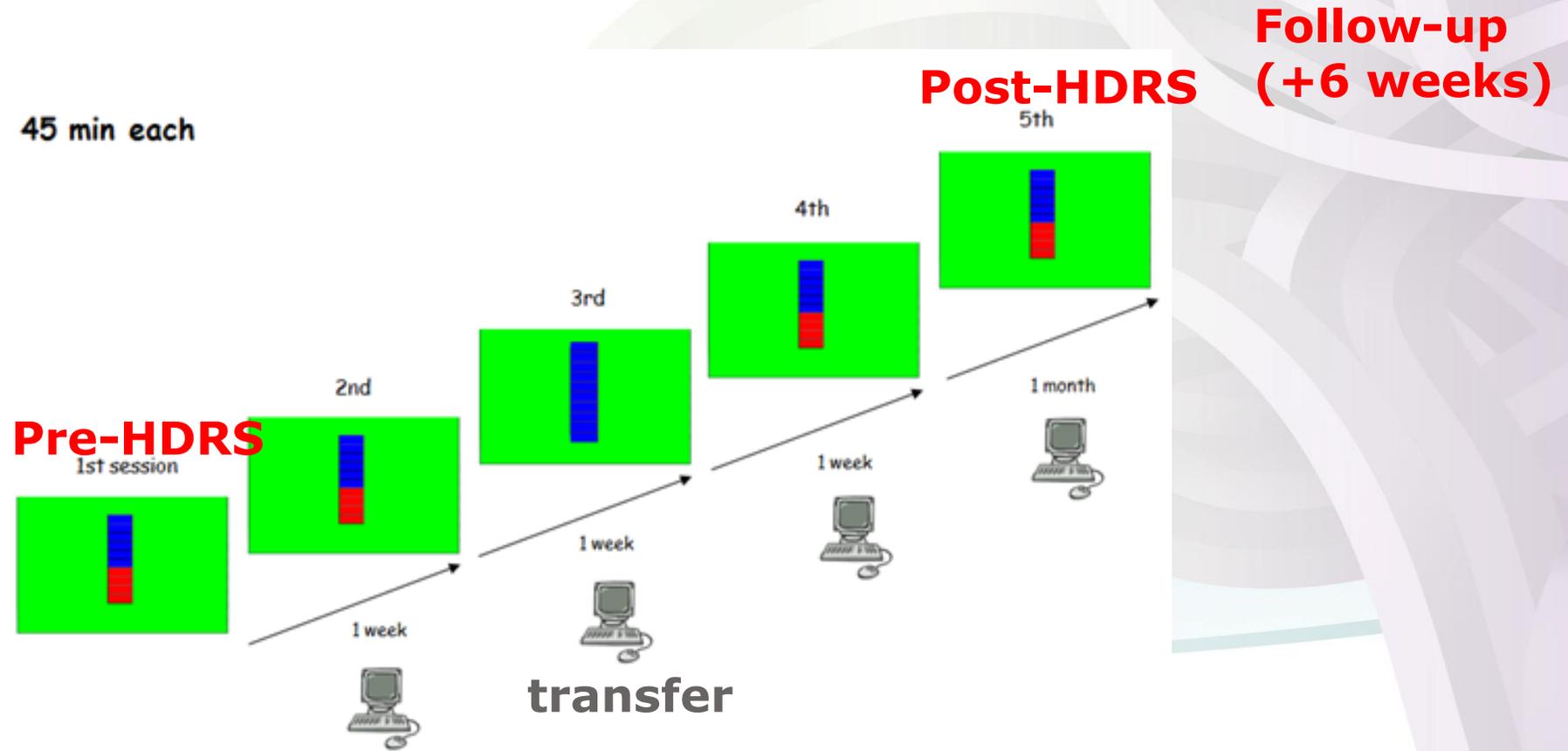
# Target areas (localiser)





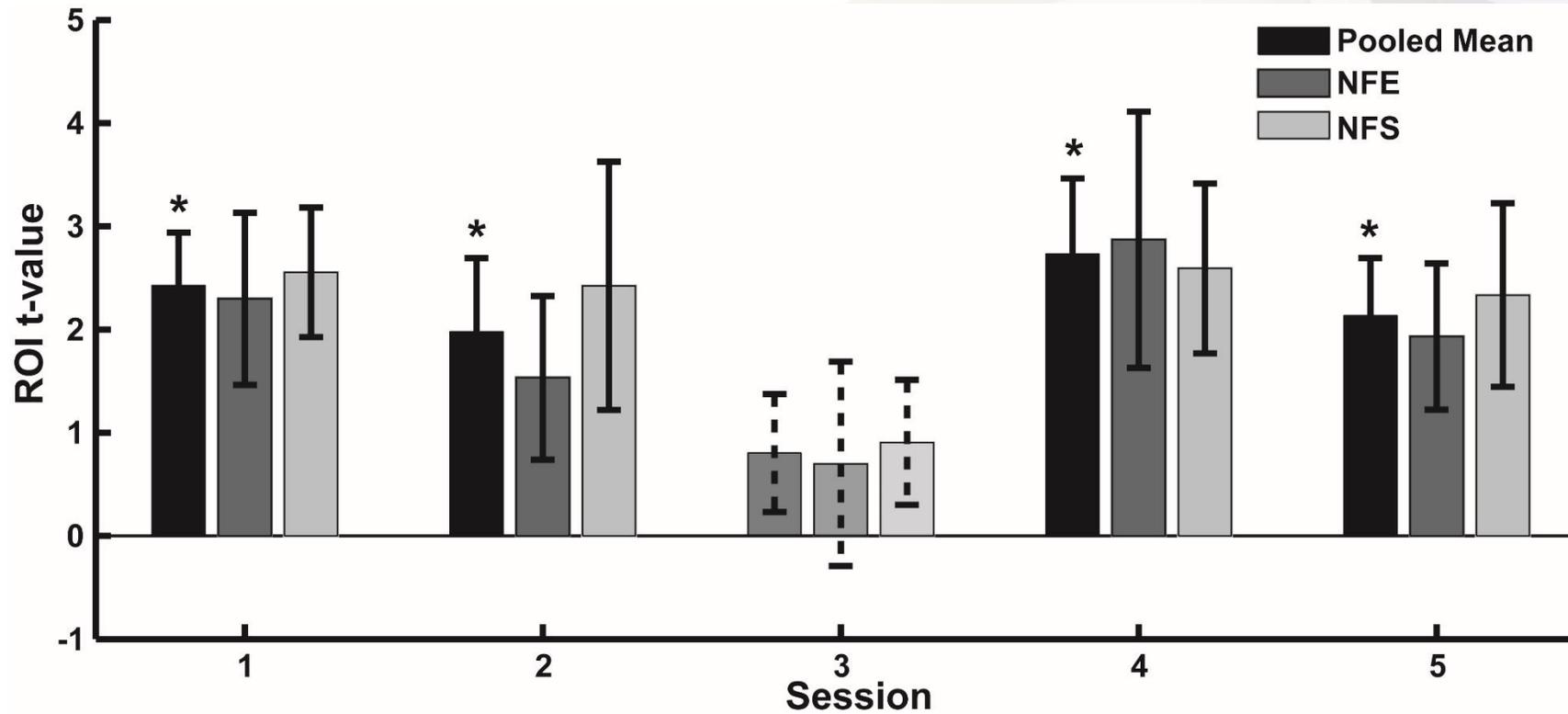
# Study Design

45 min each





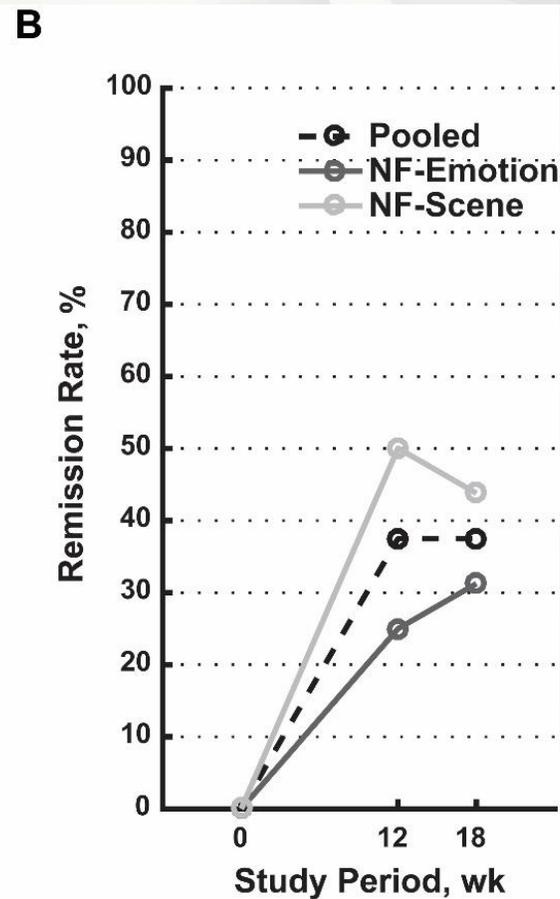
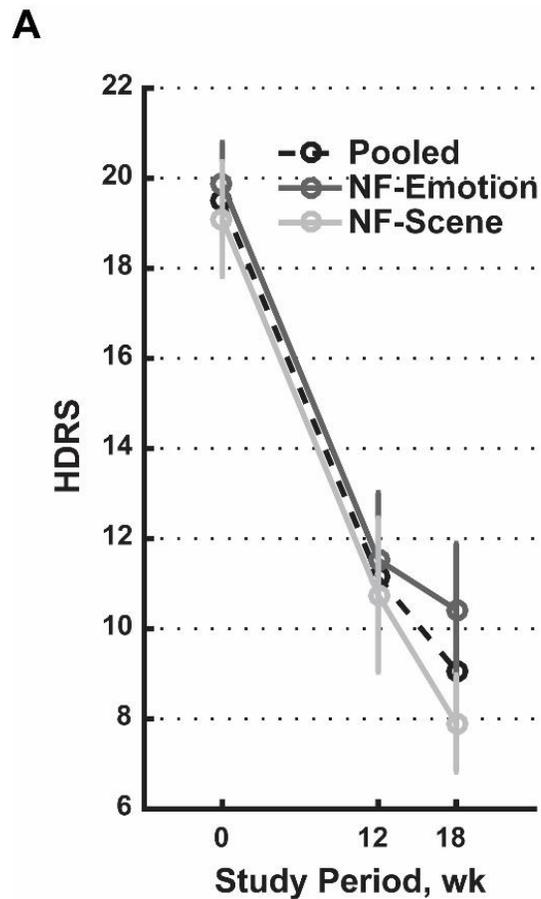
# Target region upregulation





# Clinical improvement, but no difference between groups

~40%  
improvement in  
both groups





## Comparison with other NF work

# Randomized Clinical Trial of Real-Time fMRI Amygdala Neurofeedback for Major Depressive Disorder: Effects on Symptoms and Autobiographical Memory Recall

Kymerly D. Young, Ph.D., Greg J. Siegle, Ph.D., Vadim Zotev, Ph.D., Raquel Phillips, B.S., Masaya Misaki, Ph.D., Han Yuan, Ph.D., Wayne C. Drevets, M.D., Jerzy Bodurka, Ph.D.

Young, AJP (2017)



# real vs. sham feedback

| Measure and Group                             | Visit 1: Baseline |     | Visit 2: rtfMRI-nf |     | Visit 3: rtfMRI-nf |     | Visit 4: Follow-Up |     |
|---|-------------------|-----|--------------------|-----|--------------------|-----|--------------------|-----|
|   | Mean              | SD  | Mean               | SD  | Mean               | SD  | Mean               | SD  |
| Hamilton Depression Rating Scale<br>(21 item) |                   |     |                    |     |                    |     |                    |     |
| Experimental group                            | 19.4              | 7.9 | 19.1               | 8.2 | 12.8 <sup>a</sup>  | 7.5 | 10.4 <sup>a</sup>  | 7.1 |
| Control group                                 | 19.1              | 4.4 | 19.3               | 5.6 | 17.2 <sup>b</sup>  | 5.8 | 17.2 <sup>b</sup>  | 5.0 |



# Complementary designs

| Study                                 | Specificity (NF)            | Self-regulation | positive reinforcement |
|---------------------------------------|-----------------------------|-----------------|------------------------|
| Young et al., AJP, 2017               | Amygdala $>$ control region | —               | —                      |
| Mehler et al., Neuropsychopharm, 2018 | NFE $\approx$ NFS           | NFS             | NFS                    |

# The Braintrain Project

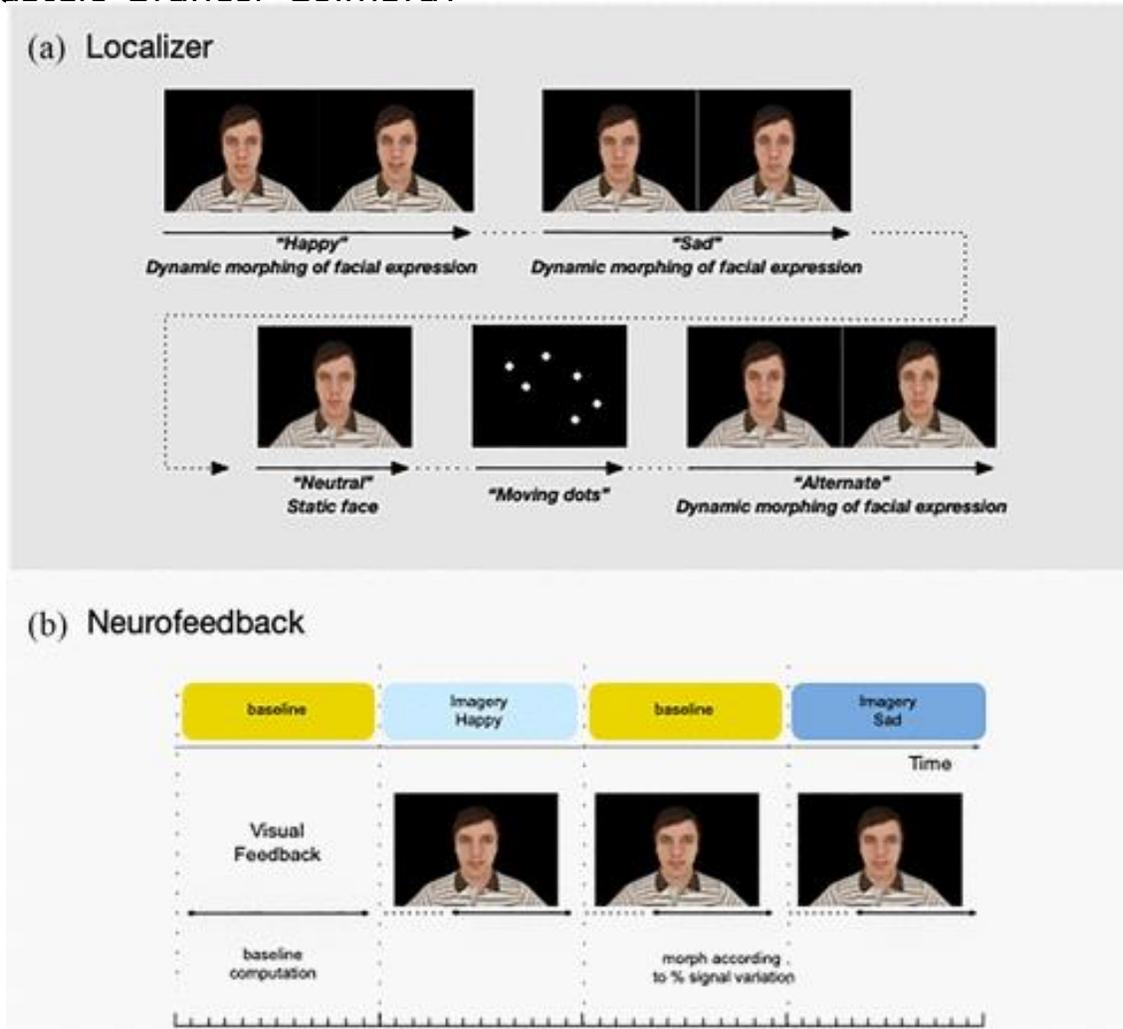
[www.braintrainproject.eu](http://www.braintrainproject.eu)

- 5-year collaborative project funded by the European Commission 2013-2018
- Consortium goal: Adapt and improve fMRI-Neurofeedback (NF) for clinical use
- Central component: Assessment of feasibility and clinical effects of NF through randomised clinical trials
- Targeted mental disorders characterised by dysfunctions in motivation, emotion regulation, and social communication and by therapeutic gaps

| Participant                              | Targeted disorder         |
|--|---------------------------|
| Universidade de Coimbra                  | Autism Spectrum Disorder  |
| Eberhard Karls Universitaet Tuebingen    | Eating disorders/ Obesity |
| King's College London/ Oxford University | Childhood anxiety         |
| Tel Aviv University                      | PTSD                      |
| Cardiff University                       | Alcohol Addiction         |

# NF-ASD: Training the social brain - 8-week real-time fMRI NF Imaging Feasibility Trial

(PI: Miguel Castelo-Branco/ Coimbra)



- Intervention Model:
  - **Single arm**
- Primary Purpose:
  - **Basic Science and clinical feasibility study**
- Participants:
  - **15 ASD subjects** (no drop outs)

**Findings** (Direito et al., *Autism*, 2021): Improvement in recognition of Fear in Faces (FEEST battery) and global significant improvements in adaptive behavior (VABS and ATEC) and in specific clinical subscales of ATEC, VABS, and POMS



## Progress & challenges

- Promising efficacy results in depression
- Feasibility in Autism, feasibility and early efficacy data in PTSD
- Idiosyncratic protocol development (disease- and investigator-specific paradigms) and lack of standardisation
- Picking the right control conditions/ interventions
- Difficulty of moving to adequately powered efficacy studies

# Clinical research with fMRI-NF: a growing community, and growing interest worldwide

Original Article

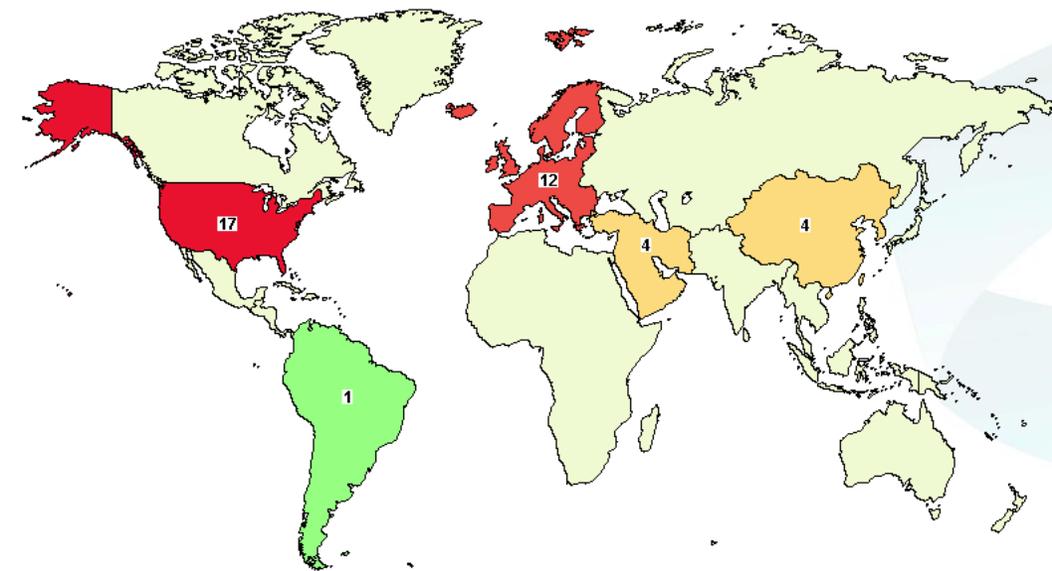
## Current practices in clinical neurofeedback with functional MRI— Analysis of a survey using the TIDieR checklist

Elizabeth Randell<sup>a,\*</sup>, Rachel McNamara<sup>a</sup>, Leena Subramanian<sup>b,c</sup>, Kerenza Hood<sup>a</sup>,  
David Linden<sup>b,c</sup>

<sup>a</sup> Centre for Trials Research, Cardiff University, Neuadd Meirionnydd, Heath Park, Cardiff, UK

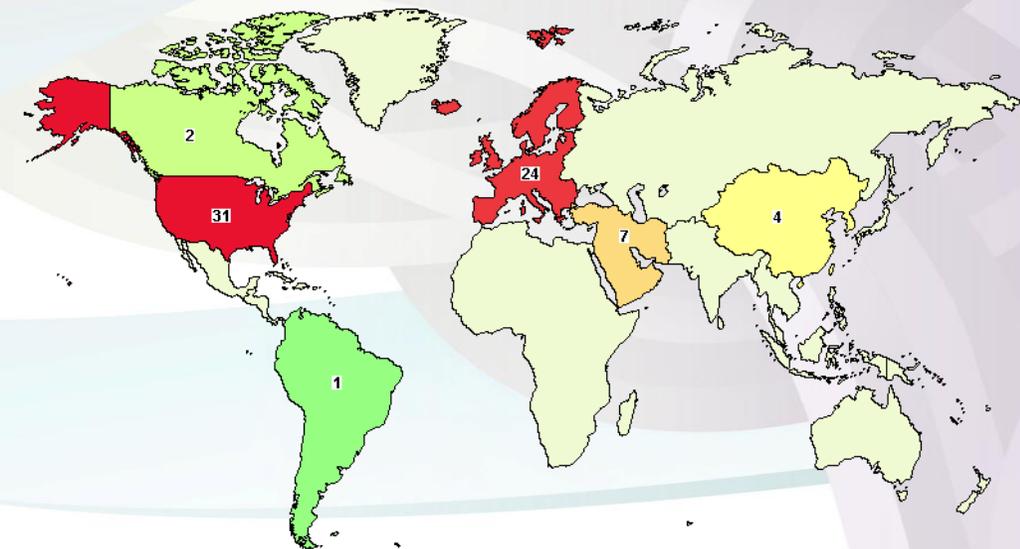
<sup>b</sup> Division of Psychological Medicine and Clinical Neurosciences, School of Medicine, Cardiff University, Hadyn Ellis Building, Maindy Road, Cardiff, UK

<sup>c</sup> Cardiff University Brain Research Imaging Centre, School of Psychology, Cardiff University, Maindy Road, Cardiff, UK



May 2018

source: [clinicaltrials.gov](https://clinicaltrials.gov)



May 2021

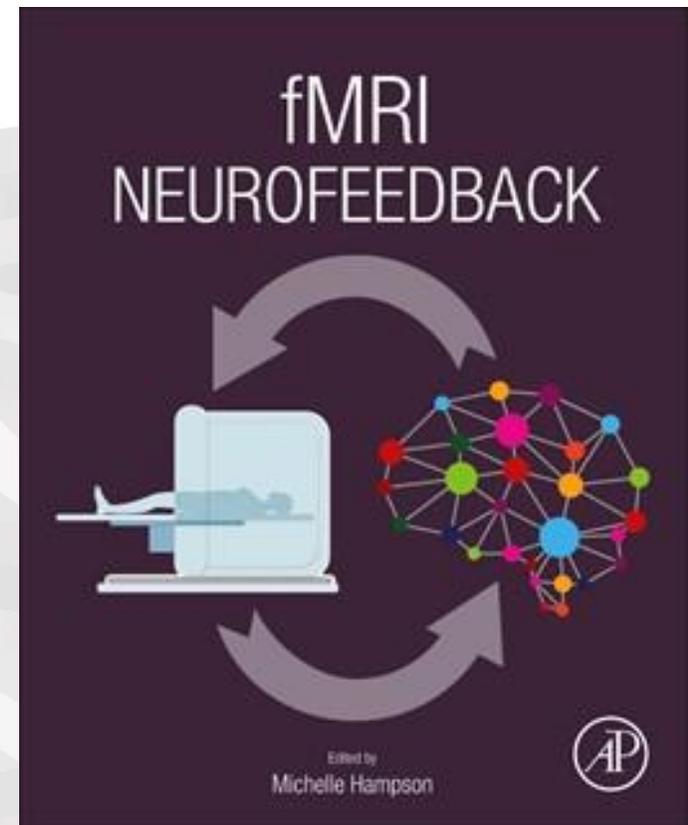
# Teaching resources on neurofeedback

Link to keynote lectures real-time fMRI:

<https://www.rtfin2019.org/107020/wiki/484037/keynote-speakers>

Training workshop rtfin2019:

<https://www.rtfin2019.org/107020/wiki/484025/main-speakers>



real-time functional imaging  
and neurofeedback conference

*December 7- 11, 2019*