Escola de verão CIBIT-ICNAS 2022

Neuroimagem e neuroreabilitação

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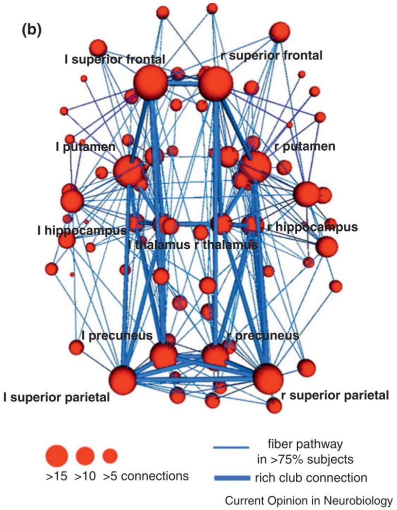
Universidade de Coimbra

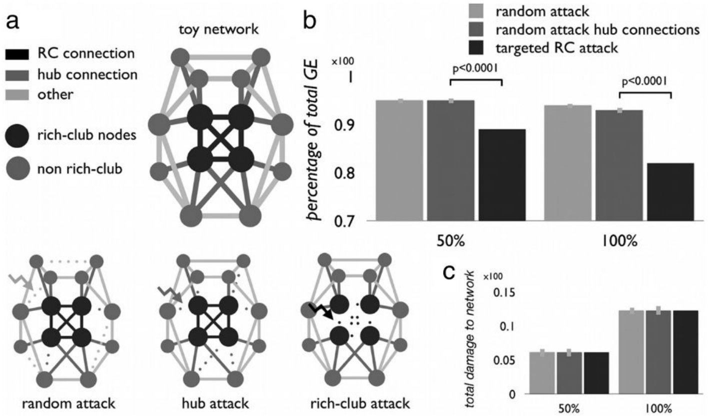
Instituto de Ciências Nucleares Aplicadas à Saúde

Overview

- Neurorehabilitation from a engineering perspective
- Network neuroscience
- Network analysis
- How to identify a target

Neurorehabilitation from a engineering perspective





How to define this structure and which node should we consider as a target region?

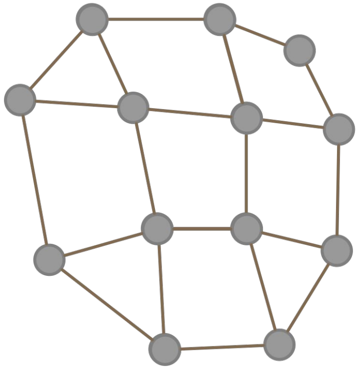
Gu, S., et al. (2015). Controllability of structural brain networks. Nature Communications, 6, 1–10

To an integrated view of the brain.

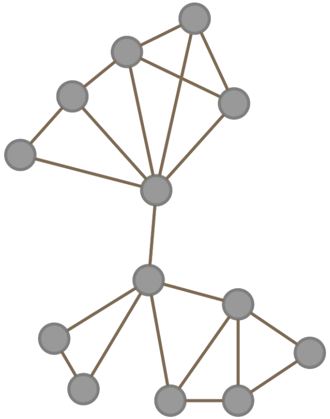
The brain is a **giant interconnected, feed-forward and feed-back recurrent network**

These systems, also known as Non-linear dynamical systems, **cannot be predicted looking at specific components of the systems** - they have emergent properties from the whole, connected components- consciousness or thought is the most relevant in humans.

Graph theory - Exploring ***network structure***

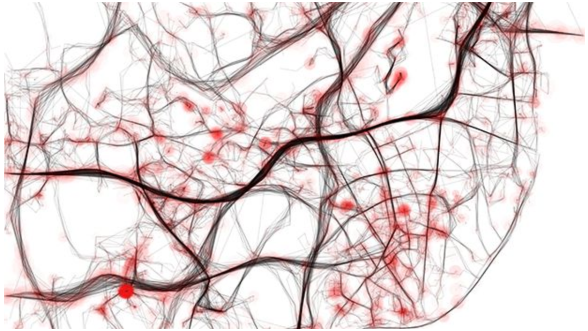


most nodes are connected
with 3/4 other nodes

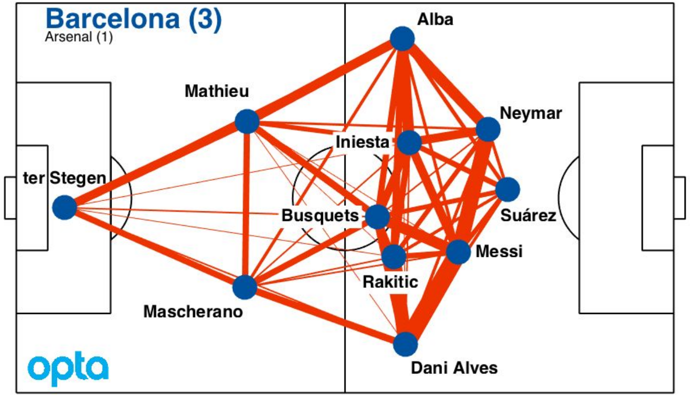


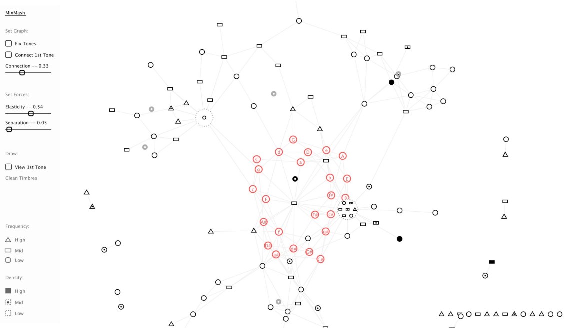
Some nodes connect
different ‘modules’

Graphs as generic models for characterization of networks



https://cdv.dei.uc.pt/lisbons-blood-vessels/



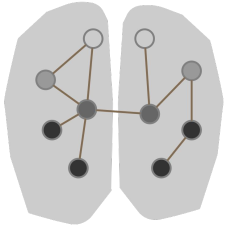


Connectome

Structural description of the

network elements and connections

forming the human brain



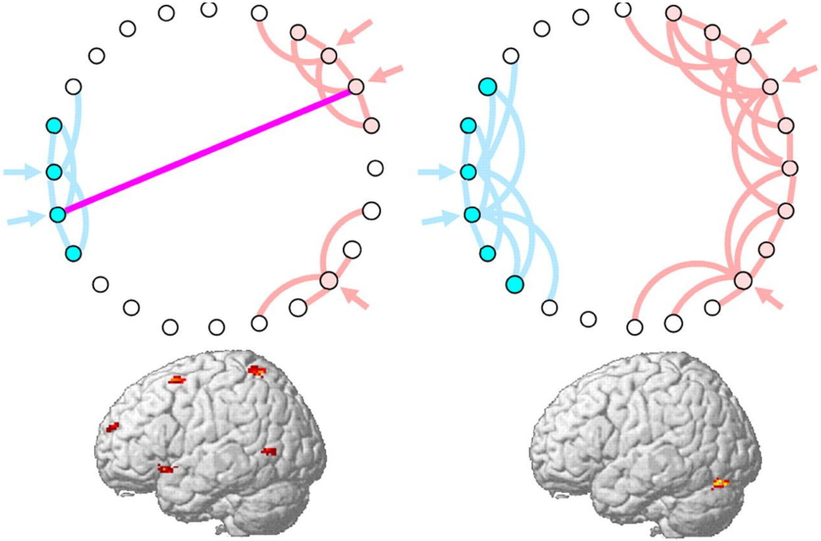
...forms the structure for the...

"understanding of how human cognitive function emerges from neuronal structure and dynamics."

Connectivity and network neuroscience

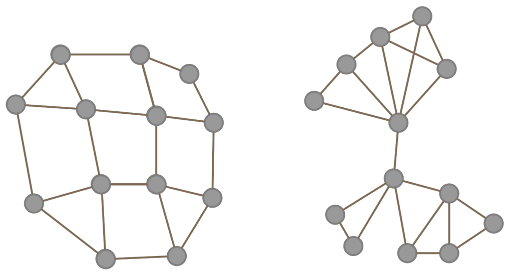
Sporns, O., Tononi, G., & Kötter, R. (2005). The human connectome: A structural description of the human brain. PLoS Computational Biology, 1(4), 0245–0251.

Functional connectivity as a **biomarker - an example**



In the network on the left, a combination of strong local connectivity within delimited groups of neural units and selective long-range connectivity between local groups (…) information can be efficiently represented and efficiently propagated.
The brain images at bottom, from a visual attention task, display distributed patterns of functional activation in the normal brain (left) and abnormally intense and regionally localized activation in the autistic brain (right), a pattern that may stem from such differences at the network level.

The Journal of Neuroscience, October 20, 2004 24(42):9228 –923

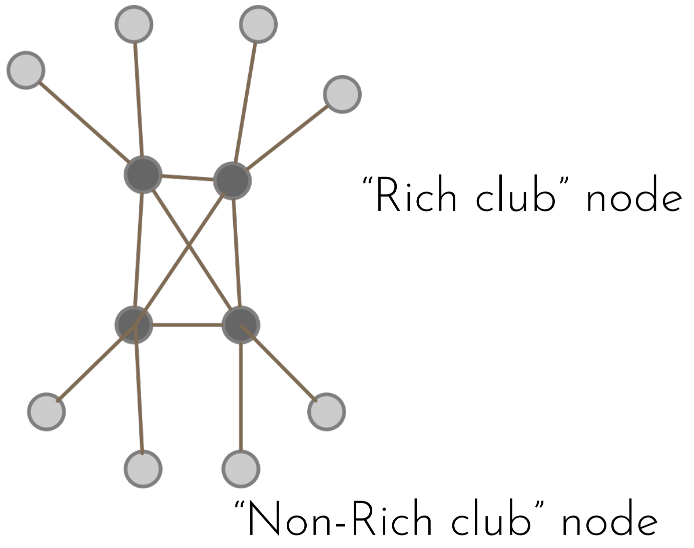


Network analysis - basic concepts and examples

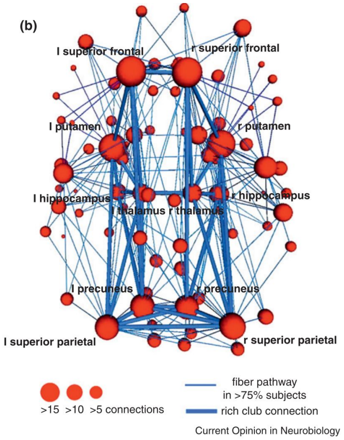
Characterize the connections per node - local vs. global properties of a network

One simple, yet important, local statistic of a node is **centrality**—how influential a node is in the context of the broader network

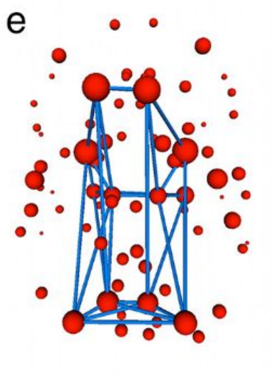
e.g. “**Rich Club**” coefficient
- Network’s hub (high-degree node) **are on average more interconnected** than lower-lower-degree nodes.



Connectome

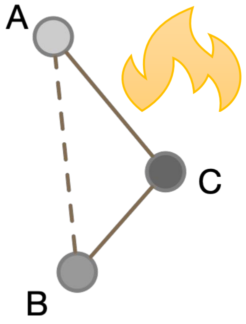


"Almost all regions the brain have at least one link directly to the rich club."



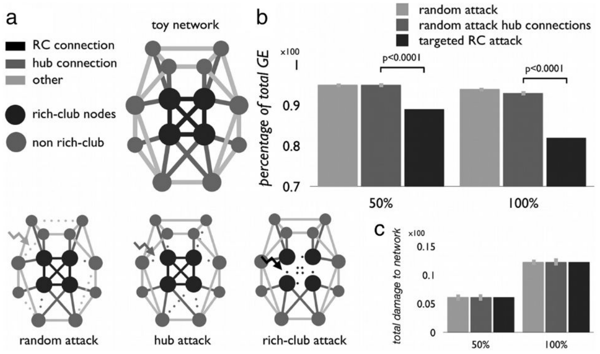
"These **12 hubs** have twice the connections of other brain regions"
"Best connected of all is the precuneus."
(Van den Heuvel, 2011)

Sporns, O. (2013). Network attributes for segregation and integration in the human brain. Current Opinion in Neurobiology, 23(2), 162–171. https://doi.org/10.1016/j.conb.2012.11.015
van den Heuvel, M. P., & Sporns, O. (2011). Rich-Club Organization of the Human Connectome. Journal of Neuroscience, 31(44), 15775–15786.



Targeting connectivity markers in novel interventions - basic concepts and examples

"Attacking" the network and controllability



Differential outcome based on the edge/node "under attack"

nature COMMUNICATIONS

ARTICLE

Received 7 Apr 2015 | Accepted 19 Aug 2015 | Published 1 Oct 2015 DOI: 10.1038/ncomms9414 OPEN

Controllability of structural brain networks

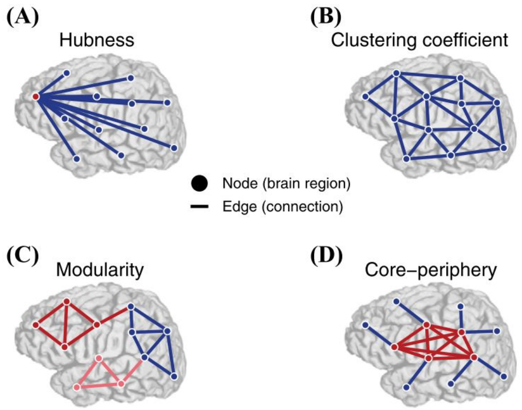
Shi Gu[1,2], Fabio Pasqualetti[3], Matthew Cieslak[4], Qawi K. Telesford[2,5], Alfred B. Yu[5], Ari E. Kahn[2], John D. Medaglia[2], Jean M. Vettel[4,5], Michael B. Miller[4], Scott T. Grafton[4] & Danielle S. Bassett[2,6]

First studies on the controllability - characterization of the nodes/edges in terms of the stability of the system

- ***intervention target?***

van den Heuvel, M. P., & Sporns, O. (2011). Rich-Club Organization of the Human Connectome. Journal of Neuroscience, 31(44),
Gu, S., et al. (2015). Controllability of structural brain networks. Nature Communications, 6, 1–10

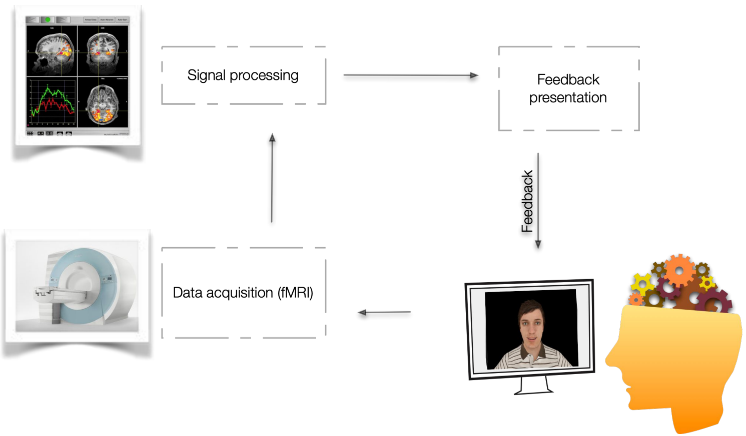
Neurorehabilitation - Fundamental principles of organization



Bassett, D. S., & Khambhati, A. N. (2017). A network engineering perspective on probing and perturbing cognition with neurofeedback. Annals of the New York Academy of Sciences, 1396, 126–143. https://doi.org/10.1111/nyas.13338

Cognitive neuroscience, the potential to use a **perturbative approach like neurofeedback** becomes particularly interesting when viewed in light of the emerging field of **connectomics**.

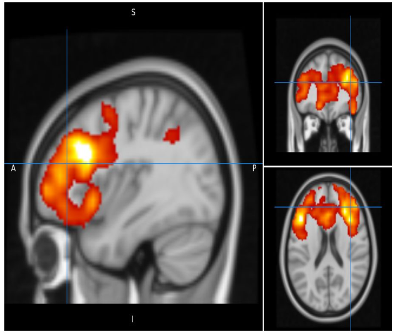
real-time fMRI neurofeedback

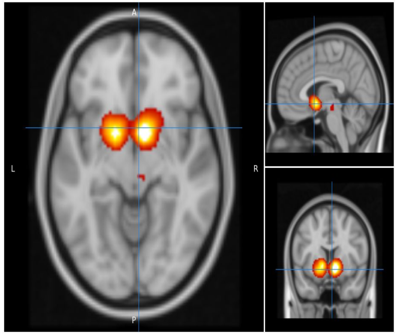


- Uses information from neuroimaging in (pseudo) real-time
  - Allows to present this information to the participant
  - The participants can regulate their own brain activity

Mechanisms and networks involved in NF success

- Cognitive control
  - Feedback monitoring
  - strategy adaptation
- Reinforcement Learning
  - reward mechanisms involved?





Training and self-regulation of brain activity

- Modulation of the activity of specific brain regions and/or neural networks
  - Restore function
    - Improve clinical symptoms
  - Induce changes on impaired underlying mechanisms
  - Optimization / functional reorganization
    - Neuroplasticity

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *The Year in Cognitive Neuroscience*
REVIEW

A network engineering perspective on probing and perturbing cognition with neurofeedback

Danielle S. Bassett[1,2] and Ankit N. Khambhati[1]

The potential to use a perturbative approach like neurofeedback becomes particularly interesting when viewed in light of the emerging field of connectomics.
(…)
manipulating the activity in one area can have nontrivial effects on other areas.

Bassett, D. S., & Khambhati, A. N. (2017). A network engineering perspective on probing and perturbing cognition with neurofeedback. Annals of the New York Academy of Sciences, 1396, 126–143. https://doi.org/10.1111/nyas.13338

rt-fMRI Neurofeedback as an interventional tool

OXFORD

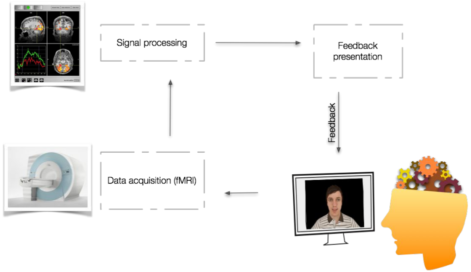
International Journal of Neuropsychopharmacology (2017) 20(10): 769–781

doi:10.1093/ijnp/pyx059
Advance Access Publication: July 17, 2017
Review

REVIEW

Resting-State Functional Connectivity-Based Biomarkers and Functional MRI-Based Neurofeedback for Psychiatric Disorders: A Challenge for Developing Theranostic Biomarkers

Takashi Yamada, MD, PhD; Ryu-ichiro Hashimoto, PhD; Noriaki Yahata, PhD; Naho Ichikawa, MA; Yujiro Yoshihara, MD, PhD; Yasumasa Okamoto, MD, PhD; Nobumasa Kato, MD, PhD; Hidehiko Takahashi, MD, PhD; Mitsuo Kawato, PhD



Study the relationship between **normalizing the biomarker** and **symptom changes** using fMRI-based neurofeedback

RESEARCH ARTICLE

WILEY

Stimulating neural plasticity with real-time fMRI neurofeedback in Huntington's disease: A proof of concept study

Marina Papoutsi[1] | Nikolaus Weiskopf[2,3] | Douglas Langbehn[4] | Ralf Reilmann[5,6] | Geraint Rees[3,7*] | Sarah J Tabrizi[1*]

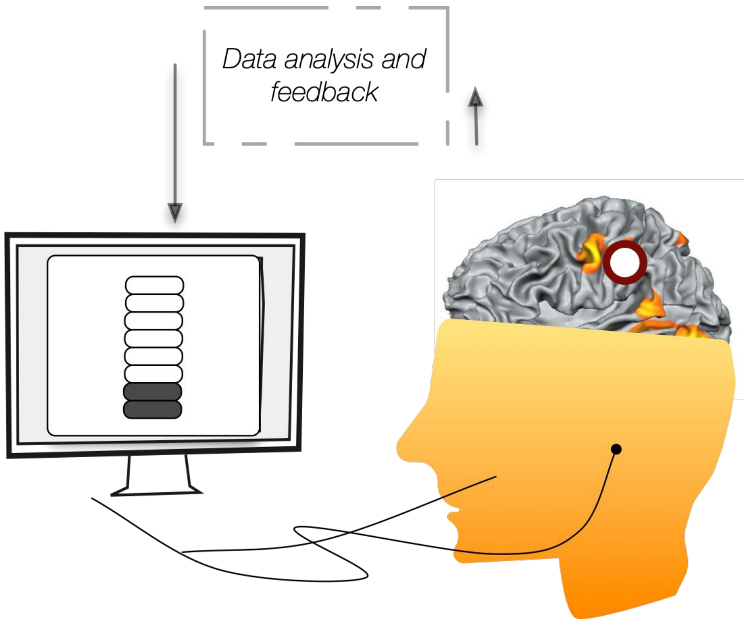
[1]UCL Huntington's Disease Centre, Institute of Neurology, University College London, London, United Kingdom
[2]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
[3]Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London, United Kingdom
[4]Carver College of Medicine, University of Iowa, Iowa City, Iowa
[5]George Huntington Institute and Department of Radiology, University of Muenster, Münster, Germany
[6]Section for Neurodegeneration and Hertie Institute for Clinical Brain Research, University of Tuebingen, Tübingen, Germany
[7]Institute of Cognitive Neuroscience, University College London, London, United Kingdom

Preliminary evidence show **neuroplasticity** associated with neurofeedback training

- not only **target-region specific** but the whole network involved

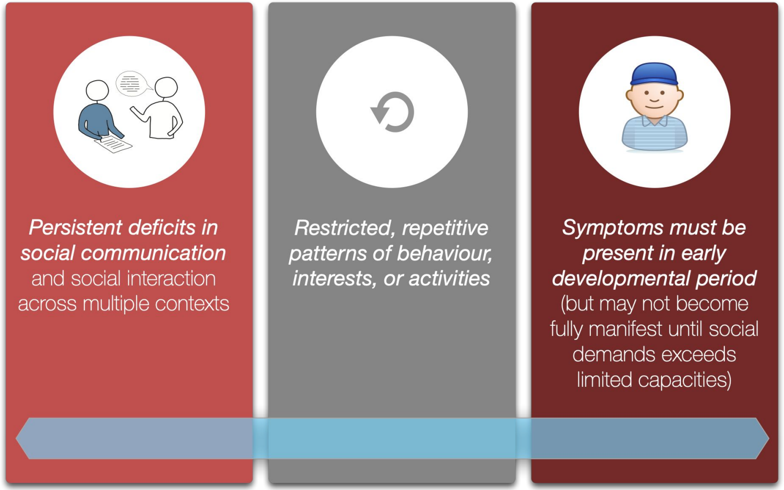
rt-FMRI nf examples

BrainTrain



Assess validity of rt-fMRI neurofeedback in autism

BrainTrain - ASD



main features of ASD

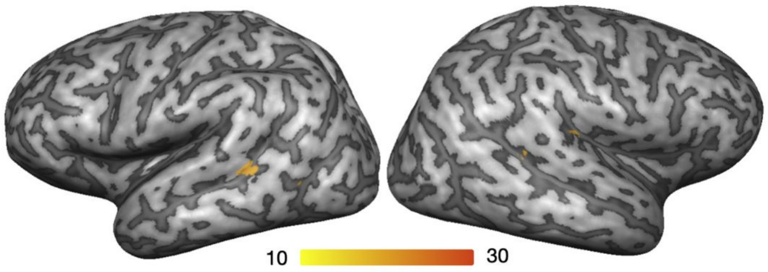
Target brain regions impaired in ASD patients

- face recognition, perception areas (prior work at CIBIT's on social cognition)

- posterior Superior Temporal Sulcus

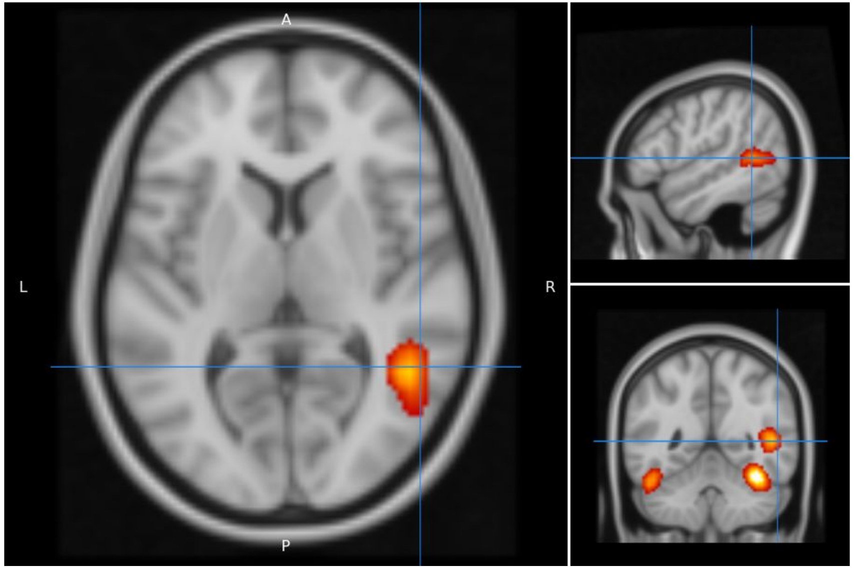
NF-ASD A neurofeedback strategy for the improvement of facial expression recognition/perception in ASD

- Identification, perception and mental imagery of facial expressions
  - Brain activity in areas related to social cognition and facial expression interpretation
    - posterior portion of the superior temporal sulcus (pSTS)



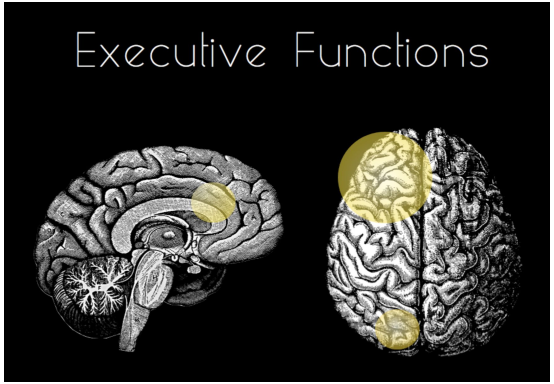
Social cognition, Face processing networks

- Social Cognition Network
  - impairments in ASD



dlPFC as NF target

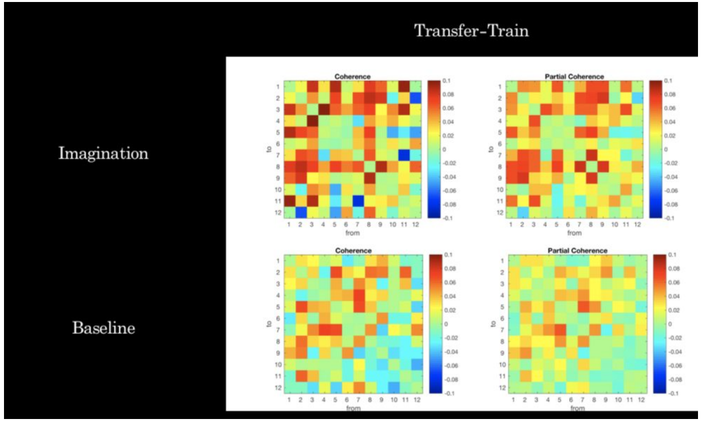
- Neurofeedback-rtfMRI protocol based on the dorsolateral prefrontal cortex (dlPFC), rationale
  - Self-modulation of fronto-parietal network, responsible for Executive Functions (EF)
  - Contribute to improve quality of life in autism, with possible future applications in other mental disorders - EF dysfunction,
- n-back (invert numbers sequence) task
  - EF training in clinical populations
    - Brain region functional impairments and underconnectivity



Pereira, D et al. (in preparation, 2022).

Connectivity analysis

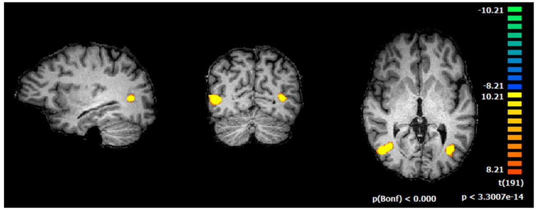
- Connectivity patterns are also quite different in the neurofeedback runs
- Hypothesis: Neurofeedback promotes connectivity

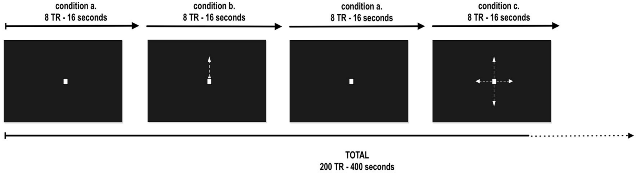


Connectivity matrix between the most important cluster of the EF network during imagination and baseline periods.

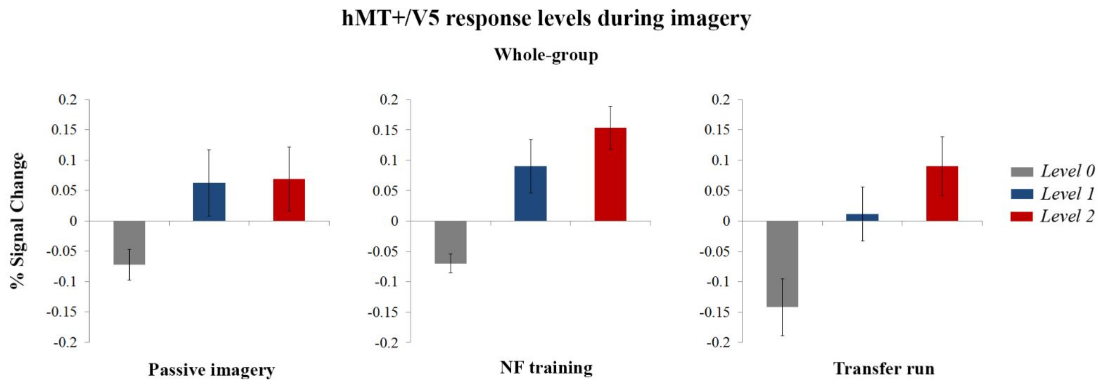
Parametric neurofeedback - exploring level-based control for BCI

- Hypothesis
  - more than two modulation levels can be achieved in a single brain region
  - hMT+/V5 complex
- Participants
  - performed three distinct imagery tasks during neurofeedback training:
    - imagery of a stationary dot, imagery of a dc with two opposing motions and imagery of a dot with four opposing motions.
  - The larger the number of motion alternations, tł higher the expected hMT+/V5 response





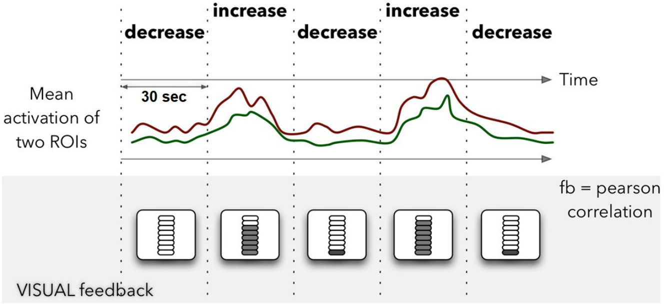
Sousa, T., Direito, B.,et al. (2016). Control of Brain Activity in hMT+/V5 at Three Response Levels Using fMRI-Based Neurofeedback/BCI. Plos One, 11(5)



- 17 (of 20) of participants achieved successful binary level of control
- 12 were able to reach even 3 significant levels of control within the same session,
- it is possible to design a parametric system of control based on activity modulation of a specific brain region with at least 3 different levels.
- Particular imagery task instructions, based on different number of motion alternations, provide feasible achievement of different control levels in BCI and/or neurofeedback applications.

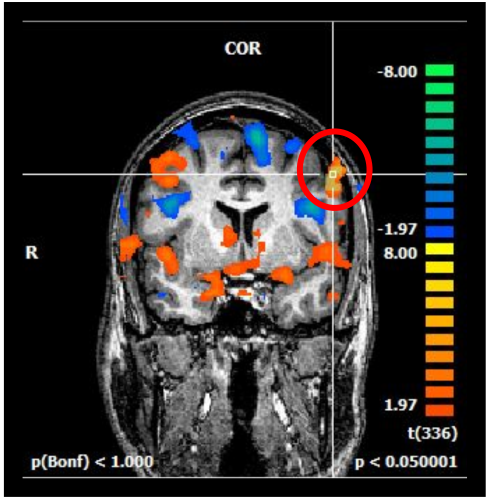
Connectivity-based neurofeedback

- Can we control not only a region but their connectivity?
  - "Functional connectivity measures (…) are emerging as potential intermediate biomarkers for many diseases"
  - "Functional connectivity markers (…) may indeed provide a valuable tool to enhance and monitor learning within an fMRI neurofeedback setup"

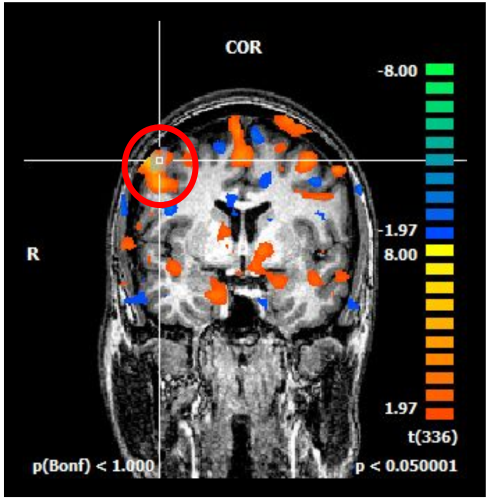


Feedback is based on an 8 point sliding window - Pearson's Correlation Coefficient

Connectivity-based neurofeedback

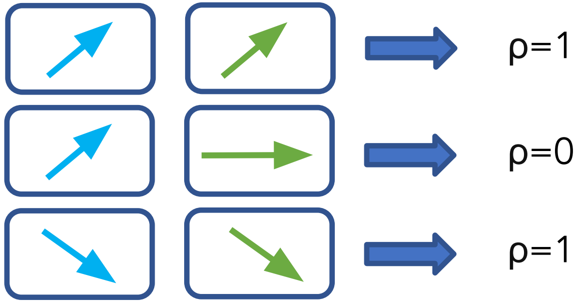


Left
Premotor
Cortex
(lPMC)



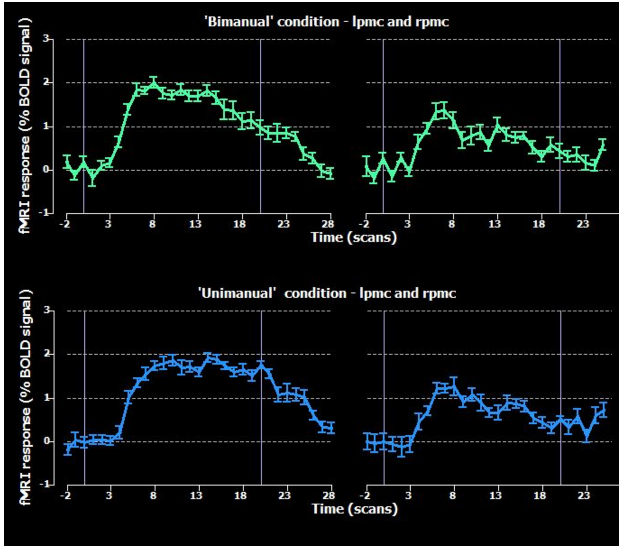
Right
Premotor
Cortex (rPMC)

Motor imagery paradigm

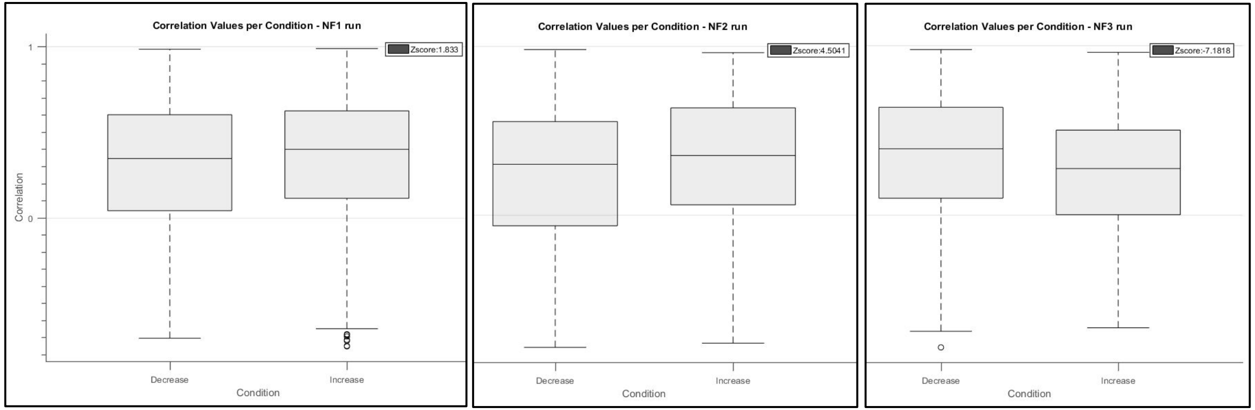


Connectivity-based neurofeedback

Activation patterns



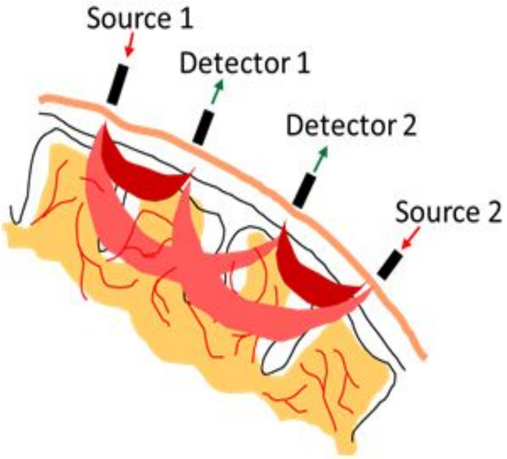
Connectivity patterns

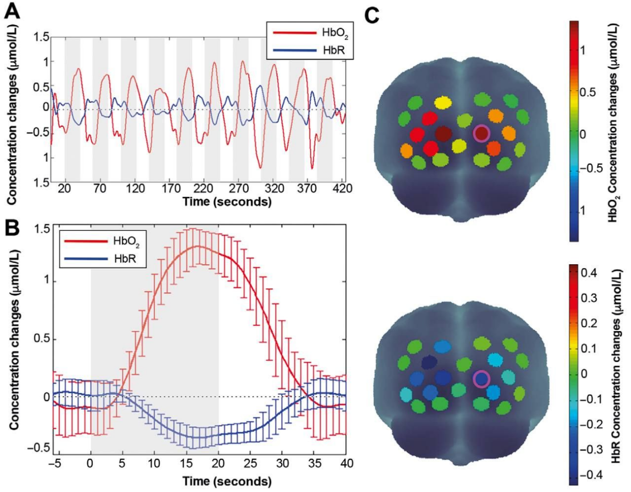


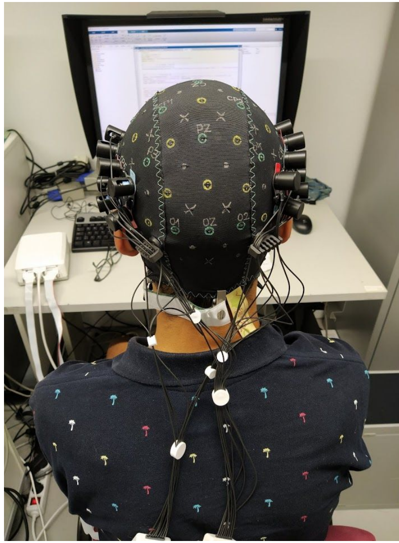
Pereira, J., Direito, B., Sayal, A., Ferreira, C., & Castelo-Branco, M. (2019). Self-Modulation of Premotor Cortex Interhemispheric Connectivity in a Real-Time Functional Magnetic Resonance Imaging Neurofeedback Study Using an Adaptive Approach. Brain Connectivity, 9(9), 662–672. https://doi.org/10.1089/brain.2019.0697

Inducing neuroplasticity in stroke using <u>fNIRS</u>

A low-cost, portable, highly correlated with fMRI, and clinically-friendly <u>optical</u> neuroimaging technique : able to measure the brain's haemodynamic response.

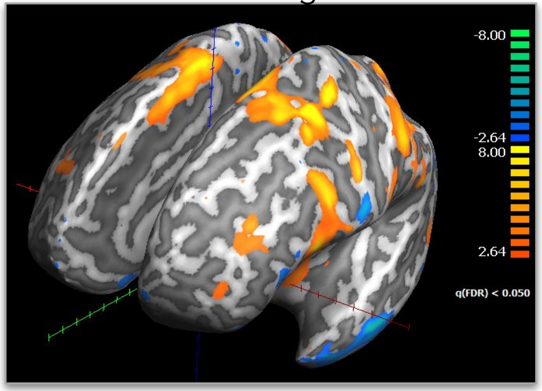


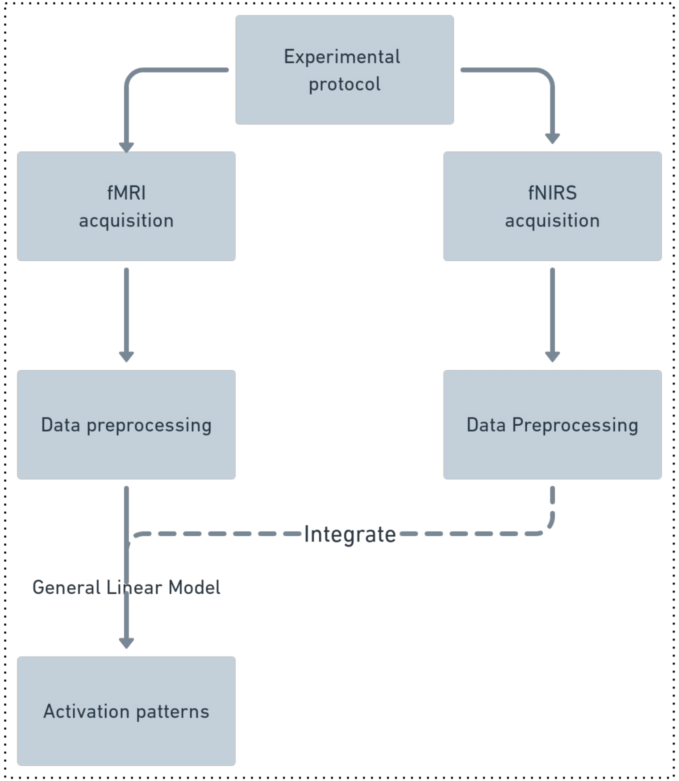




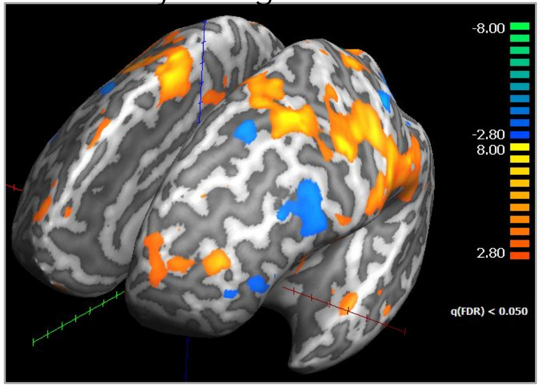
Multimodal fNIRS/fMRI correspondence

BOLD signal

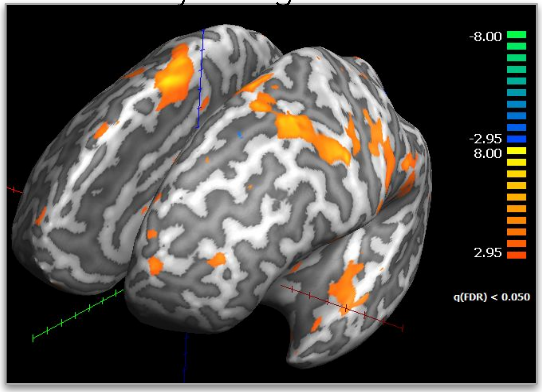




oxyhemoglobin data



deoxyhemoglobin data



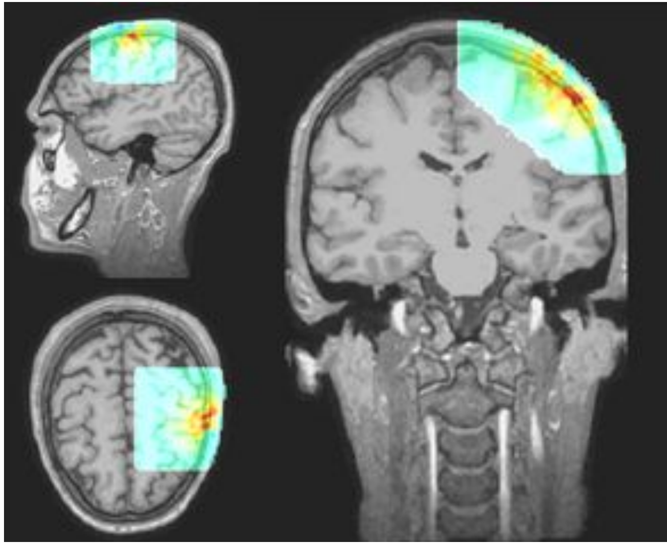
fNIRS as a neuroimaging modality

Advantages

- Safe and non-invasive
- Small, relatively inexpensive technology
- Good temporal resolution
- Correction of noise

Downsides

- Only cortical measures: no whole brain analysis
- Spatial resolution

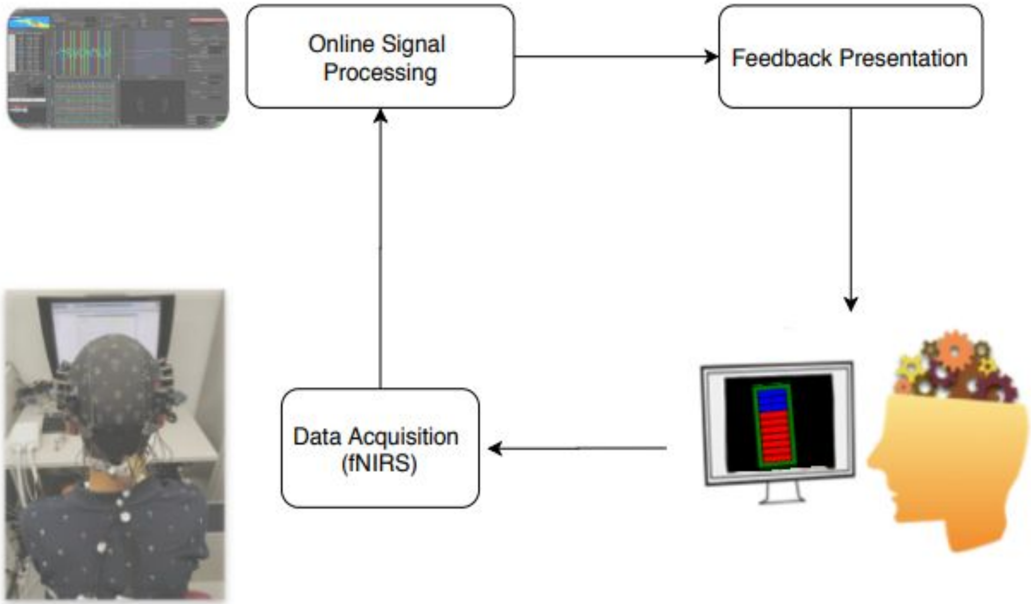


Ferrari, Marco, and Valentina Quaresima. "A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application." Neuroimage 63.2 (2012): 921-935.

What can we get with fNIRS

Source: Nirx Medical Technologies.

fNIRS-based neurofeedback

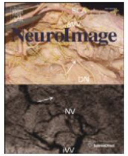


NeuroImage 62 (2012) 2232–2243

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



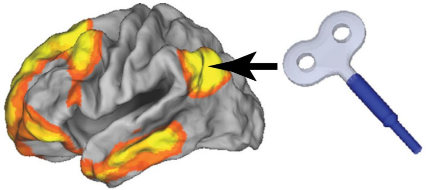
Review

Measuring and manipulating brain connectivity with resting state functional connectivity magnetic resonance imaging (fcMRI) and transcranial magnetic stimulation (TMS)

Michael D. Fox [a,b,*], Mark A. Halko [b], Mark C. Eldaief [b,c], Alvaro Pascual-Leone [b,d]

[a] Partners Neurology Residency, Massachusetts General Hospital, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[b] Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA
[c] Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
[d] Institut Guttmann, Hospital de Neurorehabilitació, Institut Universitari adscrit a la Universitat Autònoma de Barcelona, Barcelona, Spain

"(…)TMS to modulate pathological network interactions identified with resting state fcMRI."



"Inhibitory TMS resulted in pronounced increases in functional connectivity between the stimulation site and the medial temporal lobe"