BCI application in neuroimaging - Neurofeedback

Principles and Organization

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Universidade de Coimbra
Instituto de Ciências Nucleares Aplicadas à Saúde

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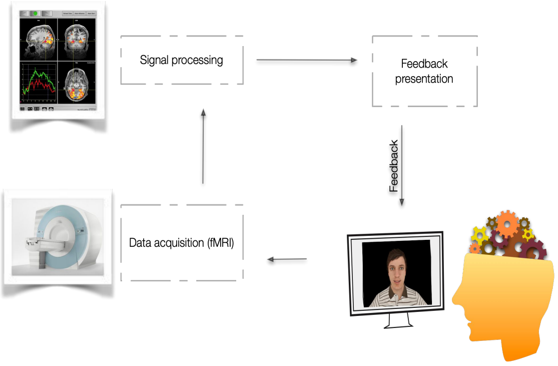
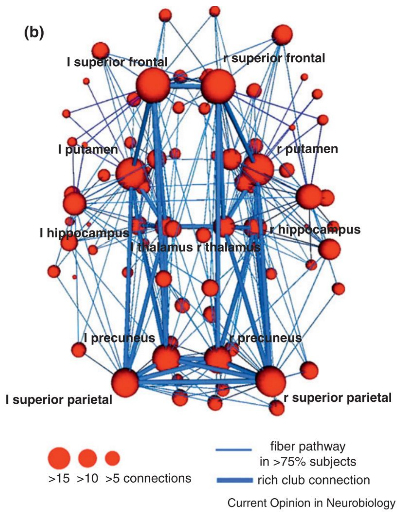
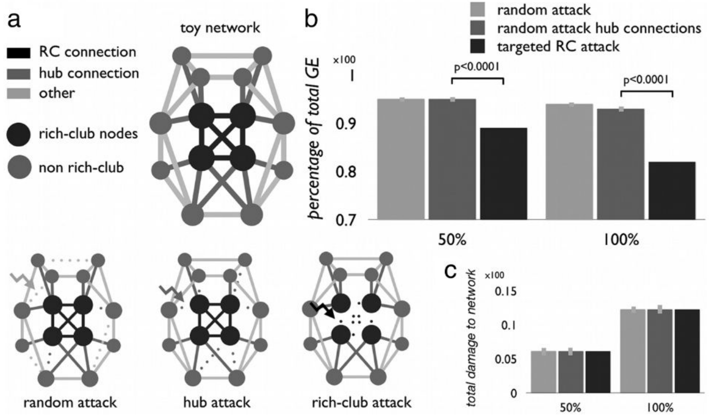
Neurofeedback from a engineering perspective



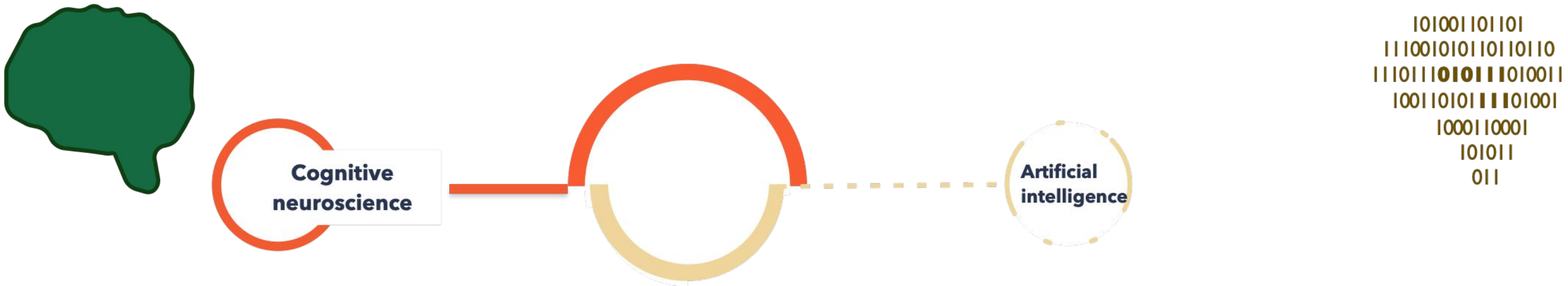




How to define this structure and which node should we consider as a target region?

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

The relationship between cognitive science and artificial intelligence

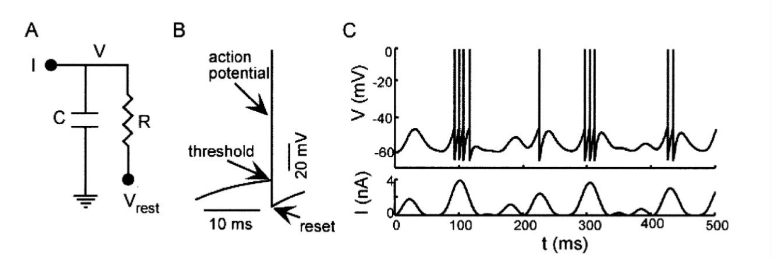


"One of the goals of the cybernetics movement was to find common elements in the functioning of animals and machines."

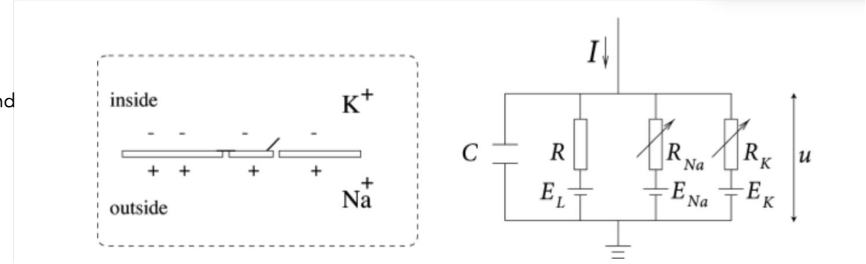
Abraham, T. H. (2002). (Physio)logical circuits: The intellectual origins of the McCulloch-Pitts neural networks. J. Hist. Behav. Sci. 38, 3–25. doi:10.1002/jhbs.1094.

An historical view - neuron model

1907 Lapicque's model



1952 A. L. Hodgkin and A. F. Huxley



An historical view

Attempted to create an alphabet of human thought, each letter of which represented a concept and could be combined and manipulated according to a set of logical rules to compute all knowledge
Gottfried Leibniz

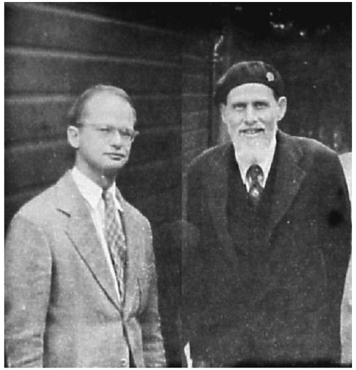
17th century

1910-1913

"Principia Mathematica"
Bertrand Russell, Alfred Whitehead

1943

"A logical calculus of the ideas immanent in nervous activity"
Warren McCulloch
Walter Pitts



McCulloch (right) and Pitts (left) in 1949, source: www.semanticscholar.com

The relationship between cognitive science and artificial intelligence

- The radical story written by McCulloch-Pitts (neurons perform logical calculus) was the first to adapt the principles of computation to mind-body connection
- These notions would support the idea that neural networks can form formal logical systems
- A network can carry out endless computations
  - Basis of the human thought

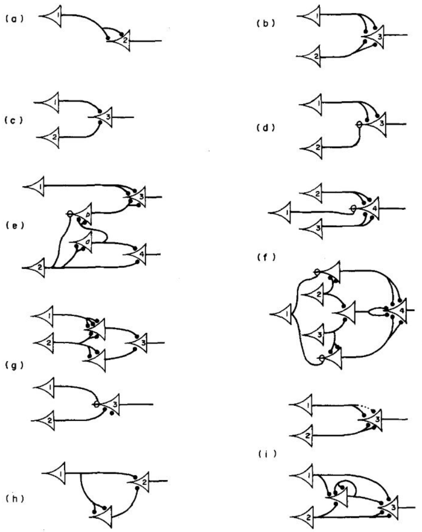


Figure 1. The neuron c_i is always marked with the numeral i upon the body of the cell, and the corresponding action is denoted by "N" with i s subscript, as in the text:

(a) $N_2(t) . \equiv . N_1(t-1);$

(b) $N_3(t) . \equiv . N_1(t-1) \vee N_2(t-1);$

(c) $N_3(t) . \equiv . N_1(t-1) . N_2(t-1);$

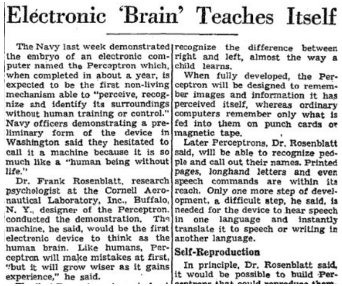
(d) $N_3(t) . \equiv N_1(t-1) . \sim N_2(t-1);$

(e) $N_3(t) : \equiv : N_1(t-1) . \vee . N_2(t-3) . \sim N_2(t-2);$
$N_4(t) . \equiv . N_2(t-2) . N_2(t-1);$

(f) $N_4(t) : \equiv : \sim N_1(t-1) . N_2(t-1) \vee N_3(t-1) . \vee . N_1(t-1).$
$N_2(t-1) . N_3(t-1)$

Abraham, T. H. (2002). (Physio)logical circuits: The intellectual origins of the Mcculloch-Pitts neural networks. J. Hist. Behav. Sci. 38, 3–25. doi:10.1002/jhbs.1094.

Computational models guiding cognitive neuroscience



Electronic 'Brain' Teaches Itself

The Navy last week demonstrated the embryo of an electronic computer named the Perceptron which, when completed in about a year, is expected to be the first non-living mechanism able to "perceive, recognize and identify its surroundings without human training or control." Navy officers demonstrating a preliminary form of the device in Washington said they hesitated to call it a machine because it is so much like a "human being without life."

Dr. Frank Rosenblatt, research psychologist at the Cornell Aeronautical Laboratory, Inc., Buffalo, N. Y., designer of the Perceptron, conducted the demonstration. The machine, he said, would be the first electronic device to think as the human brain. Like humans, Perceptron will make mistakes at first, "but it will grow wiser as it gains experience," he said.

recognize the difference between right and left, almost the way a child learns.

When fully developed, the Perceptron will be designed to remember images and information it has perceived itself, whereas ordinary computers remember only what is fed into them on punch cards or magnetic tape.

Later Perceptrons, Dr. Rosenblatt said, will be able to recognize people and call out their names. Printed pages, longhand letters and even speech commands are within its reach. Only one more step of development, a difficult step, he said, is needed for the device to hear speech in one language and instantly translate it to speech or writing in another language.

Self-Reproduction

In principle, Dr. Rosenblatt said, it would be possible to build Perceptrons that could reproduce them-

1958

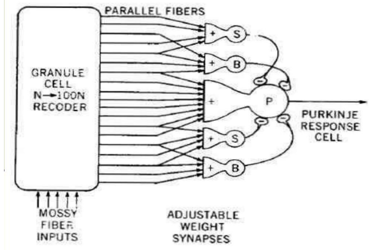
"Electronic brain teaches itself"
Perceptron, Frank Rosenblatt

Function emerges from a network (distributed across its neurons and connections between them)

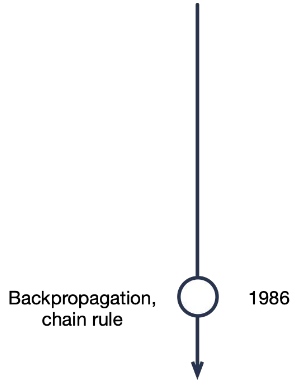
1971

Perceptron at work, the cerebellum model (James Albus).

Model of Cerebellar Perceptron, James Albus 1971

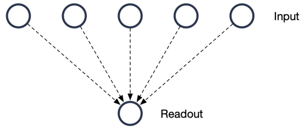


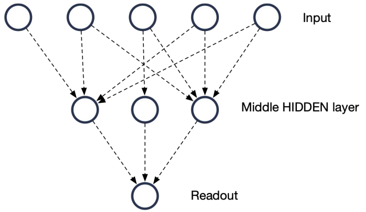
Cognitive neuroscience guiding computational intelligence



- Intelligence and learning needs more than one layer
  - Generalization capability, memory etc.
  - Hidden layers
    - An additional layer would allow some generalization

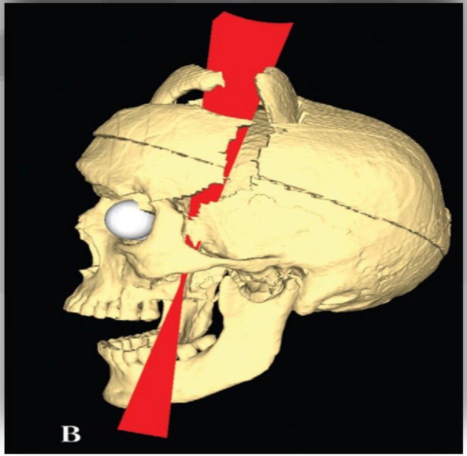
But how about *learning?*
Backpropagation



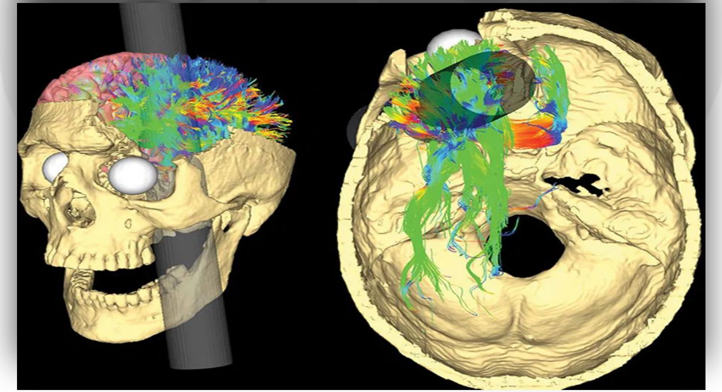


Fundamental principles of organization

Segregation



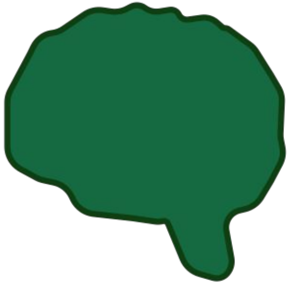
Integration



van Horn, J. D., et al.(2012). Mapping connectivity damage in the case of phineas gage. PLoS ONE, 7(5). https://doi.org/10.1371/journal.pone.0037454

From a "segregation" viewpoint toward,

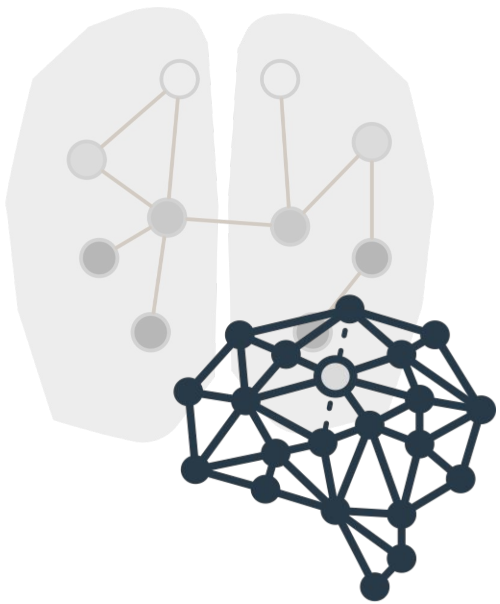
"In the past decade functional neuroimaging has been (…) successful in establishing functional segregation as a principal of organization (…).
Functional segregation is inferred by the presence of activation foci in change score or statistical parametric maps."
Friston (1994)



"A notion of cortical function has prevailed in which different parts specialize in performing particular processing of the sensory input".
Zamora-López et al. (2011)

Friston, K. J. (1994). Functional and effective connectivity: A synthesis. Human Brain Mapping, 2, 56–78
Zamora-López, G., Zhou, C., & Kurths, J. (2011). Exploring brain function from anatomical connectivity. Frontiers in Neuroscience, 5, 1–11

To an integrated view of the brain.



"Newer approaches have addressed the integration of functionally specialized areas through characterizing neurophysiological activations in terms of distributed changes."

Friston (1994)

"This proposal ***rejects*** a single anatomical site for the integration of memory and motor processes and a single store for the meaning of entities of events."

Damasio (1989)

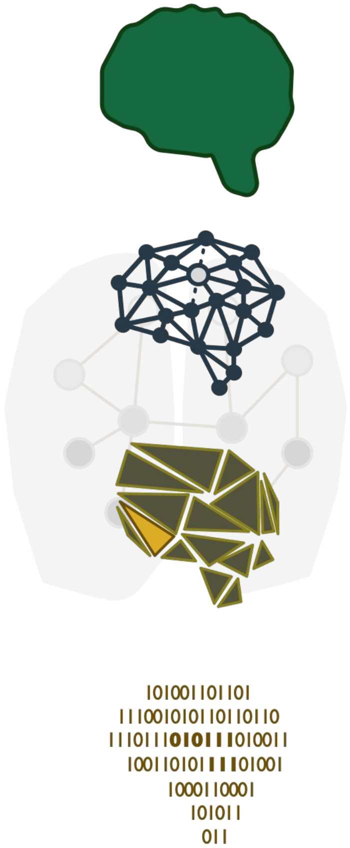
Friston, K. J. (1994). Functional and effective connectivity: A synthesis. Human Brain Mapping, 2, 56–78

Damasio, A. (1989). Time-locked multiregional retroactivation: a systems-level proposal for the neural substrates of recall and recognition. Cognition, 33(1–2), 25–62.

To an integrated view of the brain.

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

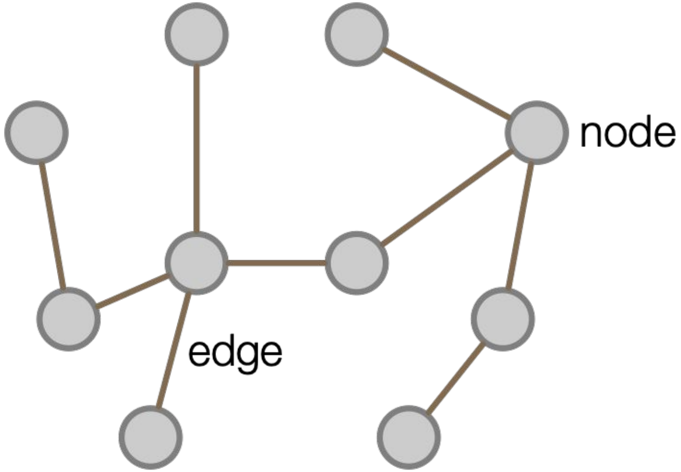
These systems, also known as Non-linear dynamical systems, cannot be predicted looking at specific components of the systems - they have emergent properties from the whole, connected components- consciousness or thought is the most relevant in humans.



Network Neuroscience

Modeling networks as graphs

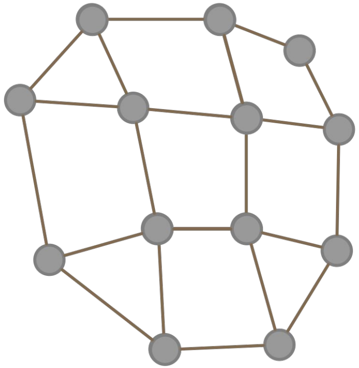
Networks can be modeled as graph of nodes connected by edges

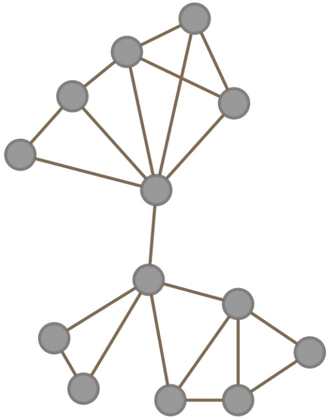


nodes. Represent basic units - structural, functional, processing units (e.g. neuron or population of neurons)

edges. Represent the interactions between units or nodes (structural or functional connection between units)

Graph theory - Exploring *network structure*

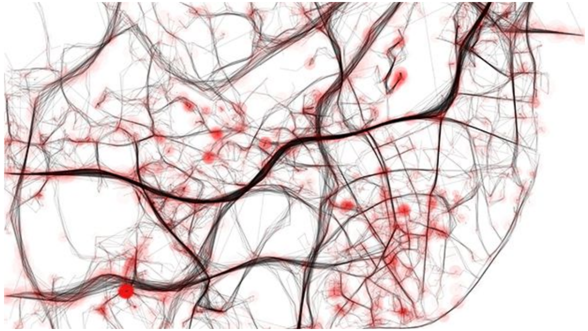




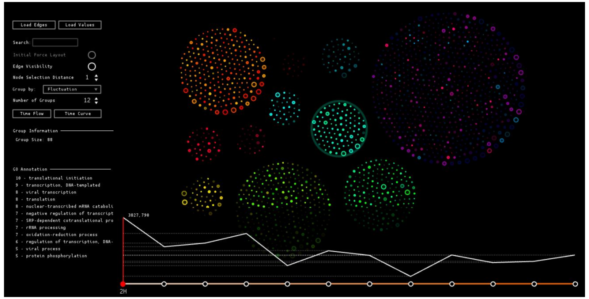
most nodes are connected with 3/4 other nodes

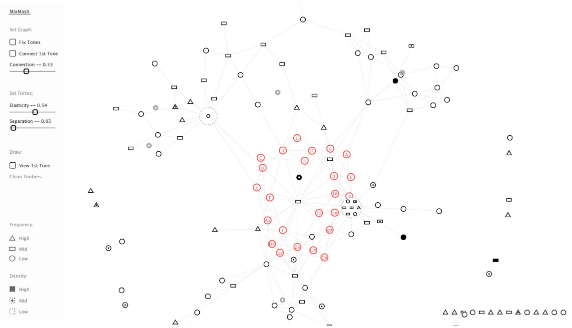
Some nodes connect different ‘modules’

Graphs as generic models for characterization of networks

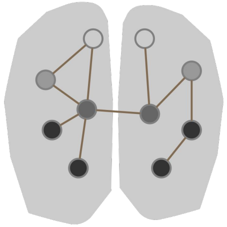


https://cdv.dei.uc.pt/lisbons-blood-vessels/





Connectome
Structural description of
the **network elements and connections**
forming the human brain



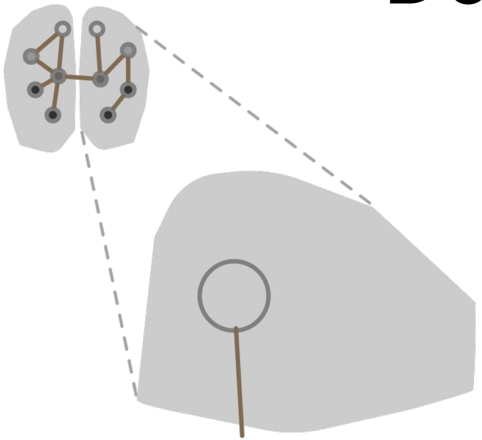
…forms the structure for the…

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

Connectivity and network neuroscience

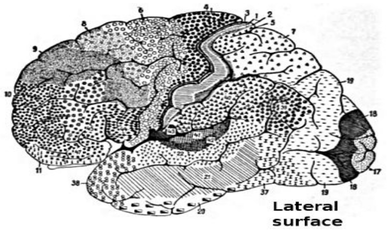
Sporns, O., Tononi, G., & Kötter, R. (2005). The human connectome: A structural description of the human brain. PLoS Computational Biology, 1(4), 0245–0251.

Defining network **nodes**

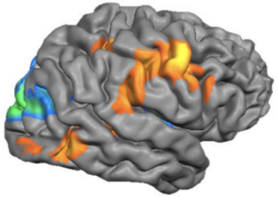


Spatially constrained,
intrinsically homogeneous and
extrinsically distinct

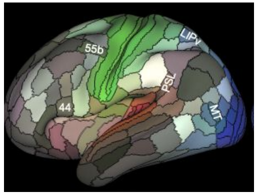
(e.g. functional, statistical,
anatomical/cytoarchitecture arguments,
multi-modal)



Brodmann areas -
citoarchitecture



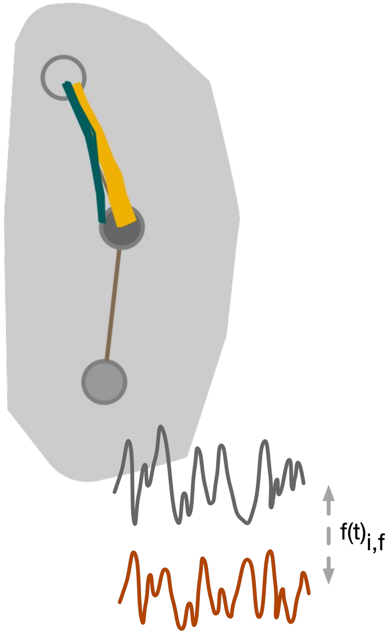
Functional-Probabilistic



Multi-modal (Glasser et al., 2016)

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

Exploring network **edges** meaning



Friston, K. J. (1994). Functional and effective connectivity: A synthesis. Human Brain Mapping, 2, 56–78

Structural connectivity

Described by physical connections between regions

- directionality cannot be resolved via data analysis (e.g. Diffusion-Weighted Imaging - DWI)

Functional connectivity

Statistical dependence between neurophysiological signals

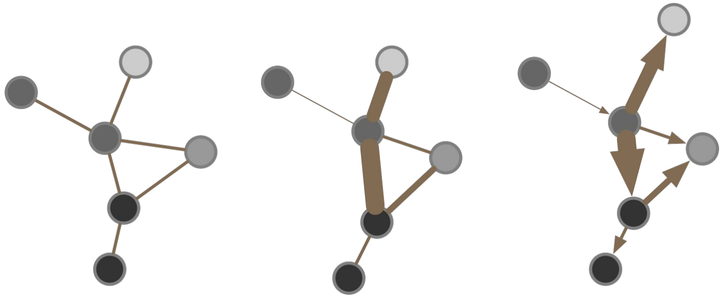
- can be directed or undirected

Effective connectivity

Influence that one node exerts over another (model-based fitting of signals)

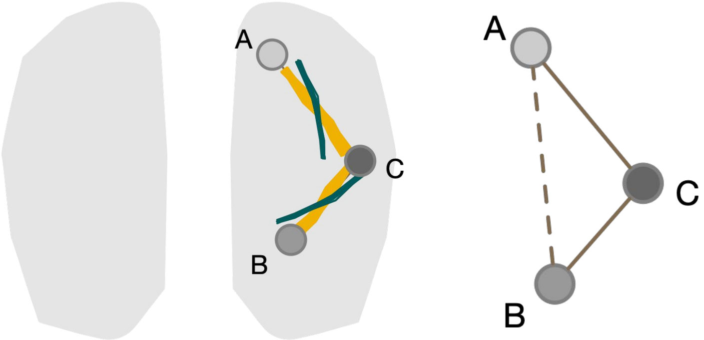
- *causal* interaction (e.g. dynamic causal modeling)

Exploring network **edges** meaning

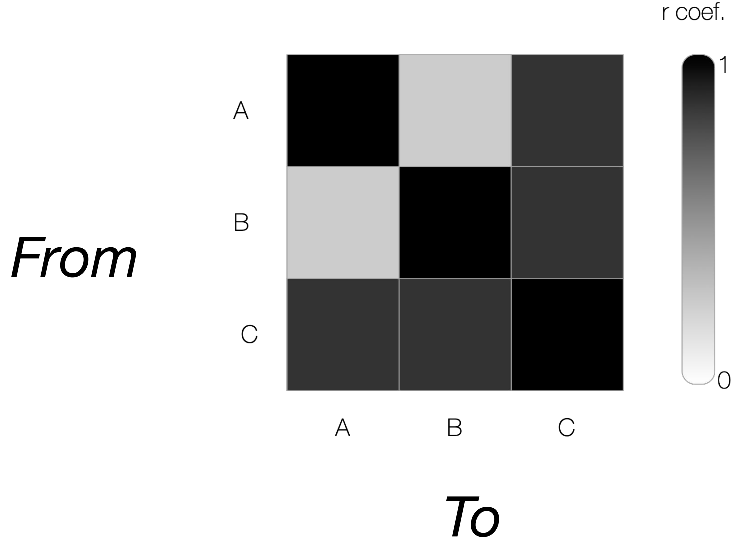


Weights	Binary	Weighted	Weighted
Direction	Undirected	Undirected	Directed

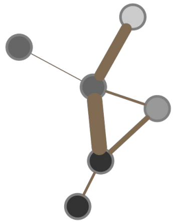
Graphical representation of Functional connectivity - graph or connectivity matrix

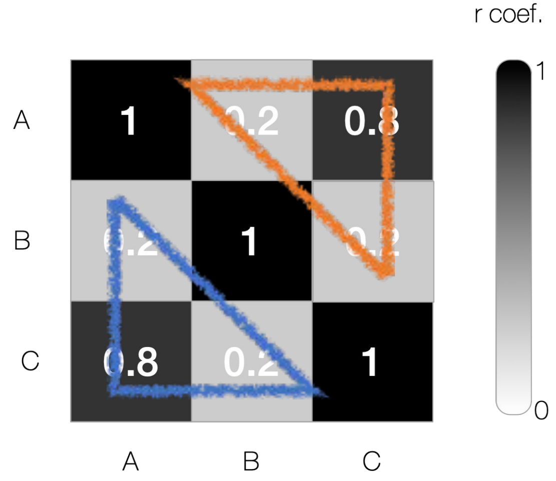


Adjacency /connectivity matrix



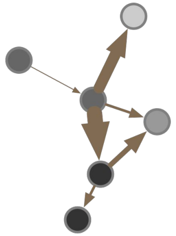
Functional connectivity as a **graph - directed vs. undirected network**

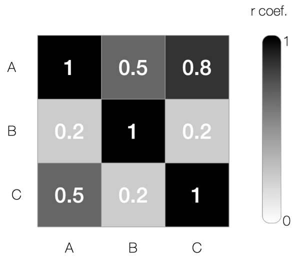




The upper triangle of the matrix is located above the diagonal

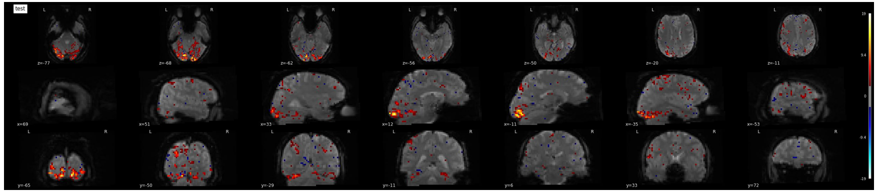
In an **undirected** network, **the upper and lower triangles are identical** - the matrix is **symmetric**
Aij=Aji



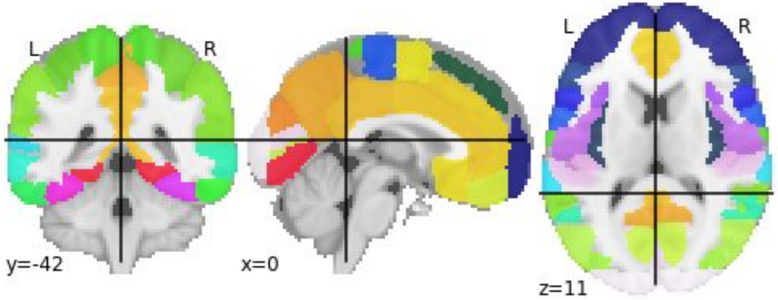


In a directed network, the upper and lower triangles may not be equal - the matrix is asymmetric

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



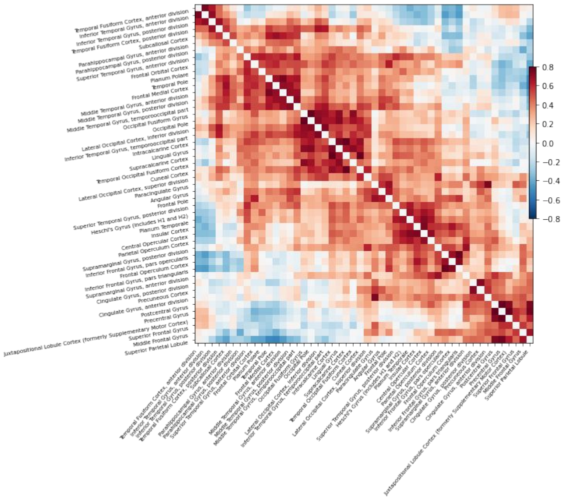
Identify nodes - e.g. functional/Anatomical masks



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

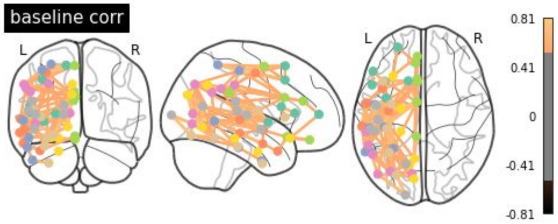
Rest

Phonologic task

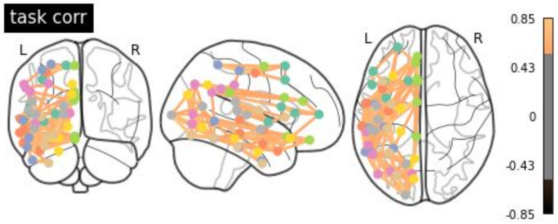


Functional connectivity as a **graph - an example**

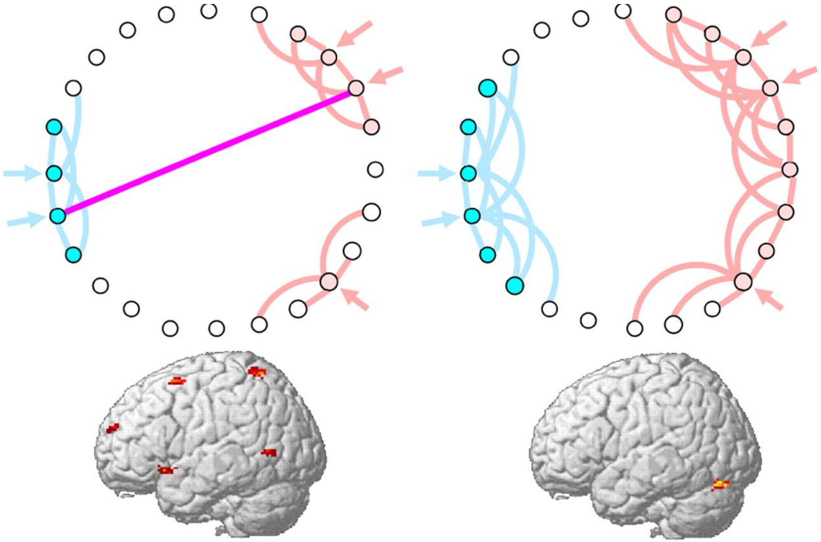
Rest



Phonologic task

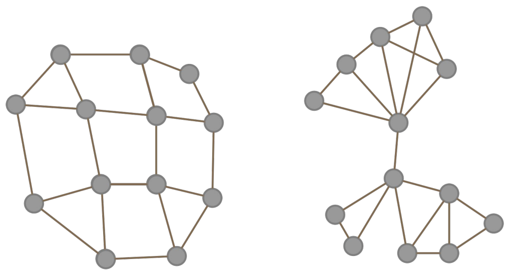


Functional connectivity as a **biomarker - an example**



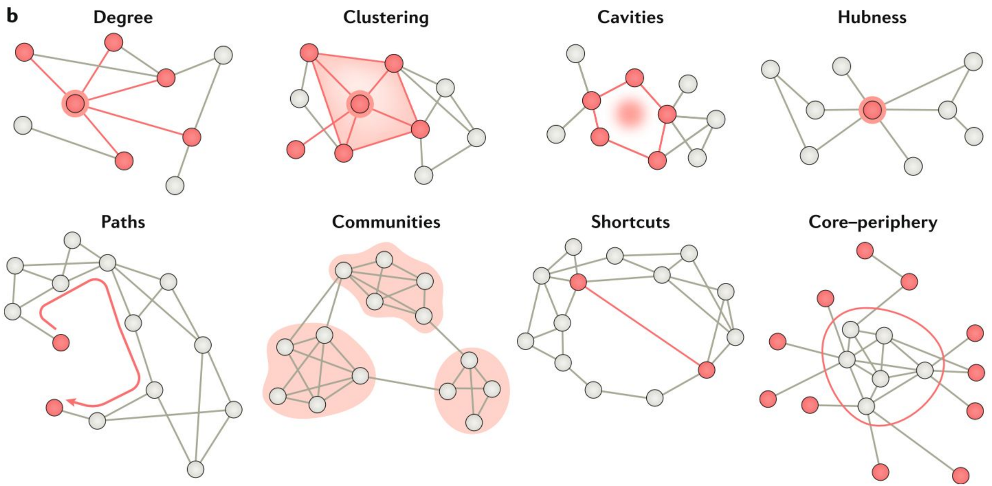
In the network on the left, a combination of strong local connectivity within delimited groups of neural units and selective long-range connectivity between local groups (...) information can be efficiently represented and efficiently propagated.
The brain images at bottom, from a visual attention task, 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

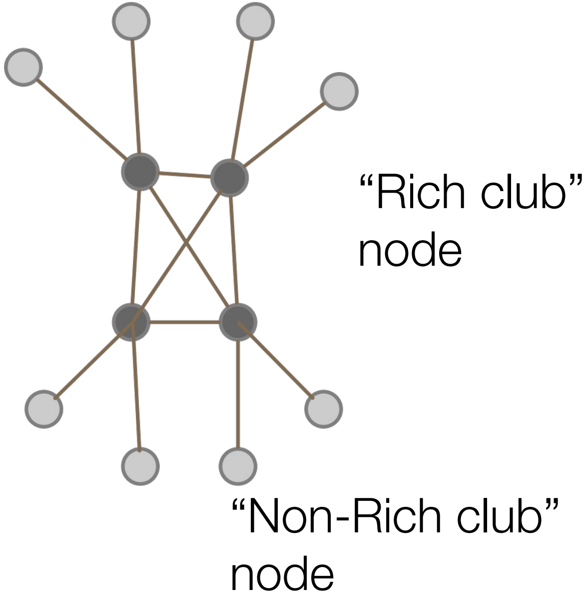
Common measures of interest in **Network Analysis**



Bassett, D. S., Zurn, P., and Gold, J. I. (2018). On the nature and use of models in network neuroscience. Nat. Rev. Neurosci. 19, 566–578. doi:10.1038/s41583-018-0038-8.

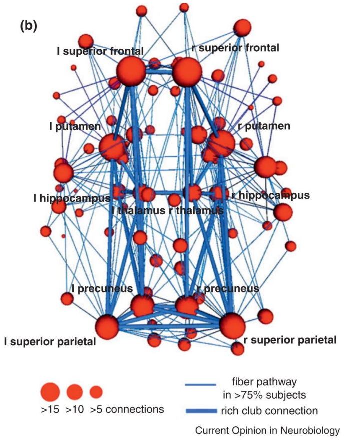
Characterize the connections per node - local vs. global properties of a network

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

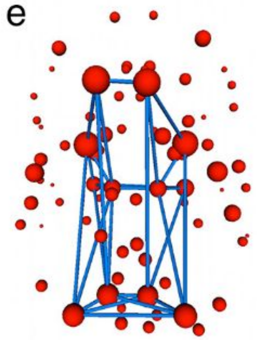


e.g. “**Rich Club**” coefficient
- Network’s hub (high-degree node) **are on average more interconnected** than lower-lower-degree nodes.

Connectome

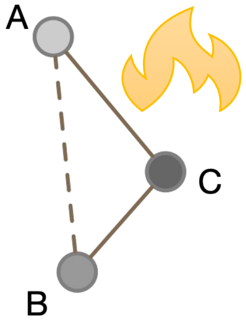


“Almost all regions the brain have at least one link directly to the rich club.”



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

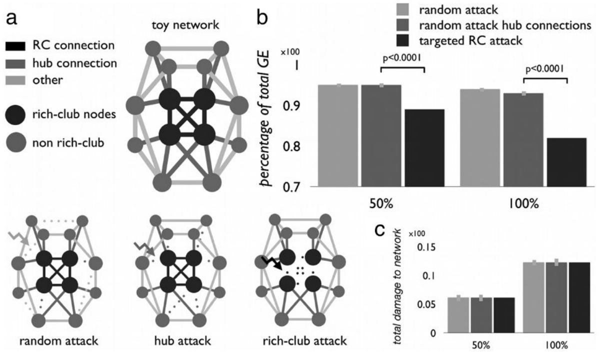
Sporns, O. (2013). Network attributes for segregation and integration in the human brain. Current Opinion in Neurobiology, 23(2), 162–171. https://doi.org/10.1016/j.conb.2012.11.015
van den Heuvel, M. P., & Sporns, O. (2011). Rich-Club Organization of the Human Connectome. Journal of Neuroscience, 31(44),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

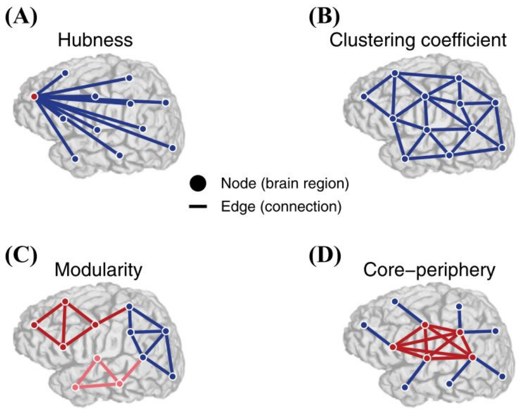
Controllability of structural brain networks

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

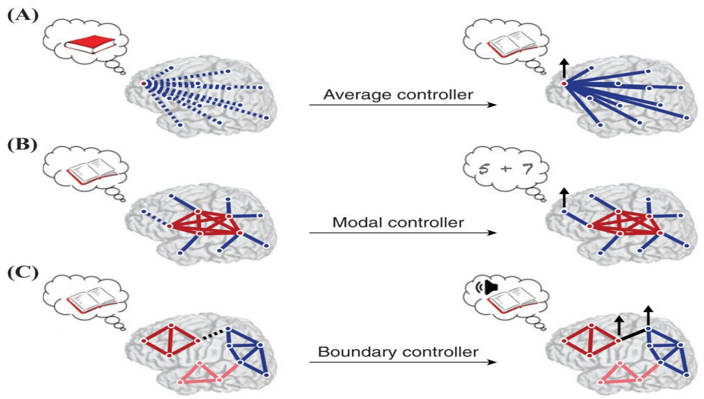
Neurorehabilitation - Fundamental principals of organization



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.**

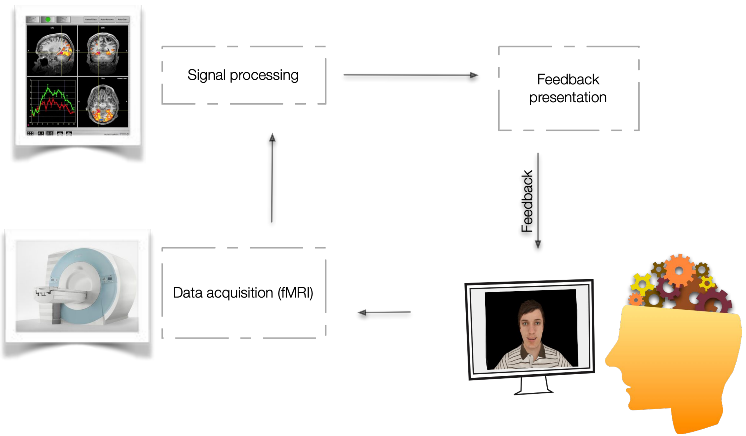
Network control and perturbing cognition with neurofeedback



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

- Definition of the network - neural basis of behavior
- Biomarker of impairment (e.g. ASD)

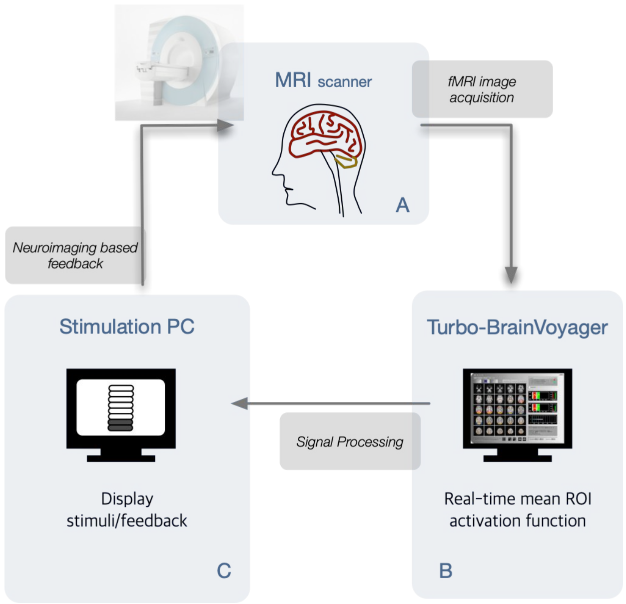
real-time fMRI neurofeedback



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

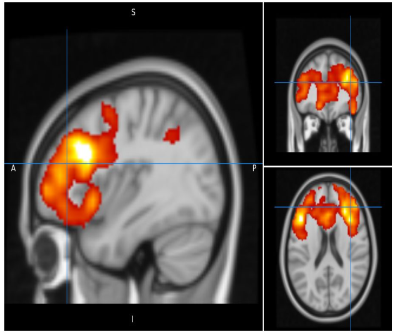
real-time fMRI neurofeedback setup

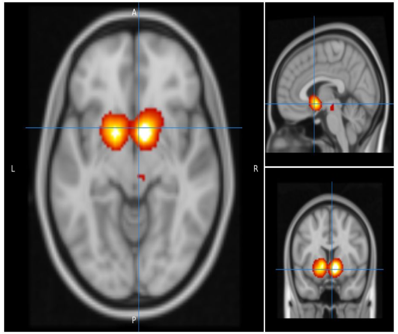
- Acquisition equipment (A)
  - MRI scanner (3T Siemens Magnetom TimTrio - Prisma update recently)
    - Collecting and saving data in a network shared folder
- Accessed by Turbo Brain-Voyager (BrainInnovation, Maastricht, Netherlands) software (B)
  - Data preprocessing (3D motion correction) and real-time statistical analysis (online GLM - General Linear Model)
- Subsystem (C) is responsible for the computation of neuroimaging-based feedback



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

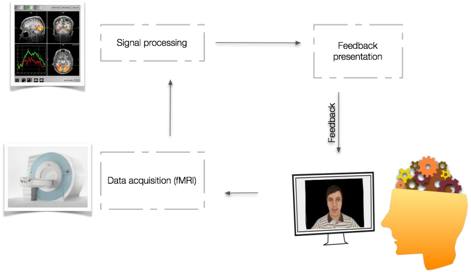
International Journal of Neuropsychopharmacology (2017) 20(10): 769–781

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

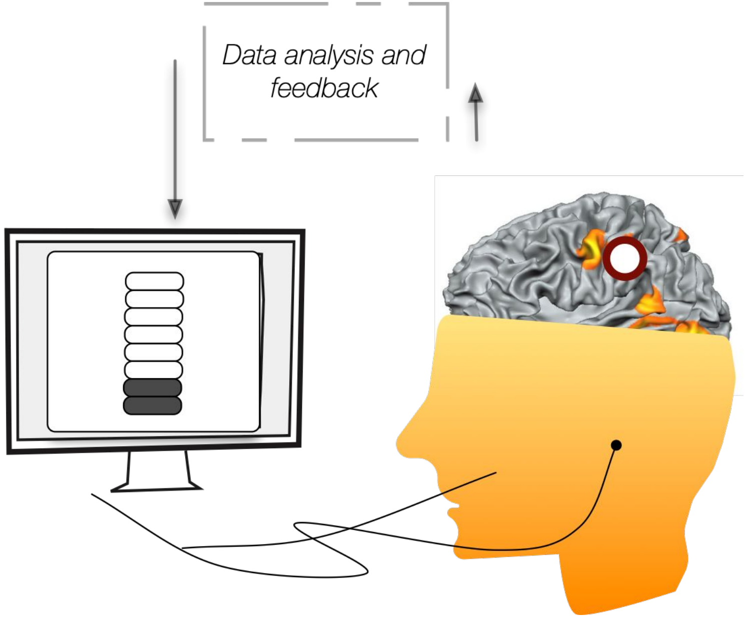
[7]Institute of Cognitive Neuroscience, University College London, London, United Kingdom

Preliminary evidence show neuroplasticity associated with neurofeedback training

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

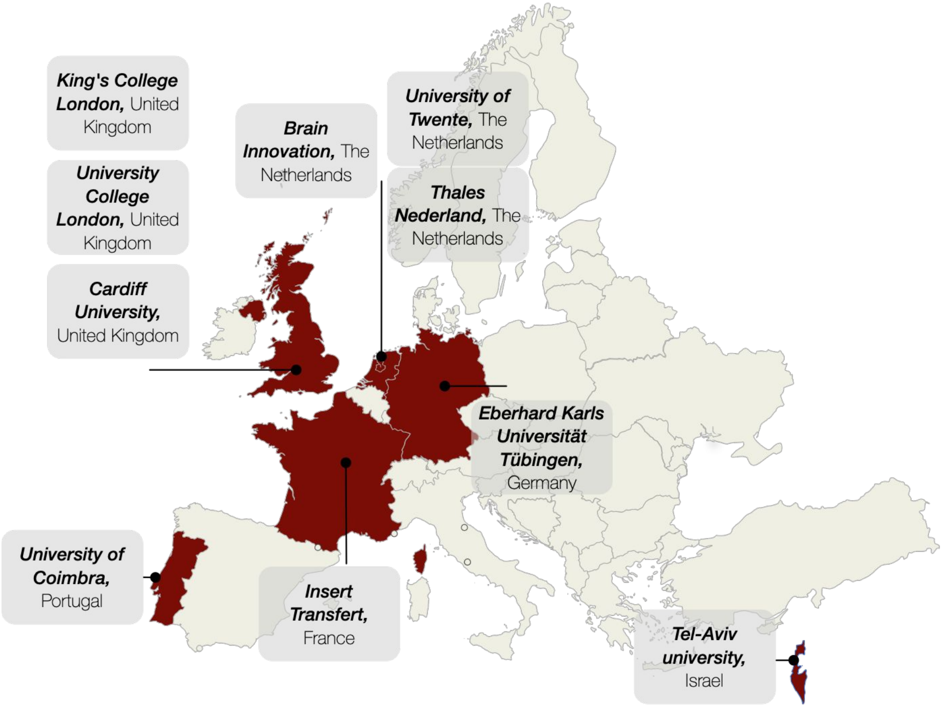
rt-FMRI nf examples

BrainTrain

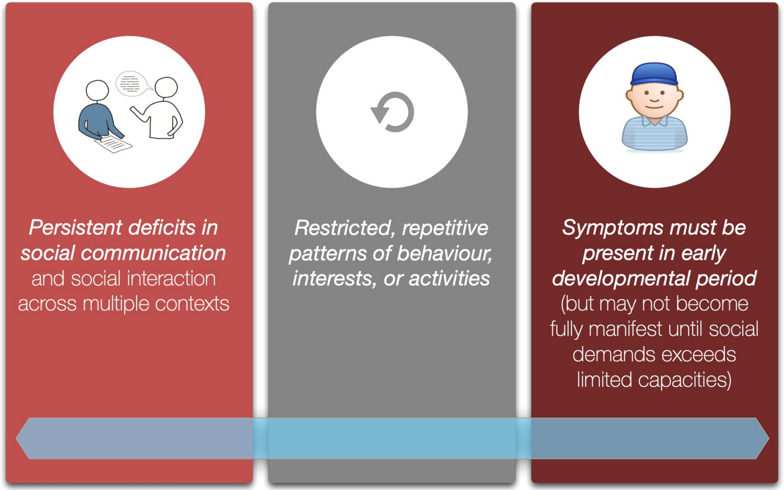


Assess validity of rt-fMRI neurofeedback in autism

BrainTrain Taking imaging into the therapeutic domain: Self-regulation of brain systems for mental disorders



BrainTrain - ASD



main features of ASD

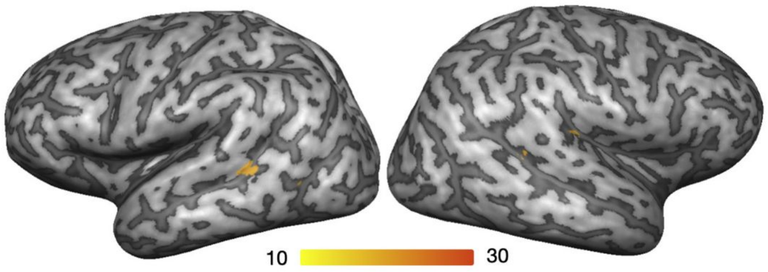
Target brain regions impaired in ASD patients

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

    - posterior Superior Temporal Sulcus

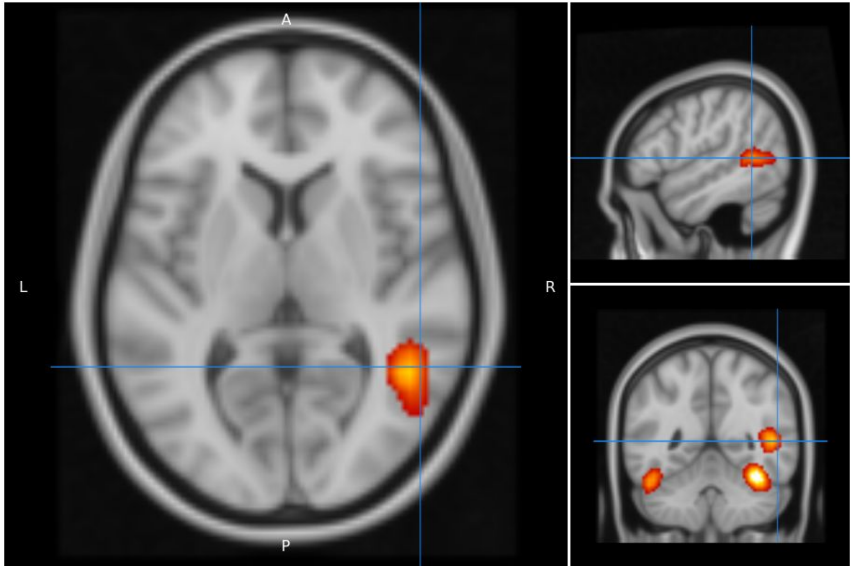
NF-ASD A neurofeedback strategy for the improvement of facial expression recognition/perception in ASD

- 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)



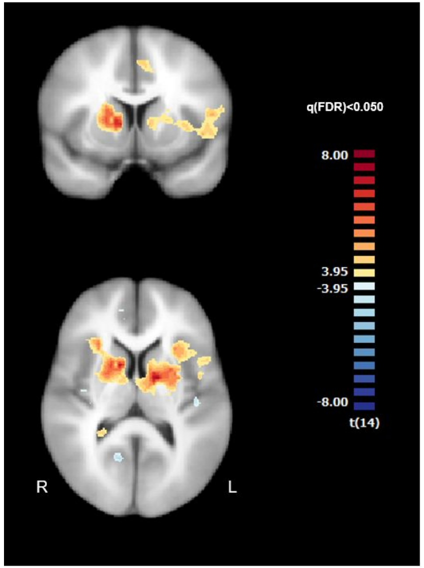
Social cognition, Face processing networks

- Social Cognition Network
  - impairments in ASD



Whole brain analysis of neurofeedback runs

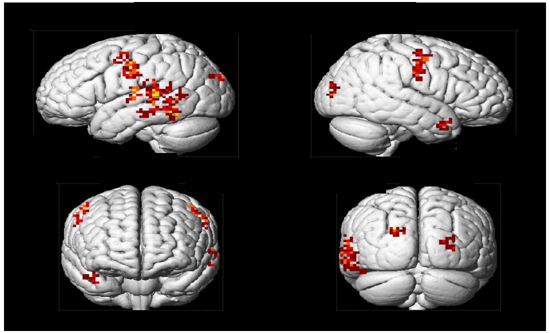
- GLM analysis (15 patients)
  - Active imagery periods vs. baseline
    - Active regions
      - anterior insula
      - caudate,
      - medial prefrontal cortex (MPFC)
      - anterior cingulate cortex (ACC)

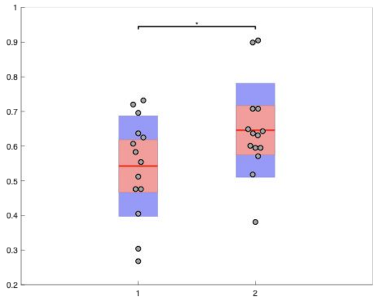


RFX-GLM, FDR corrected (p<0.05)

Basis of Neural activation of facial expressions imagery

- Identifying the neural basis of facial expression imagery
  - Accuracy **before /after** neurofeedback training increased

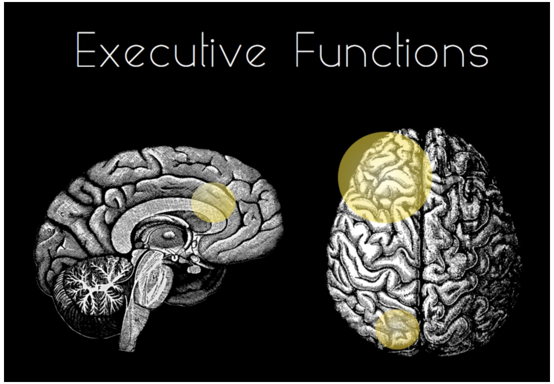




Direito et al., in preparation

dlPFC as NF target

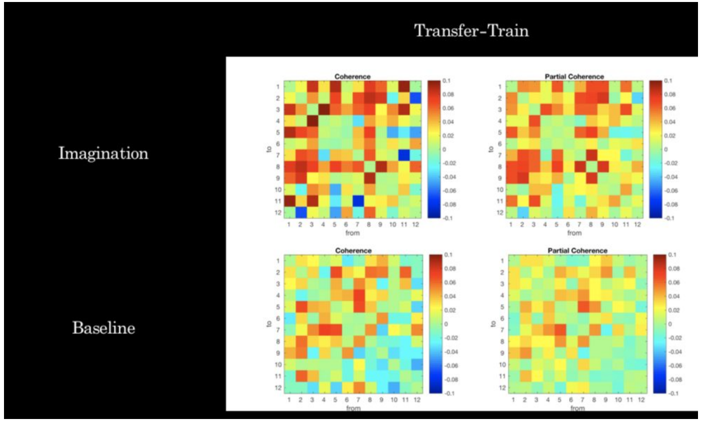
- Neurofeedback-rtfMRI protocol based on the dorsolateral prefrontal cortex (dlPFC), rationale
  - Self-modulation of fronto-parietal network, responsible for Executive Functions (EF)
  - Contribute to improve quality of life in autism, with possible future applications in other mental disorders - EF 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

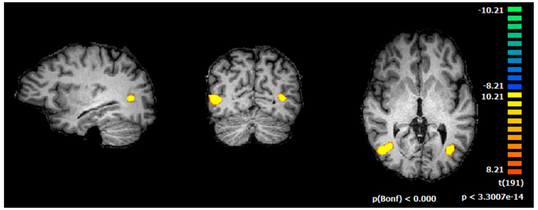
- Connectivity patterns are also quite different in the neurofeedback runs
- Hypothesis: Neurofeedback promotes connectivity

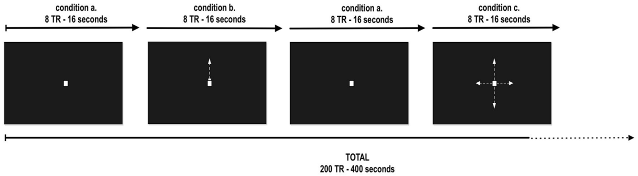


Connectivity matrix between the most important cluster of the EF network during imagination and baseline periods.

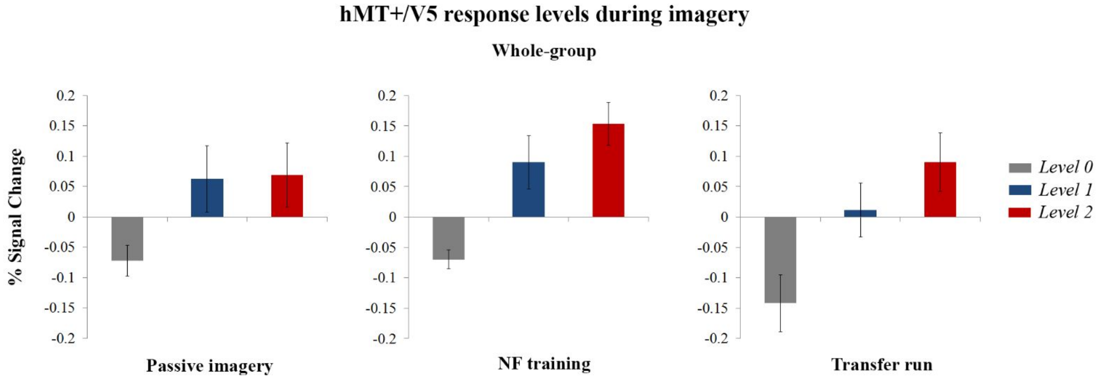
Parametric neurofeedback - exploring level-based control for BCI

- 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 dot with two opposing motions and imagery of a dot with four opposing motions.
  - The larger the number of motion alternations, th higher the expected hMT+/V5 response





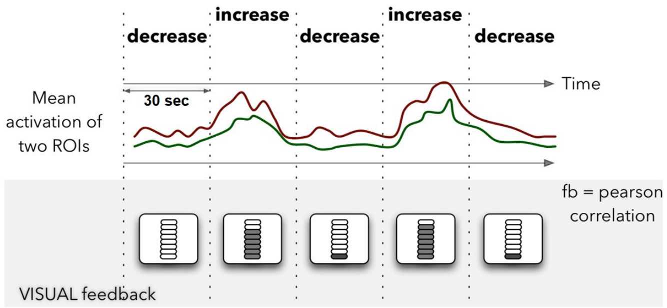
Sousa, T., Direito, B.,et al. (2016). Control of Brain Activity in hMT+/V5 at Three Response Levels Using fMRI-Based Neurofeedback/BCI. Plos One, 11(5)



- 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.

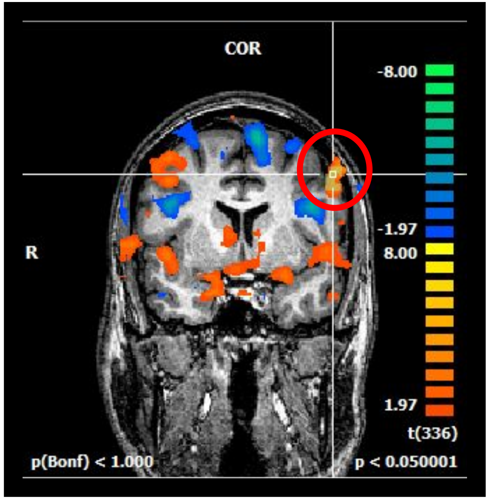
Connectivity-based neurofeedback

- 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”

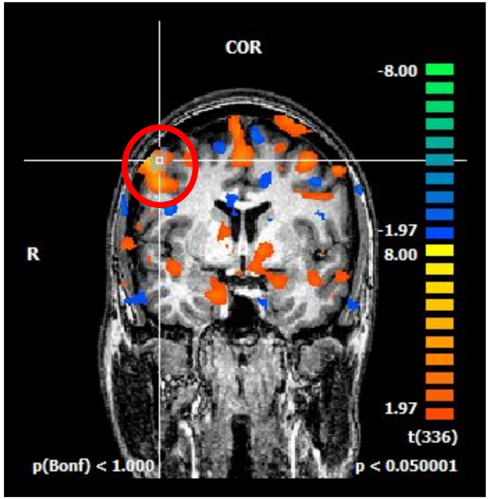


Feedback is based on an 8 point sliding window - Pearson’s Correlation Coefficient

Connectivity-based neurofeedback

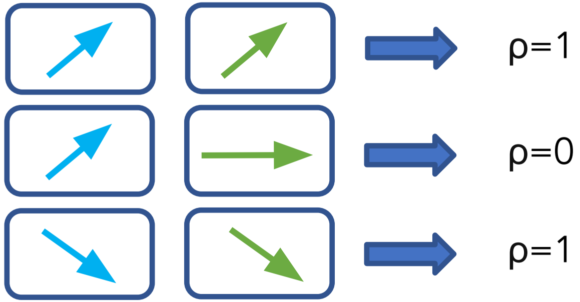


Left Premotor Cortex (lPMC)



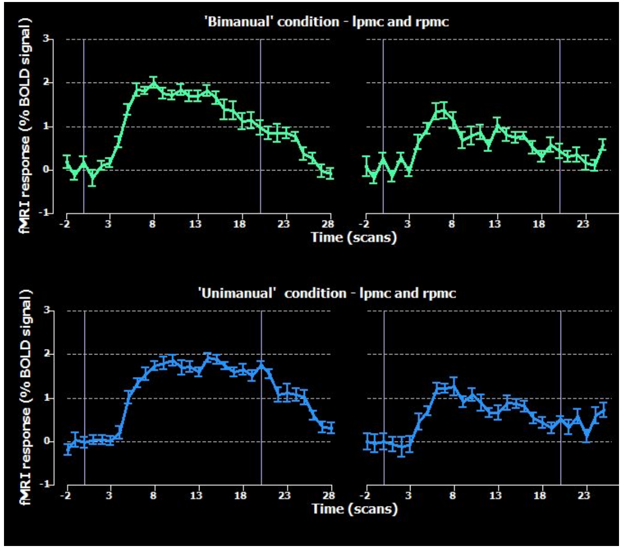
Right Premotor Cortex (rPMC)

Motor imagery paradigm

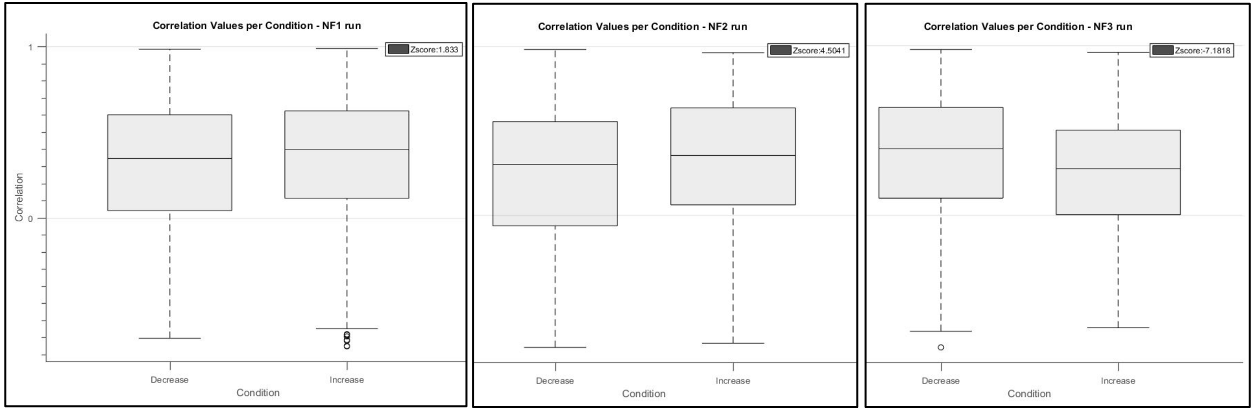


Connectivity-based neurofeedback

Activation patterns



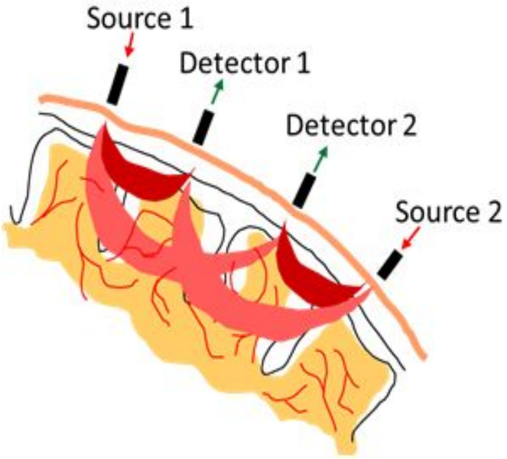
Connectivity patterns

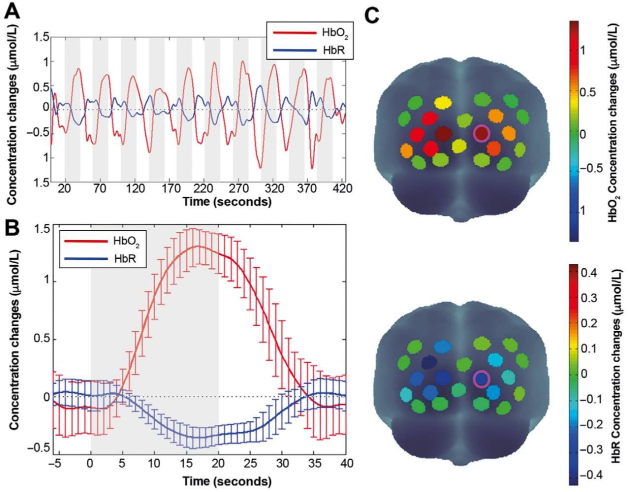


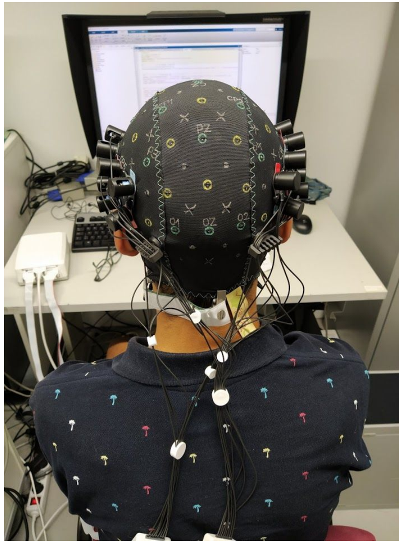
Pereira, J., Direito, B., Sayal, A., Ferreira, C., & Castelo-Branco, M. (2019). Self-Modulation of Premotor Cortex Interhemispheric Connectivity in a Real-Time Functional Magnetic Resonance Imaging Neurofeedback Study Using an Adaptive Approach. Brain Connectivity, 9(9), 662–672. https://doi.org/10.1089/brain.2019.0697

PhD Project - 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.

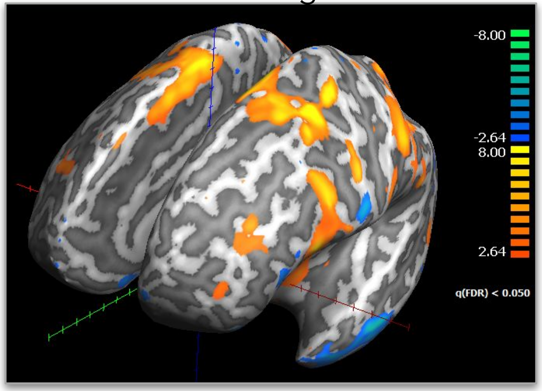


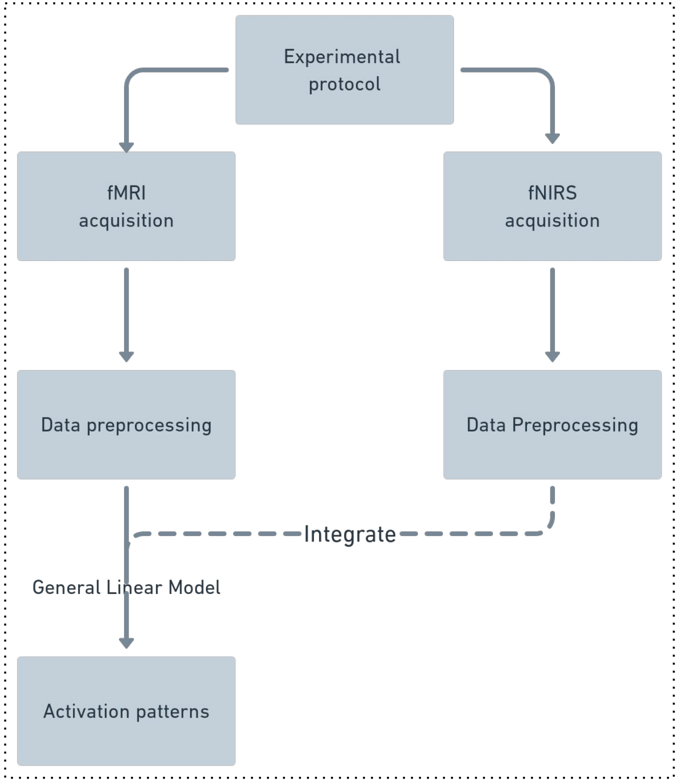




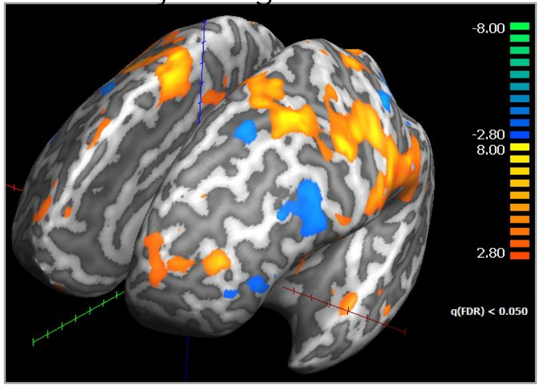
Multimodal fNIRS/fMRI correspondence

BOLD signal

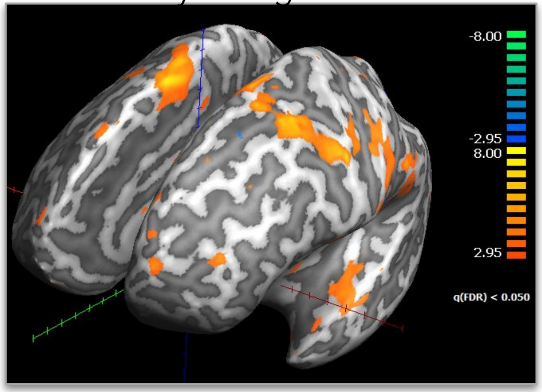




oxyhemoglobin data



deoxyhemoglobin data



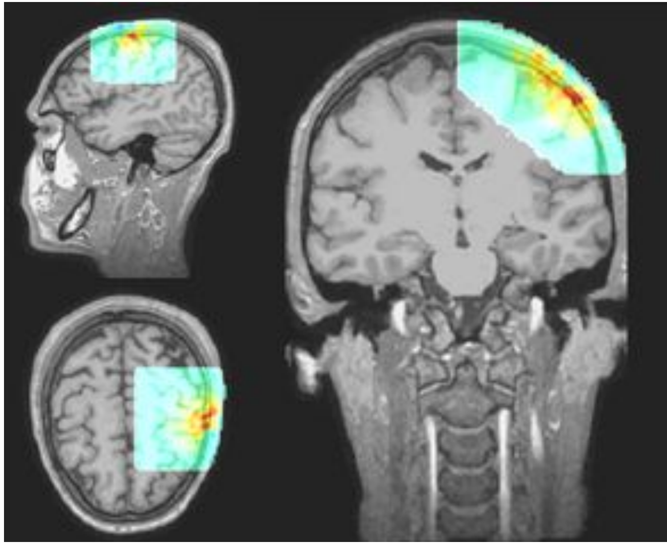
fNIRS as a neuroimaging modality

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

Review

A Mini-Review on Functional Near-Infrared Spectroscopy (fNIRS): Where Do We Stand, and Where Should We Go?

Valentina Quaresima * and Marco Ferrari

Department of Life, Health and Environmental Sciences, University of L'Aquila, 67100 L'Aquila, Italy
* Correspondence: valentina.quaresima@univaq.it

Received: 3 July 2019; Accepted: 31 July 2019; Published: 1 August 2019

Medicine	Attention deficit disorder	2018	11	C	Mauri [78]
	Auditory cortex plasticity after cochlear implant	2018	7	A	Basura [79]
	Autism spectrum disorder	2019 2019	15 30	C C	Liu [80] Zhang [81]
	Cognitive aging	2017	34	A	Agbangla [82]
	Developmental age attention deficit/hyperactivity disorder	2019	13	C	Grazioli [83]
	Eating disorders	2015	11	A	Val-Laillet [50]
	Epilepsy	2016	23	A	Peng [84]
	Gait disorders	2017	12	A	Gramigna [85]
	Mild cognitive impairment	2017	8	A	Beishon [86]
	Neurofeedback training	2018	127	A	Ehlis [87]
	Pain assessment in infants	2017	9	C	Benoit [88]
	Parkinson's disease and walking balance tasks	2018	5	A	Stuart [77]
	Prolonged disorder of consciousness	2018	7	A	Rupawala [89]
	Psychiatry	2014	168	A	Ehlis [90]
	Robot-assisted gait training	2019	2	A	Berger [91]
	Schizophrenic disorders	2017	17	A	Kumar [92]
	Stroke therapy/recovery/rehabilitation	2019	66	A	Yang [93]

A: Adults; C: Children; EEG: Electroencephalography; N: Number of reviewed articles; Ref: Reference number.

What can we get with fNIRS

Source: Nirx Medical Technologies.

Clinical need

Several technological approaches have been used to promote functional motor recovery in post-stroke patients with limited results (Teasell et al., 2003).

Inter-subject variability in functional reorganization of the brain has been identified as one of the main limitations (Gillebert et al., 2013).

Personalized interventions such as Neurofeedback are emerging as promising clinical tools (Stoeckel et al., 2014).

Motor recovery clinical trials

A systematic review by Langhorne, Coupar and Pollock (2009) summarized the reported evidence for motor function recovery post-stroke.

Several interventions demonstrated potential

a) Constraint-induced movement therapy
b) Electromyographic (EMG) biofeedback
c) Mental practice with Motor Imagery (MI)
d) Robotics

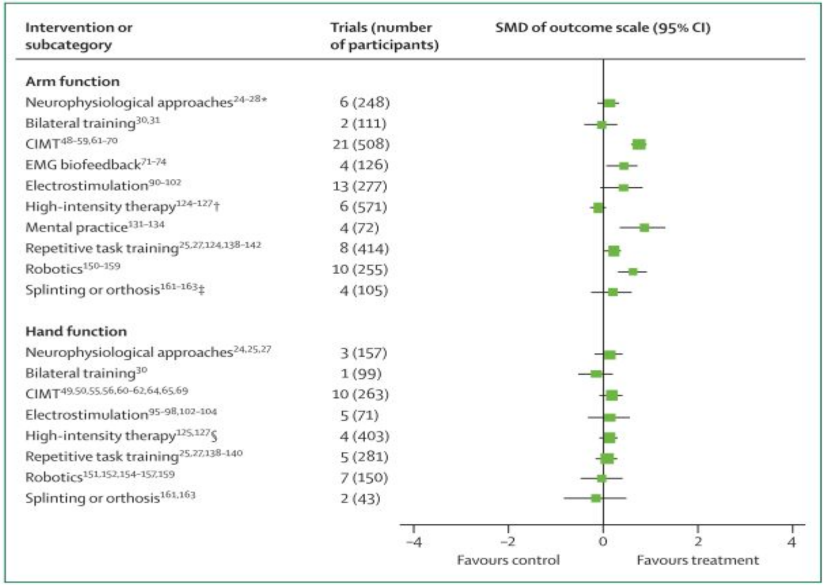


Figure 2: **Interventions to improve upper-limb motor recovery after stroke**

Motor recovery clinical trials

More recently, Stinear et al., (2020) reviewed 15 randomized clinical trials (RTCs) divided in several approaches:

a) Training
b) Technological
c) Pharmacological
d) Neuromodulation

Most proved feasible, however, only one RTC (pharmacological) reported differences between experimental and control groups.

Majority of patients in acute/subacute stage.

Neurofeedback for Stroke Rehabilitation

Wang, Mantini and Gillebert (2018) reviewed 33 NF experiments of motor network related areas.

Three stroke cohorts have proven feasible the self-modulation of neural activity and connectivity between brain areas related to impaired functions.

Learned modulation was associated with:

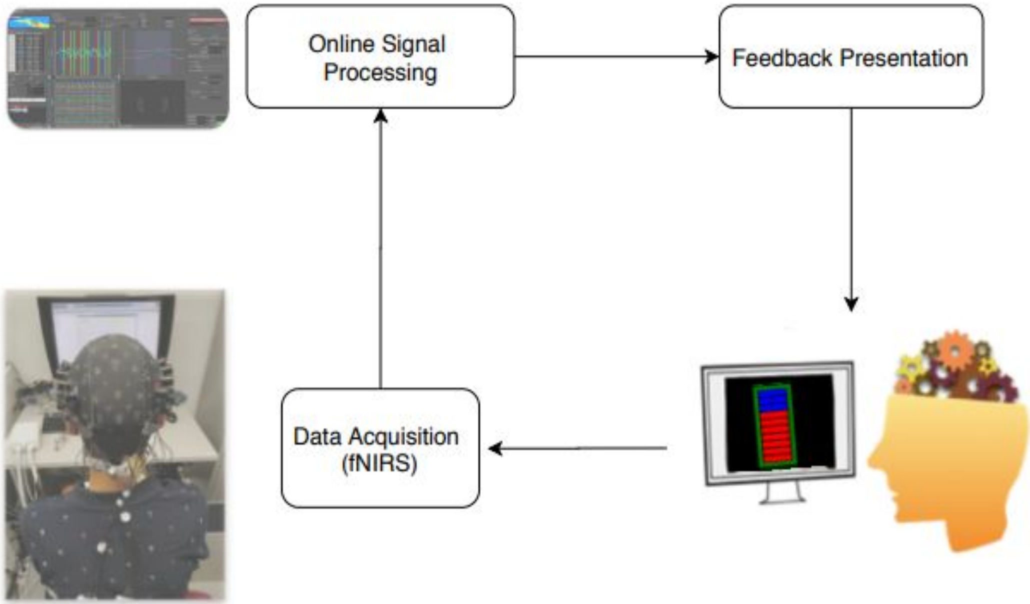
- Increased resting-state connectivity between M1 and thalamus;
- Improvements in visuomotor function;
- Reduced spatial attention bias.

Aim of the Project

Validate a functional connectivity-based fNIRS NF framework as a possible motor rehabilitation tool for post-stroke patients with upper limb hemiparesis:

- Transfer previous work in real-time fMRI NF (Pereira et al. 2019)
- Investigate NF induced changes in the motor network
- Study the role of the contralesional hemisphere in motor recovery

fNIRS-based neurofeedback

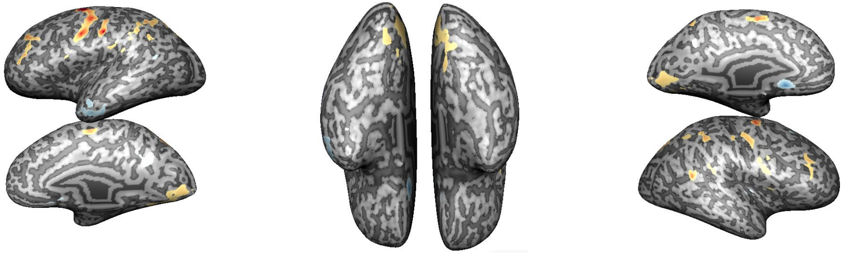


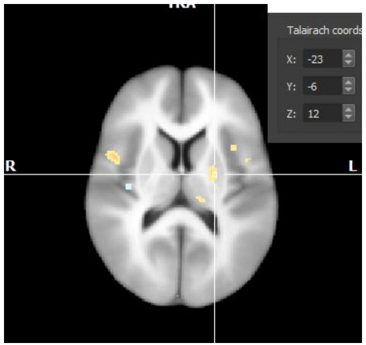
Exploring success mechanisms and reward

- Overall success rate in neurofeedback is under 50%
- Important regions for neurofeedback success?
  - How to characterize them?
  - What can we learn from them?
  - How to adapt the difficulty level?

Exploring reward

- Exploratory analysis (considered the same paradigm as three-level control - defined specific time points for feedback)
  - Neurofeedback runs
    - Whole-brain
    - 10 participants, 2-runs each
      - (RFX, p< 0.01)
      - Contrast (+) mov vs. (-) static

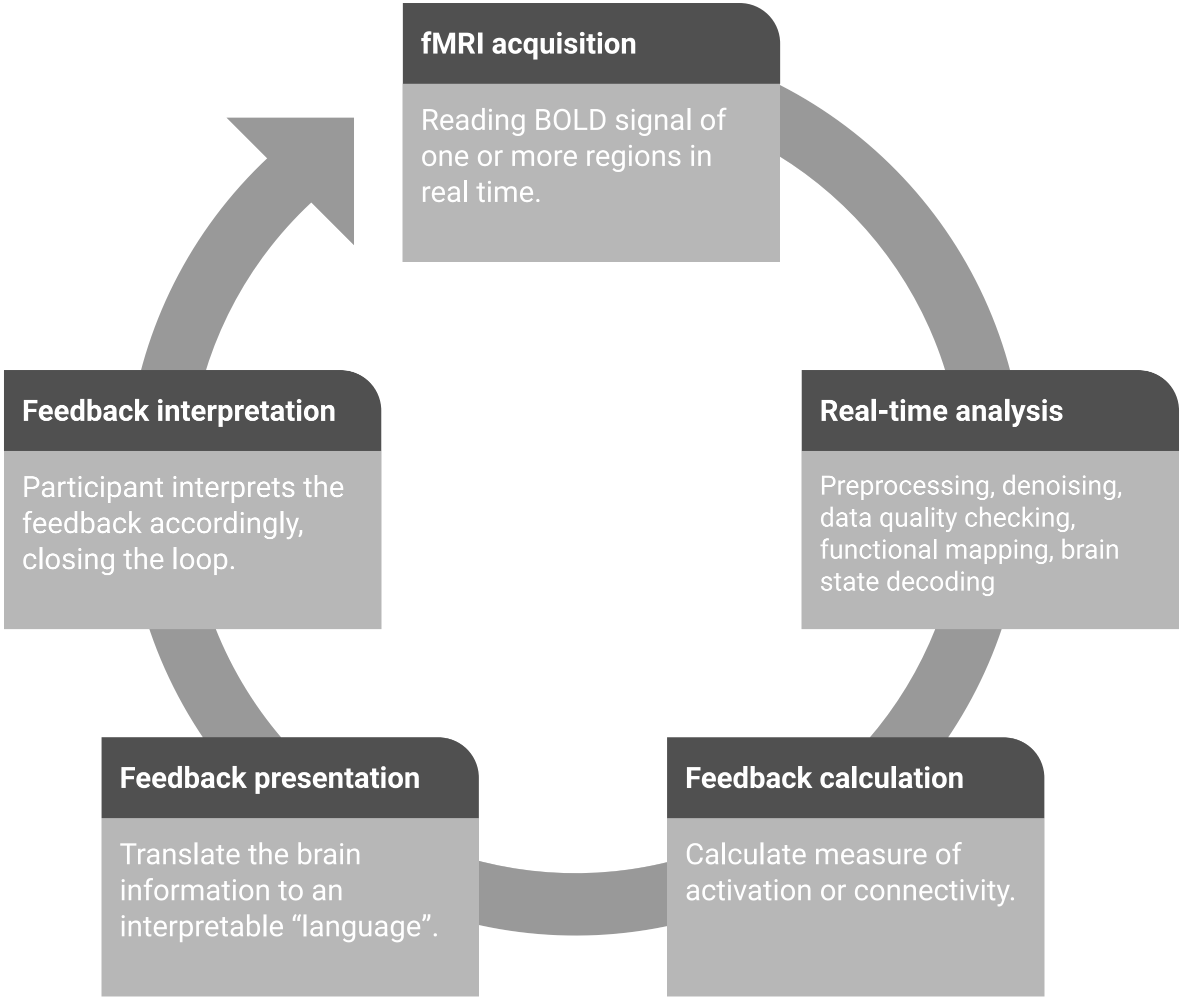




Next steps

- Neurofeedback - Define ‘learning’ or success
- Connectivity analysis
    - Modeling the interaction between nodes - bottom-up vs. top-down - which region is ‘driving’ the system on neurofeedback experiments
- Data-driven analysis of the data - machine learning (we have focused on the target region, what else?)
- How to “drive” the system towards a particular state?
- Analysis improvements
- Is NF immersive? How to improve?

Listen to your brain - PhD project


fMRI acquisition
Reading BOLD signal of one or more regions in real time.
Real-time analysis
Preprocessing, denoising, data quality checking, functional mapping, brain state decoding
Feedback calculation
Calculate measure of activation or connectivity.
Feedback presentation
Translate the brain information to an interpretable “language”.
Feedback interpretation
Participant interprets the feedback accordingly, closing the loop.

Motivation

- A number of different interfaces have been explored to communicate the neuronal information to the participant in a friendly way [Krause et al., 2017].

The engagement/immersiveness of the neurofeedback interface is of major importance.

Achieving control of a BCI is a hard learning process.

- Music is, in a way, a language we all understand, crossing cultures and dating back to our ancestors.
- Provided we validate that certain melodies elicit specific emotions [Cespedes-Guevara et al., 2018], we could take advantage of this to implement a more intuitive neurofeedback interface.
- Numerous evidence for a link between music listening/training and brain plasticity [Vik et al., 2018, Blum et al., 2017].

Main objective

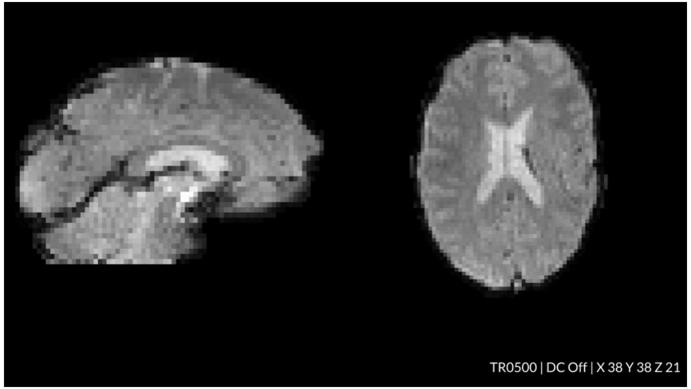
This project aims to assess the potential of using music as the interface in an fMRI-based neurofeedback experiment.

- Study the neural correlates of music processing and of its emotional content.
- Design a neurofeedback intervention taking these correlates into account.

- Evaluate how the brain's reward and emotion processing systems respond to such an intervention.

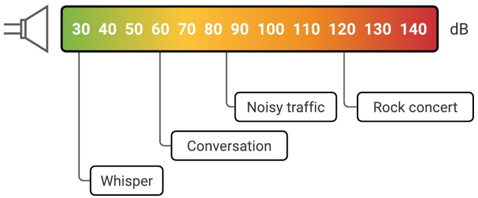
Stage 1 - Analysis

- Susceptibility artefact correction
- Image quality metrics (IQM)
    - temporal signal-to-noise ratio (tSNR)
    - (functional) contrast-to-noise ratio (CNR)
- V1 and hMT+ activity
- Seed-based functional connectivity metrics
- Extraction of neural components using ICA



Stage 2 - ANC in the MRI room

- Objective - develop a simple, open-source software/hardware solution that allows implementing ANC in any current scanner using its own audio system.



Decibel Level Comparison Chart.

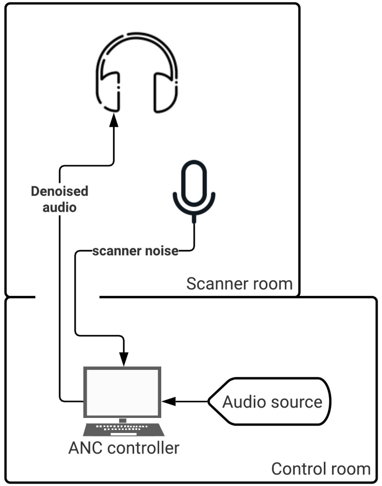


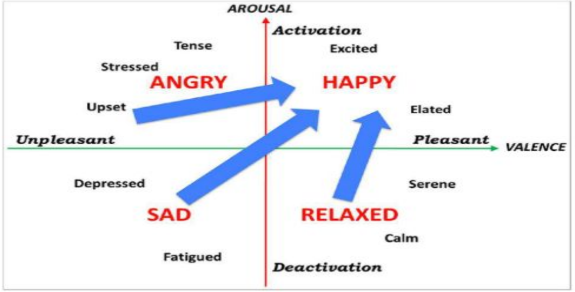
Diagram of the ANC system for the MRI and control rooms. The ANC controller receives two audio signals, one from the audio source, transmitting the signal to be heard by the participant, and the other from the internal scanner microphone, carrying the scanner noise waves. After processing, the denoised sound is fed to the headphones.

Stage 3 - music as a NF interface

- Objective - develop a neurofeedback interface using music that could be used in a wide range of experimental protocols
- A number of paradigm options have been hypothesized, differing in
  - Experimental design
  - Type of feedback presentation
  - Target region/network
  - Control groups
  - Degree of subject specificity

Stage 3 - Interface options

- Continuous feedback
  - Link brain activation to a continuous transition between white noise and music
  - Dynamically change parameters of the music, such as valence, volume, tempo, or complexity, based on brain activation patterns
  - Allow the participant to freely navigate in the arousal/valence plane



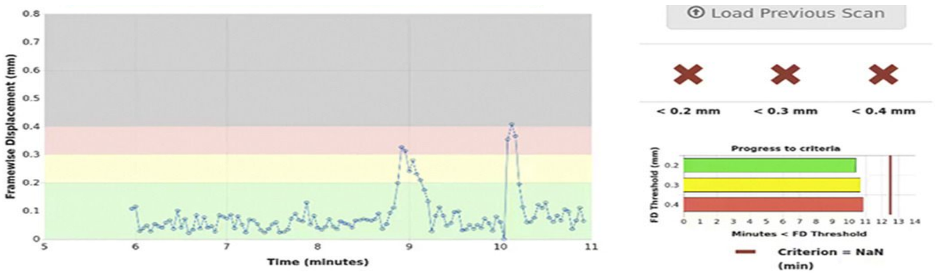
Arousal/valence plane [Ramirez et al., 2015]

- Discrete feedback
  - Present the feedback at the end or at specific timepoints of each task block, in the form of a music excerpt that translates specific emotional content

Stage 3 - Real-time analysis

We aim to advance the current NF setup:

- Real-time monitoring of participant's head motion [Dosenbach et al., 2017]



Screenshot of FIRMM running on an example run. Adapted from [Dosenbach et al., 2017].

- Real-time correction for physiological signals [Weiss et al., 2020; Heunis et al., 2020]

- Is susceptibility artefact correction possible in real time?

Network probing - alternatives

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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]

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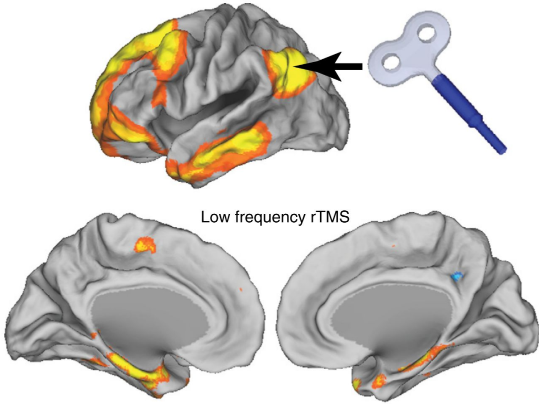
"(…)TMS to modulate pathological network interactions identified with resting state fcMRI."

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



Control groups in neurorehabilitation interventions

Sorger, B., Scharnowski, F., Linden, D. E. J., Hampson, M., and Young, K. D. (2019). Control freaks: Towards optimal selection of control conditions for fMRI neurofeedback studies. *Neuroimage* 186, 256–265. doi:10.1016/j.neuroimage.2018.11.004.