

Translational neuroimaging in addiction – from circuit mapping to neurofeedback therapies

Stimulating the Brain – Topical Round Table

Lisbon Addictions Conference, 24 October 2019

David Linden



Background

- Cue reactivity and reward studies with functional imaging have identified fronto-striatal networks of craving and habit formation – across addictions
- Opportunity (and need!) to implement neuromodulation therapies based on this substantial knowledge-base



Dysfunctional Brain Responses to Visual Alcohol Cues

Task: Passive viewing of alcohol pictures in the MRI scanner

Participants: 23 student participants who were either “heavy” or “light” drinkers



8-sec picture viewing blocks (2 sec per item)

Definition of “heavy drinking”?

Men: more than 21 alcohol units/week



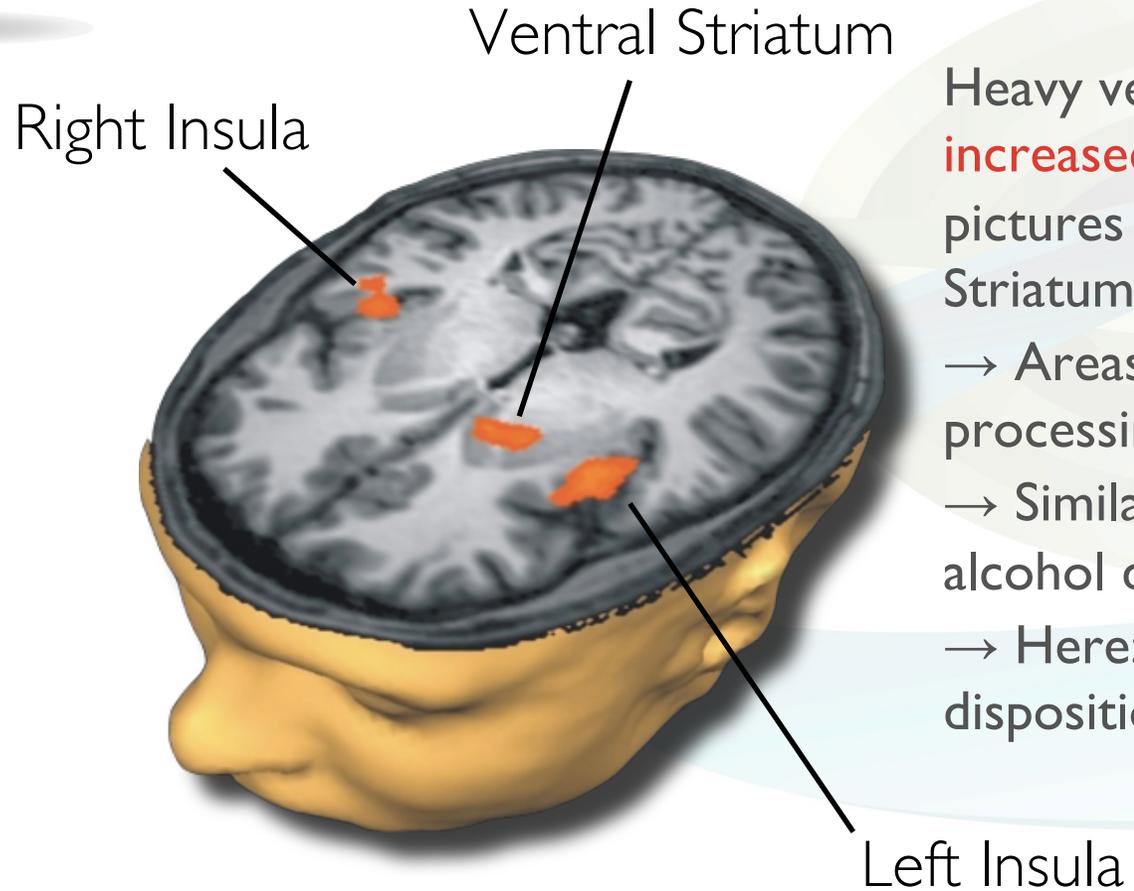
14 bottles
(330 ml)

**In our sample mean of
59 units/ week**

Ihssen et al. (2011). *Cerebral Cortex*



Alcohol Cue Reactivity in the Brain



Heavy versus light drinkers showed **increased** brain responses to alcohol pictures in the Insula and Ventral Striatum.

- Areas involved in **reward** processing and **craving**
- Similar responses can be seen in alcohol dependence.
- Here: May index addictive dispositions in preclinical stages

Ihssen et al. (2011). *Cerebral Cortex*



Reactivity to Other Cues

- Alcohol dependence is not only characterised
- by increased responsiveness to alcohol cues
 - but also by reduced responsiveness to OTHER, healthy, non-chemical incentives or life goals
- **Lack of current concerns** (Cox & Klinger, 1988)

Examples of current concerns (identified in rating studies)



Family & Relationship



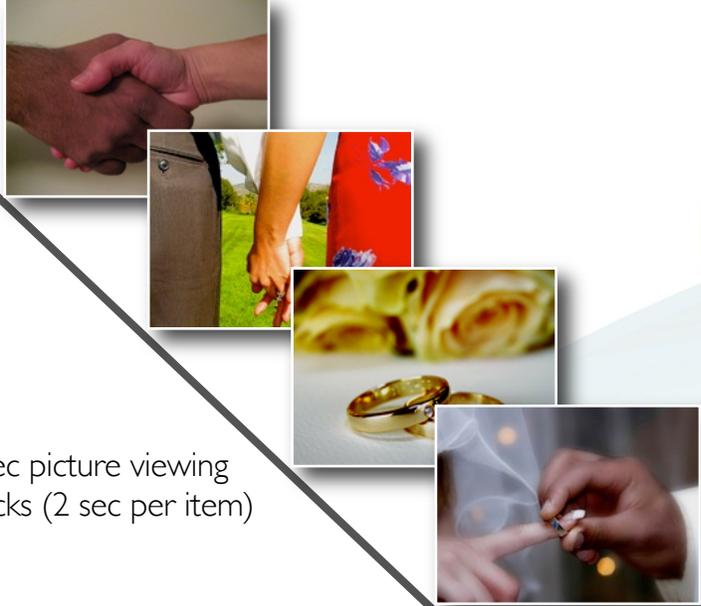
Finance & Employment



Education

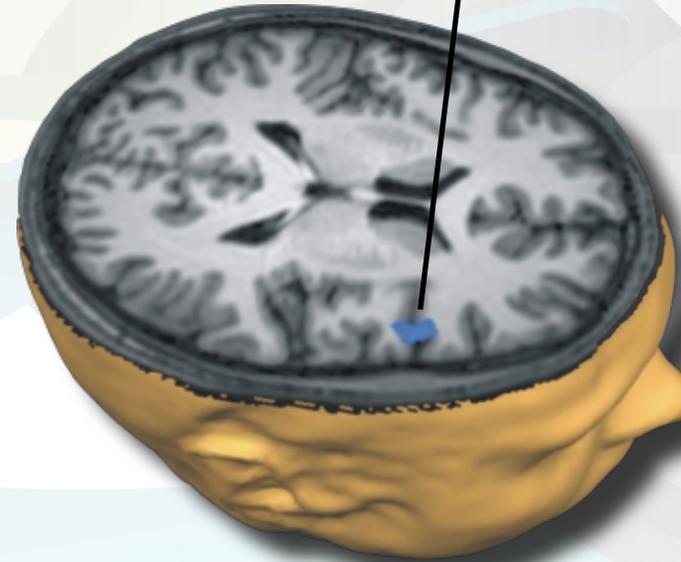


Heavy Drinkers - Reduced Responsiveness to Other (Healthy) Life Goals



8-sec picture viewing blocks (2 sec per item)

Inferior frontal gyrus (BA9)



- IFG involved in action planning & representation of action goals
- Healthy goals positioned lower in the motivational hierarchy



Why Use Neurofeedback to Treat Addictions?

There is a need to explore additional treatment options for alcohol dependence:

- Relapse rates are as high as 50-70% within one year of detoxification.
 - One key factor for relapse: Dysfunctional responses (craving) to environmental alcohol cues after treatment
 - Can neurofeedback help patients to control cue reactivity and craving?



State of the field: neurofeedback studies in alcohol use disorder

- Several pilot studies (Kirsch et al., *Addiction Biology*, 2016; Karch et al., *PLoS One* 2015)
- Several trials under way, one completed

The SyBil-AA real-time fMRI neurofeedback study: protocol of a single-blind randomized controlled trial in alcohol use disorder

Martin Fungisai Gerchen  [✉](mailto:gerchen@klinik.uni-wuerzburg.de), Martina Kirsch, Nathalie Bahs, Patrick Halli, Sarah Gerhardt, Axel Schäfer, Wolfgang H. Sommer, Falk Kiefer and Peter Kirsch

BMC Psychiatry BMC series – open, inclusive and trusted 2018 **18**:12

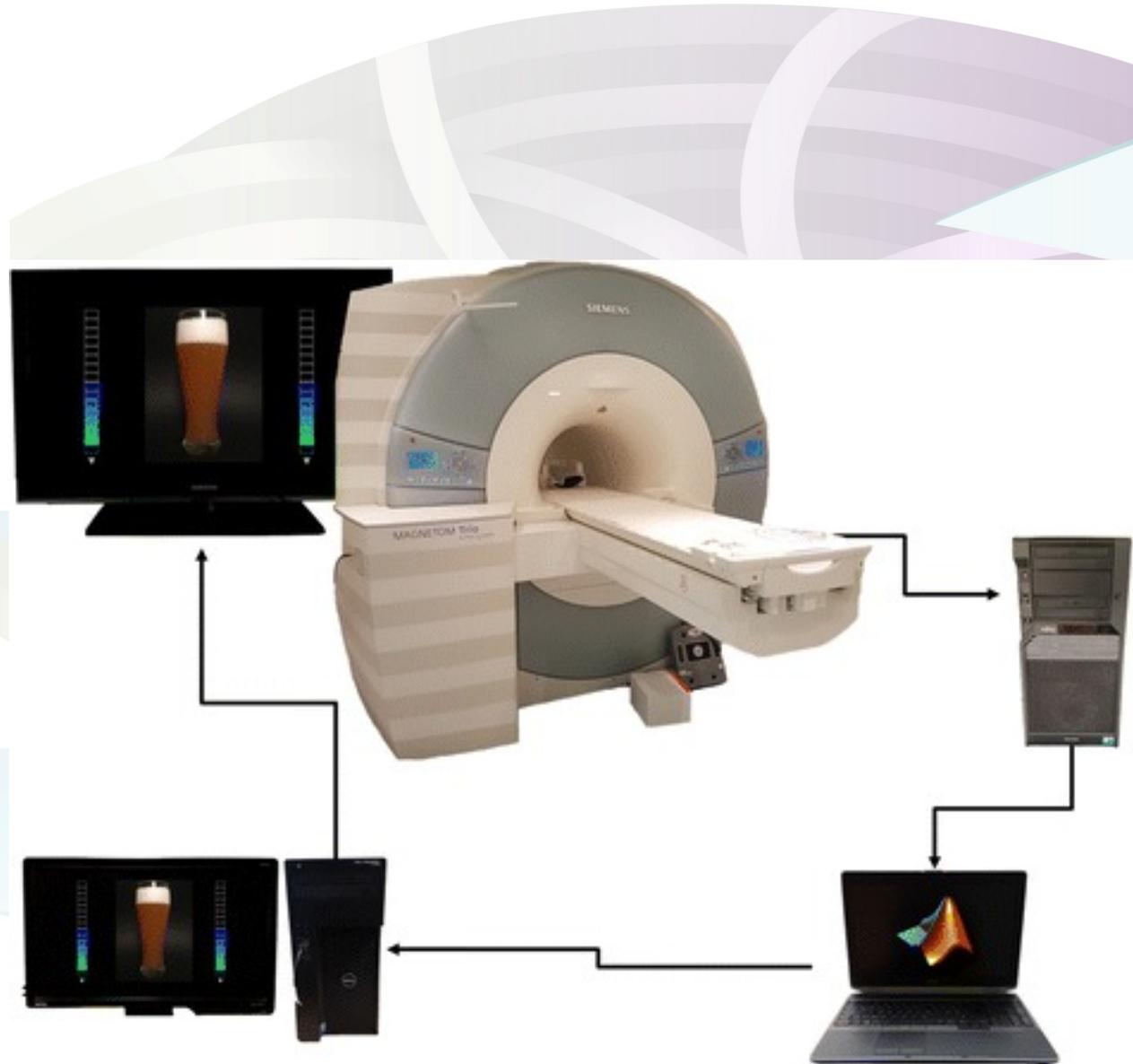
<https://doi.org/10.1186/s12888-018-1604-3> | © The Author(s). 2018

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Five groups (20 patients each):

- 1) downregulate the ventral striatum
- 2) upregulate the right inferior frontal gyrus
- 3) negatively modulate the connectivity between these regions,
- 4) upregulate auditory cortex
- 5) downregulate auditory cortex

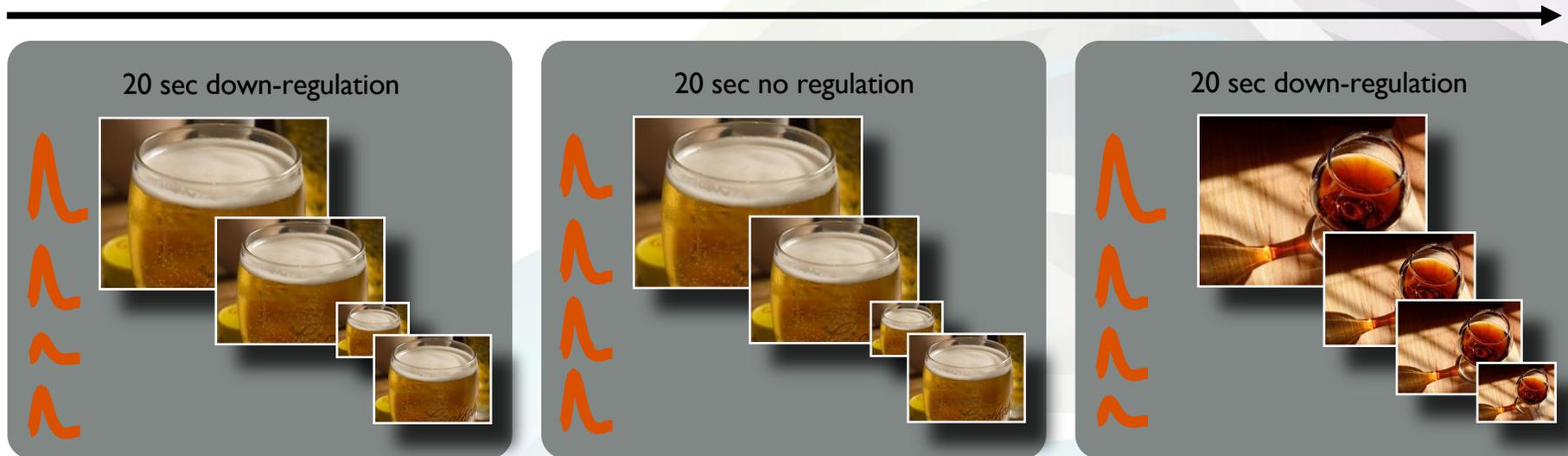
Powered for contrast between 1-3 vs. 4-5





A New 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)



Neurofeedback training for alcohol dependence versus treatment as usual: study protocol for a randomized controlled trial

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Trial Design

Neurofeedback (N=25)

Treatment-as-usual (N=27)

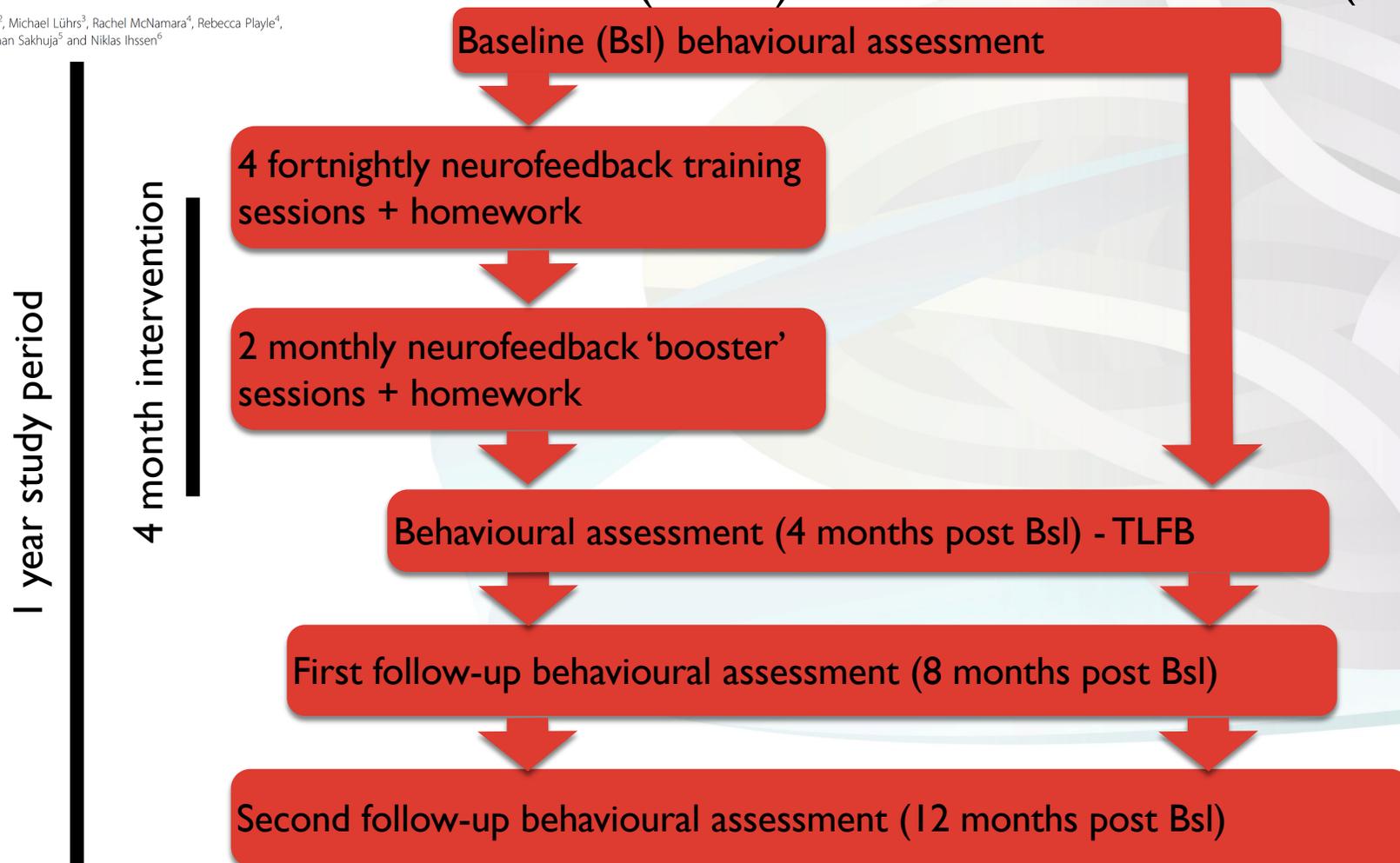




Table 1 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) diagram

	Study period					
	Enrolment	Allocation				
Timepoint	Pre intervention	Time 0	Baseline	Post intervention	8-month follow-up	12-month follow-up
Enrolment:						
Eligibility screen	X					
Informed consent	X					
Allocation						
		X				
Interventions:						
rtfMRI NFT + TAU				X		
TAU				X		
Assessments:						
Alcohol Timeline Followback	X		X	X	X	X
Drinking Urges Questionnaire			X	X	X	X
Obsessive Compulsive Drinking Scale			X	X	X	X
Alcohol Stroop Test			X	X	X	X
Severity of Alcohol Dependence			X			
Thought Control Questionnaire			X			
Thought Control Ability Questionnaire			X			
Profile of Mood States			X		X	X
Hospital Anxiety and Depression Scale			X	X	X	X
Beck Depression Inventory			X	X	X	X

rtfMRI real-time functional magnetic resonance imaging, *TAU* treatment as usual



Other ongoing trials

- **A Response Modulation Hypothesis of Socioemotional Processing Associated With Alcohol Use Disorder**
- See next slide (courtesy of Dr S Fede)
- NCT03535129 (NIAAA)
- **fNIRs-based Neurofeedback to Reduce Relapse in pOUD/AUD**
- “This study will examine the impact of functional near-infrared spectroscopy-based neurofeedback to a region within the brain's prefrontal cortex involved with self-regulation of resisting craving in alcohol use and prescription opioid use disorder patients.”
- NCT03595293 (Hershey Medical Centre)



Problems & potential solutions

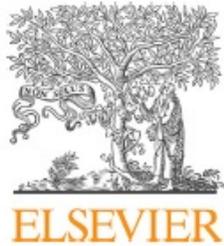
- Small N
- Need to demonstrate feasibility & efficacy
- Intervention vs. prevention trials in addiction - patient engagement, follow-up times, costs...
- Standardisation & meta-analysis
- Split in several phases/ adaptive trial design; in-built stratification
- Surrogate measures of dependence/ relapse risk, ambulatory assessments (experience-sampling)



Where do we stand

- Context of other neuromodulation approaches: For both rTMS and tDCS “a number of promising findings reported” alongside numerous negative and inconsistent outcomes (Luigjes et al., Neuropsychology Review 2019)
- EEG neurofeedback: “studies use a wide variety of outcome assessments which makes the results hard to compare and only one study used a control condition matched in time” (Luigjes et al., 2019)

Need for randomisation, blinding, standardisation (of outcome measures and protocols) and documentation of concurrent treatments/ standard care.



Contents lists available at [ScienceDirect](#)

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journal homepage: <http://www.euopsy-journal.com>



Original Article

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

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Funders & further information

MH&NS school for mental health and neuroscience

 Maastricht University

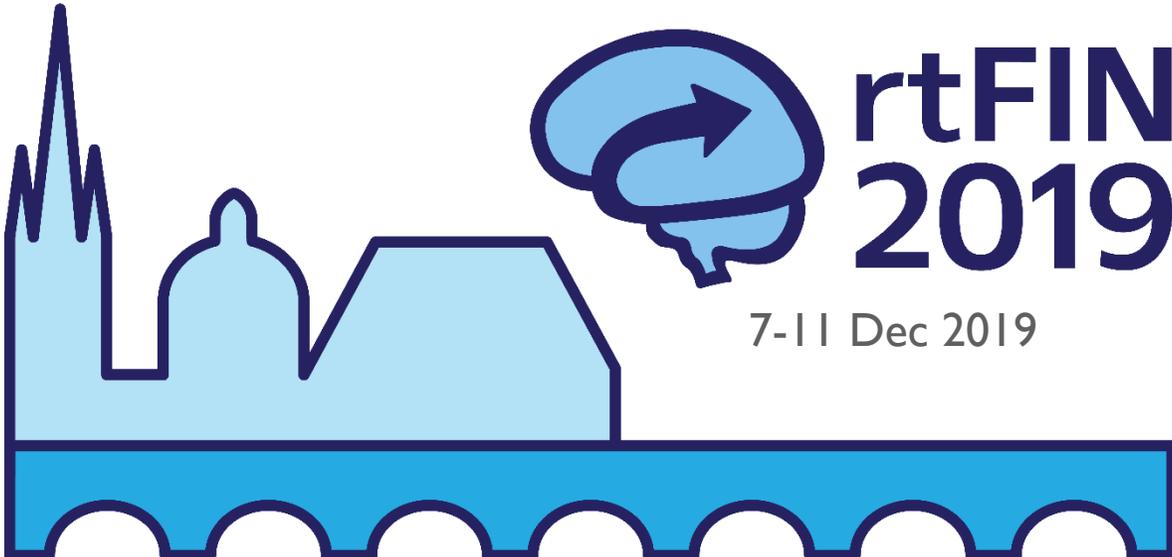
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www.braintrainproject.eu



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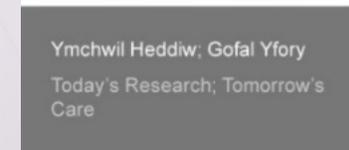
7-11 Dec 2019



Maastricht - Aachen

The central graphic features a stylized blue silhouette of the Maastricht skyline, including a prominent spire. To the right of the skyline is a circular icon containing a brain and a curved arrow, representing the rtFIN (Research Training in Financial Neuroscience) theme. The text "rtFIN 2019" and the dates "7-11 Dec 2019" are positioned to the right of the skyline. Below the skyline, the text "Maastricht - Aachen" is written in a large, bold, blue font.

wellcometrust



<https://www.rtfin2019.org/107020/wiki/423935/registration-information>

<https://twitter.com/rtFIN2019>