ICTP SAIFR International Centre for Theoretical Physics South American Institute for Fundamental Research

WORKSHOP ON DYNAMICAL PROCESSES ON COMPLEX NETWORKS

May 13 – 17, 2024

at Instituto de Física Teórica - UNESP, Brazil

IFGW UNICAMP

Neurofísica Unicamp

Complex networks to help understand brain re/organization in motor rehabilitation and brain-computer interfaces

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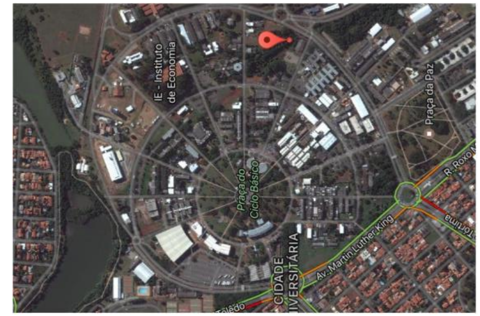
UNICAMP BRAIN BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY

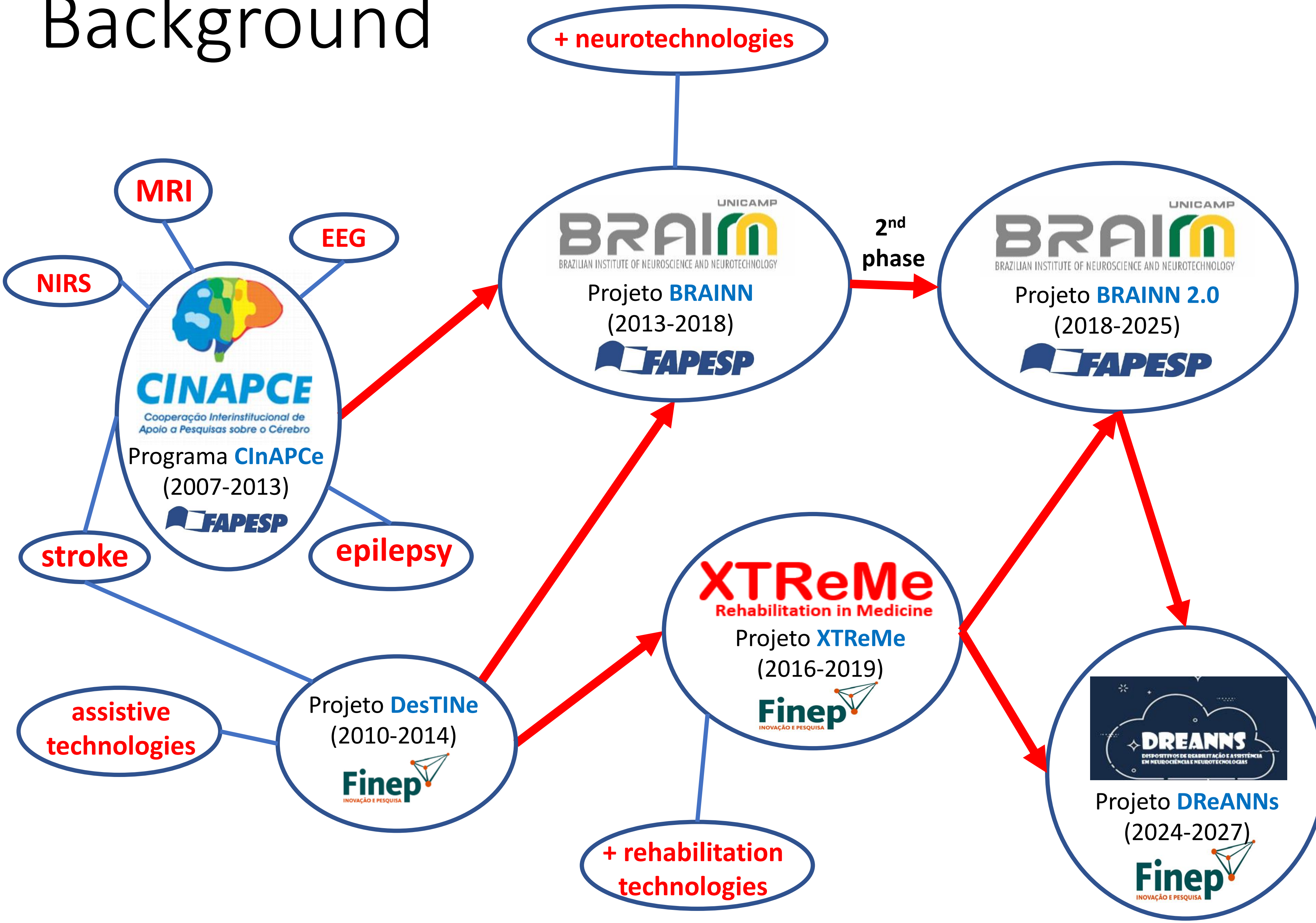
15/05/2024

Background



- Medical Physics undergraduate course (2003)
- Neurophysics group (2005)

Background


+ neurotechnologies
MRI
EEG
NIRS
CINAPCE
Cooperação Interinstitucional de Apoio a Pesquisas sobre o Cérebro
Programa CInAPCe
(2007-2013)
FAPESP
stroke
epilepsy
UNICAMP
BRAINN
BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY
Projeto BRAINN
(2013-2018)
FAPESP
2nd phase
UNICAMP
BRAINN
BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY
Projeto BRAINN 2.0
(2018-2025)
FAPESP
XTReMe
Rehabilitation in Medicine
Projeto XTReMe
(2016-2019)
Finep
INOVAÇÃO E PESQUISA
assistive technologies
Projeto DesTINe
(2010-2014)
Finep
INOVAÇÃO E PESQUISA
+ rehabilitation technologies
DREANNS
Projeto DReANNs
(2024-2027)
Finep
INOVAÇÃO E PESQUISA

BRAINN Project
(http://www.brainn.org.br/en)

- Neuroscience of healthy and diseased brain
  - Epilepsy, neurovascular diseases, neuromotor diseases, dementias, lupus
- Genetics and animal models
- Precision medicine
- Instrumentation development
  - Neural probes, NIRS systems
- Development of assistive and rehabilitation technologies
  - BCI, VR, robotic prostheses
- Image processing, analysis and visualization
  - Neuronavigation system
- Neuromodulation
- Neuroscience for education
- Big data analysis, signal processing and machine learning
- Artificial consciousness
- Biostatistics and computational biology

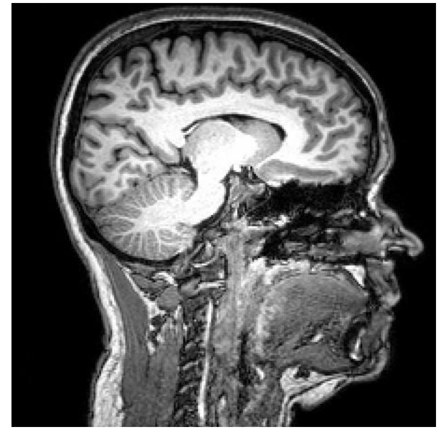
BRAINN Project

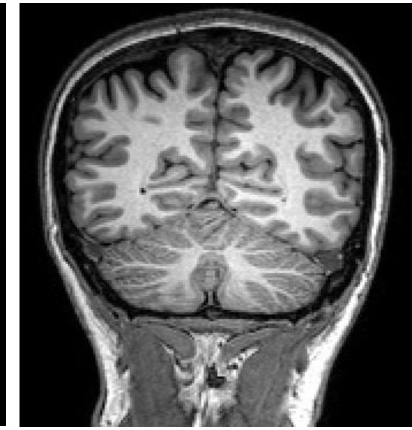
(http://www.brainn.org.br/en)

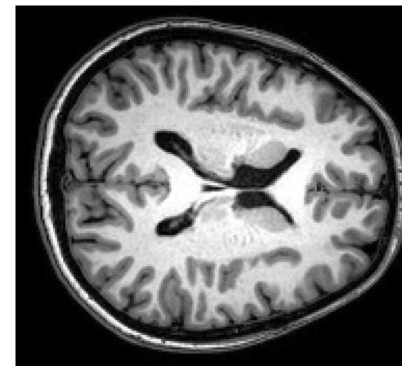
- Evaluation of assistive and rehabilitation technologies
  - Brain-computer interfaces (BCIs) and neurofeedback
  - Extended reality (XR) and transcranial direct current stimulation (tDCS)

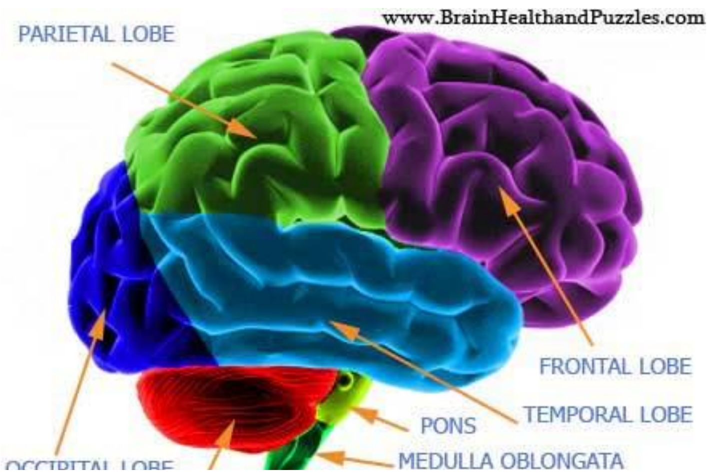
The brain

Basic structure

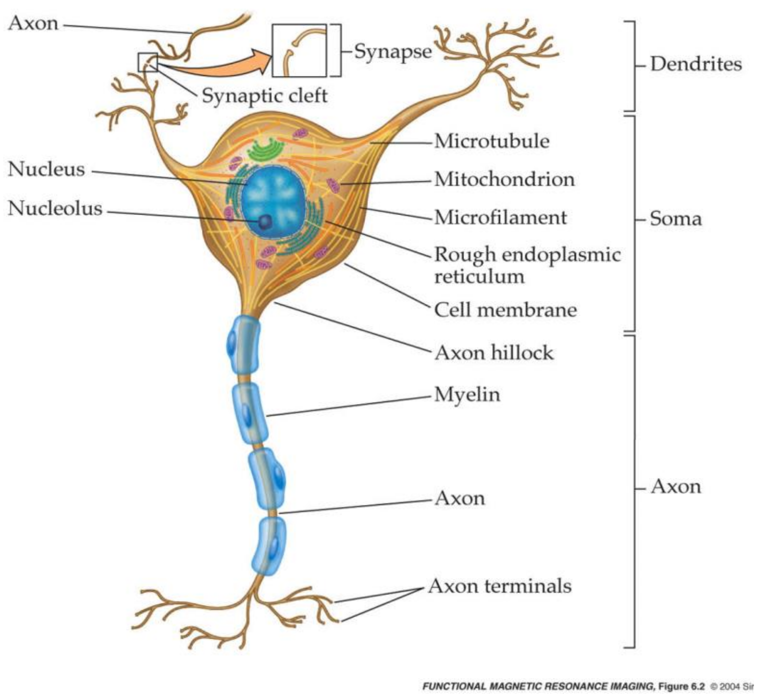


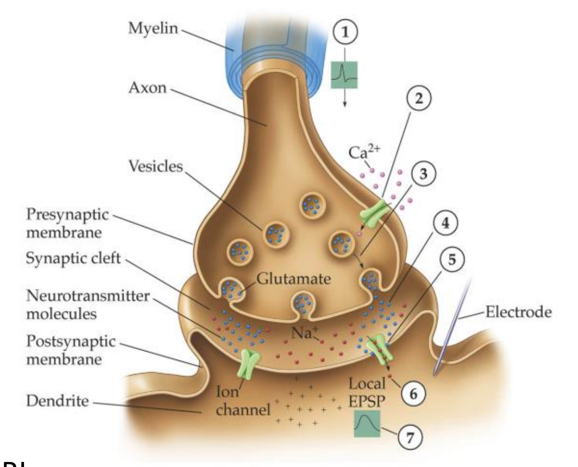






- 86 billion neurons
  - 16 billions - brain
  - 69 billions - cerebellum
- 85 billion glial cells

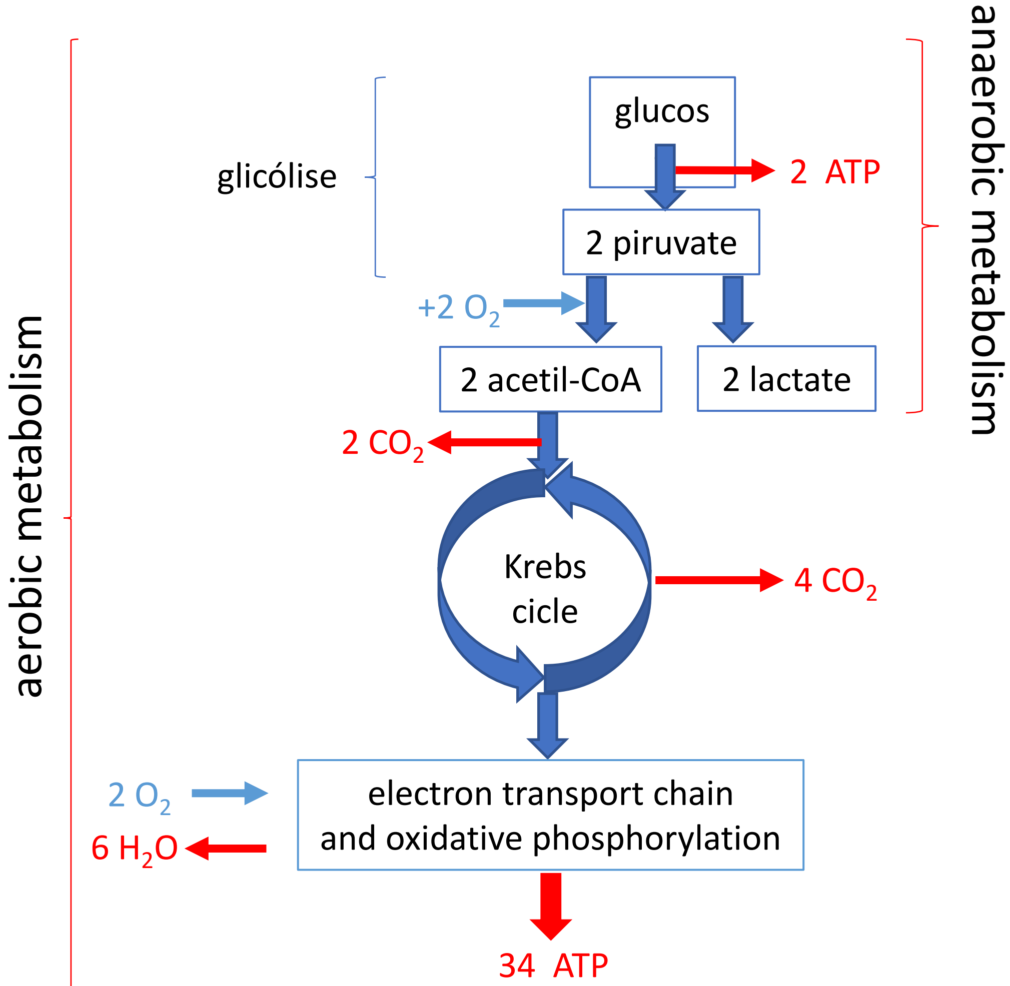


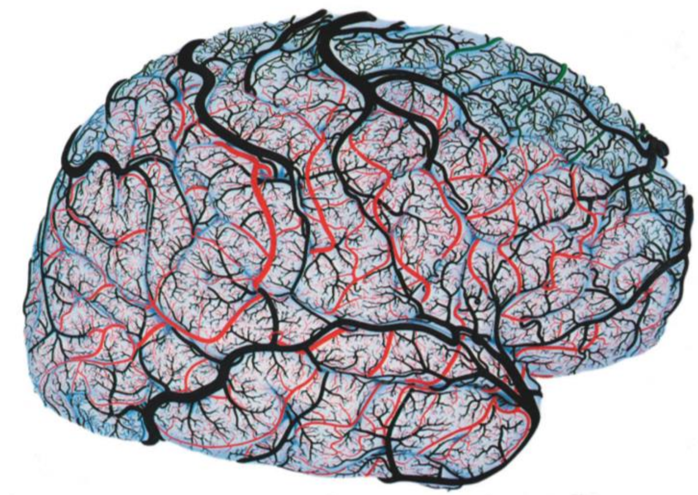


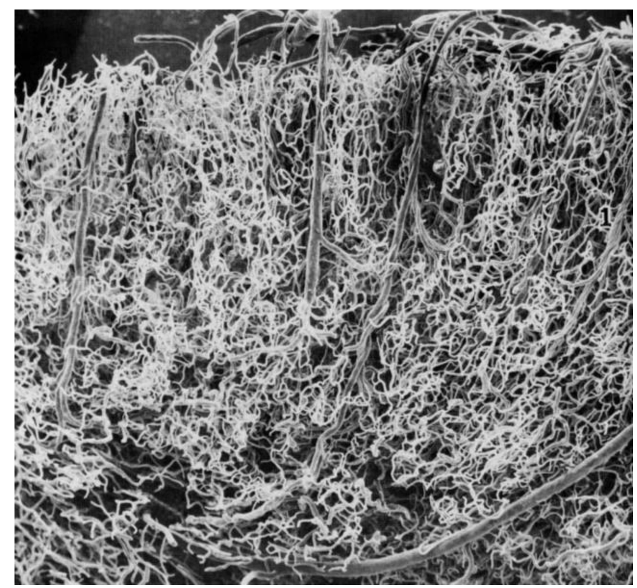
Huettel et al. 2003, FMRI

Anaerobic and aerobic metabolism

- Brain is ~2% of body mass
- It uses ~20% of body energy





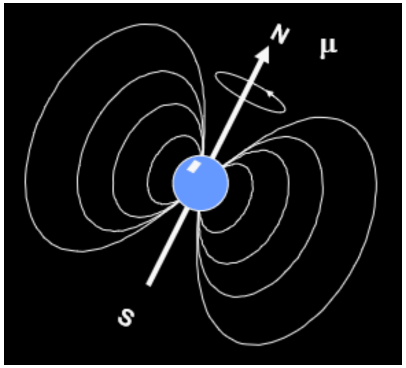


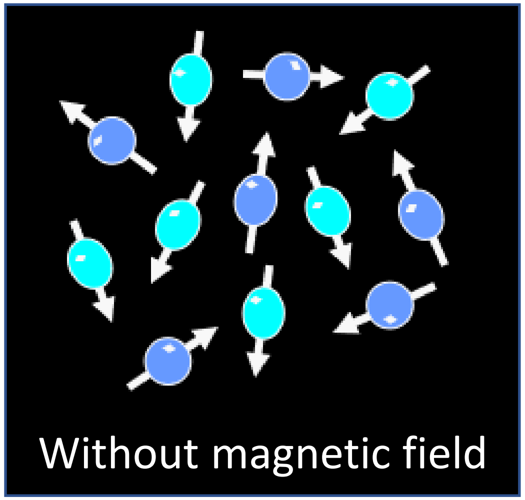
capillary network

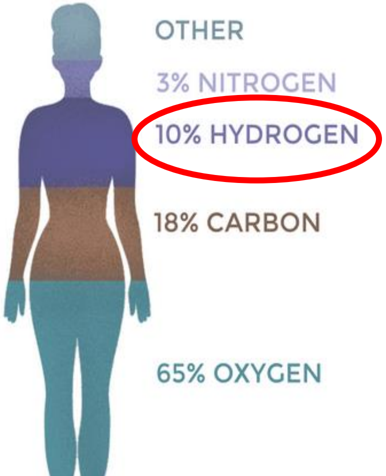
Huettel et al. 2003, FMRI

Techniques for measuring brain data

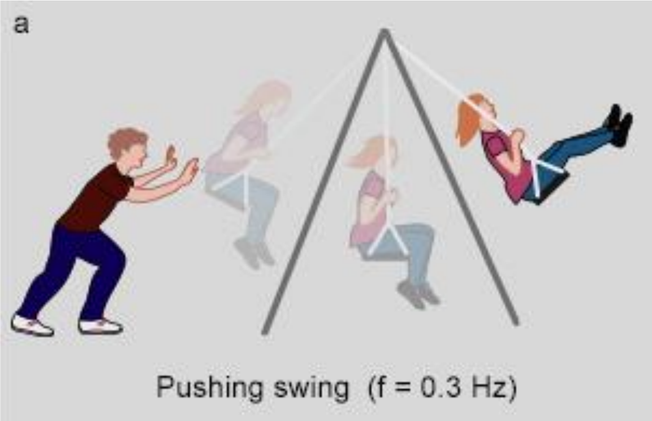
Magnetic resonance imaging (MRI)



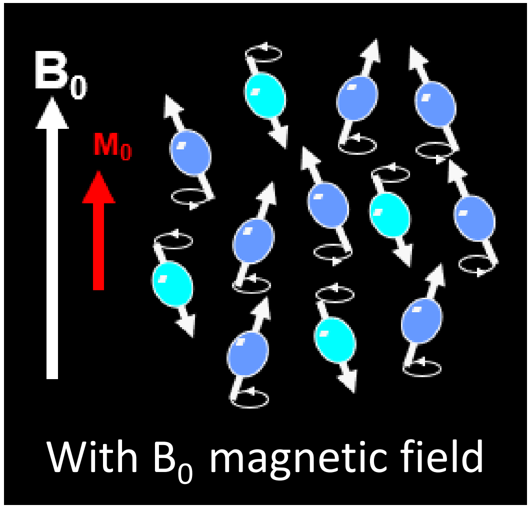


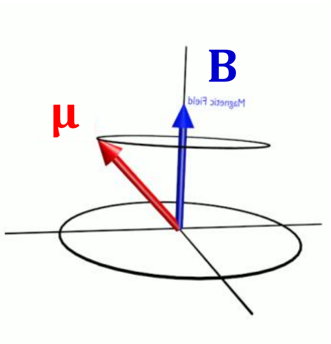


chandra.si.edu/elements/

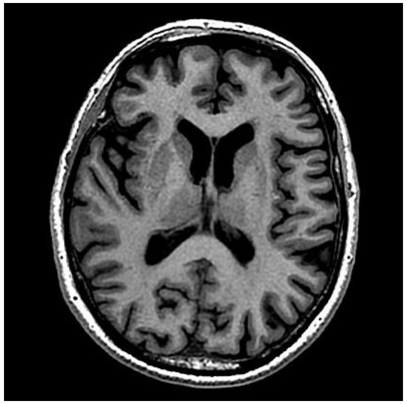


www.abc.net.au/science/articles/2014/06/16/4022877.htm



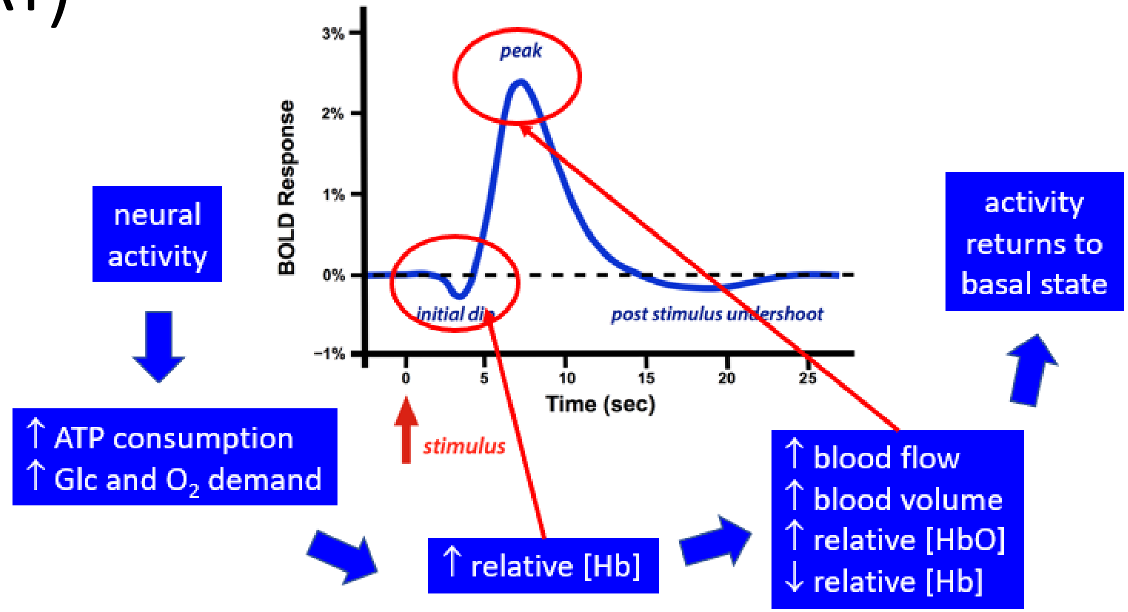


www2.chem.umd.edu/groups/efrain/Spherical_Neutron_Polarimetry.php



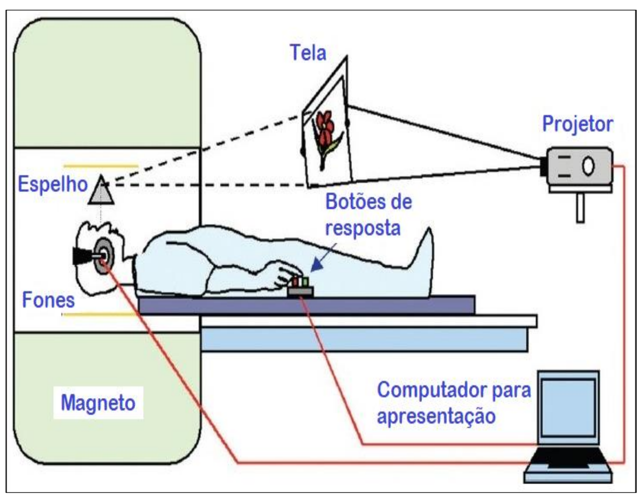
www.sciencelearn.org.nz/resources/987-looking-at-the-brain-with-mri

Functional magnetic resonance imaging (fMRI)

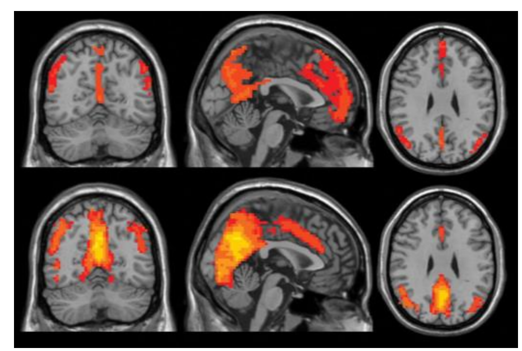


Adapted from https://mriquestions.com/does-boldbrain-activity.html

Oxyhemoglobin (HbO) and deoxyhemoglobin (Hb) have different magnetic properties



https://europepmc.org/article/pmc/pmc2747426



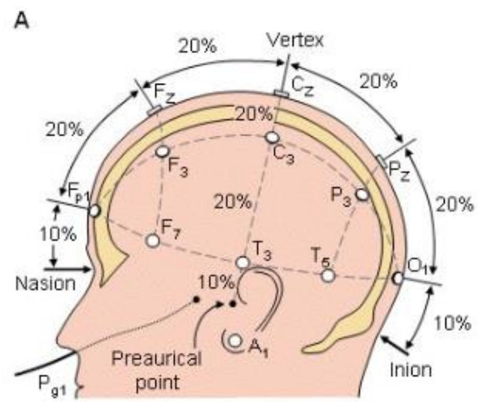
https://medium.com/swlh/functional-connectomics-a-novel-approach-to-study-the-brain-9918df14ccfc

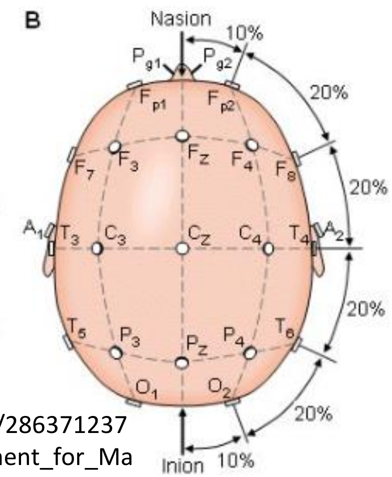
Electroencephalography (EEG)

https://www.sciencedaily.com/releases/2009/12/091204103751.htm

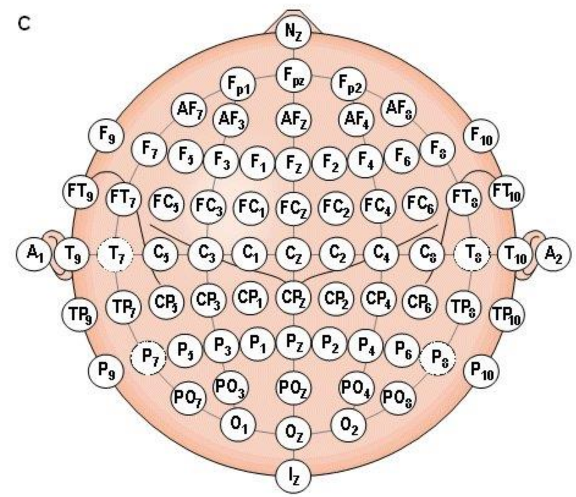
EEG signals are directly related to neuronal firing

10-20 system



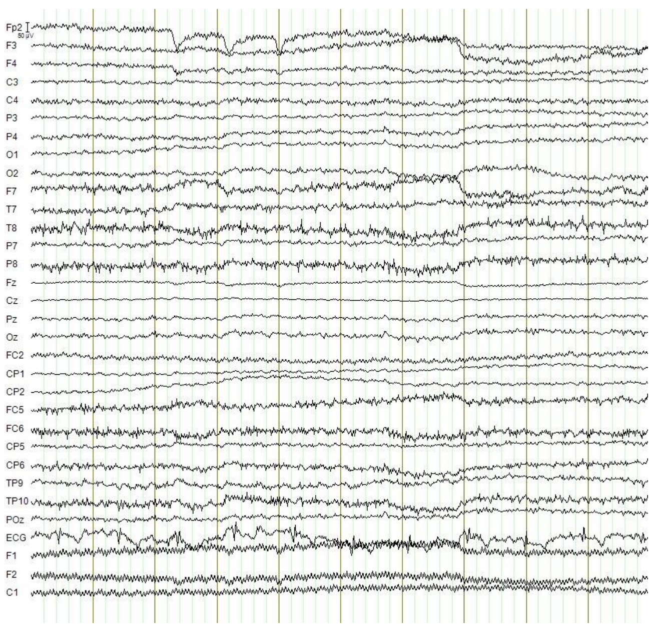


https://www.researchgate.net/publication/286371237_EEG_Based_Cognitive_Workload_Assessment_for_Maximum_Efficiency



10-10 system

https://www.researchgate.net/publication/237088559_Applying_ICA_in_EEG_Choice_of_the_Window_Length_and_of_the_Decorrelation_Method

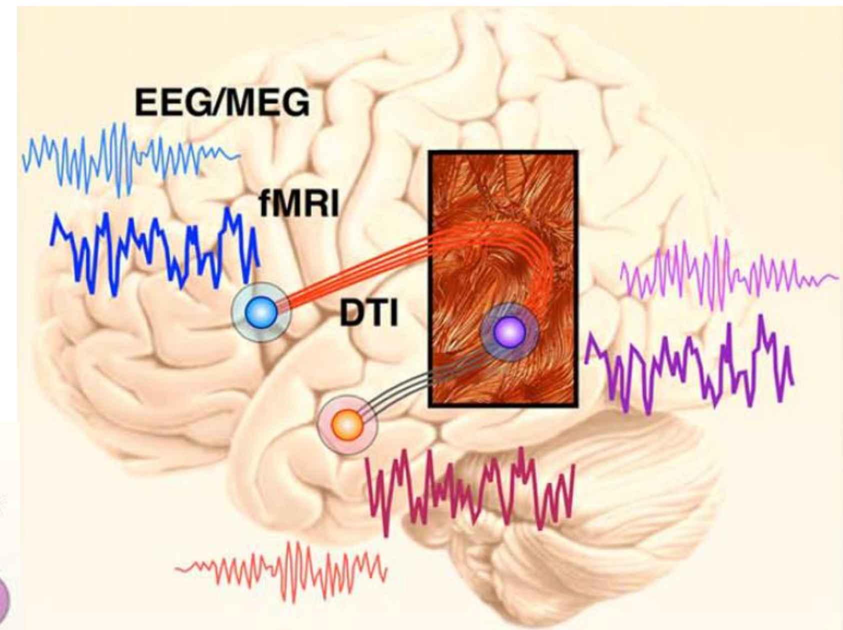


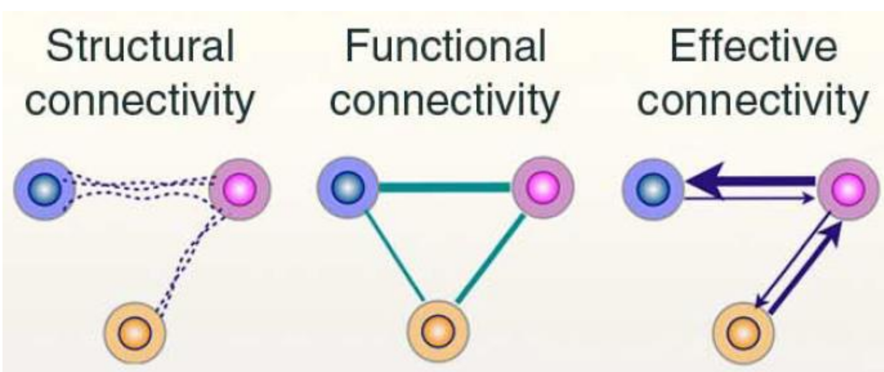
https://en.wikipedia.org/wiki/Electroencephalography

Brain connectivity

Brain connectivity

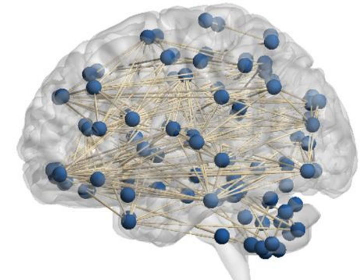
- Secondary analysis applied to (almost) any brain data
- Three types:
  - Anatomic (structural)
  - Functional
  - Effective



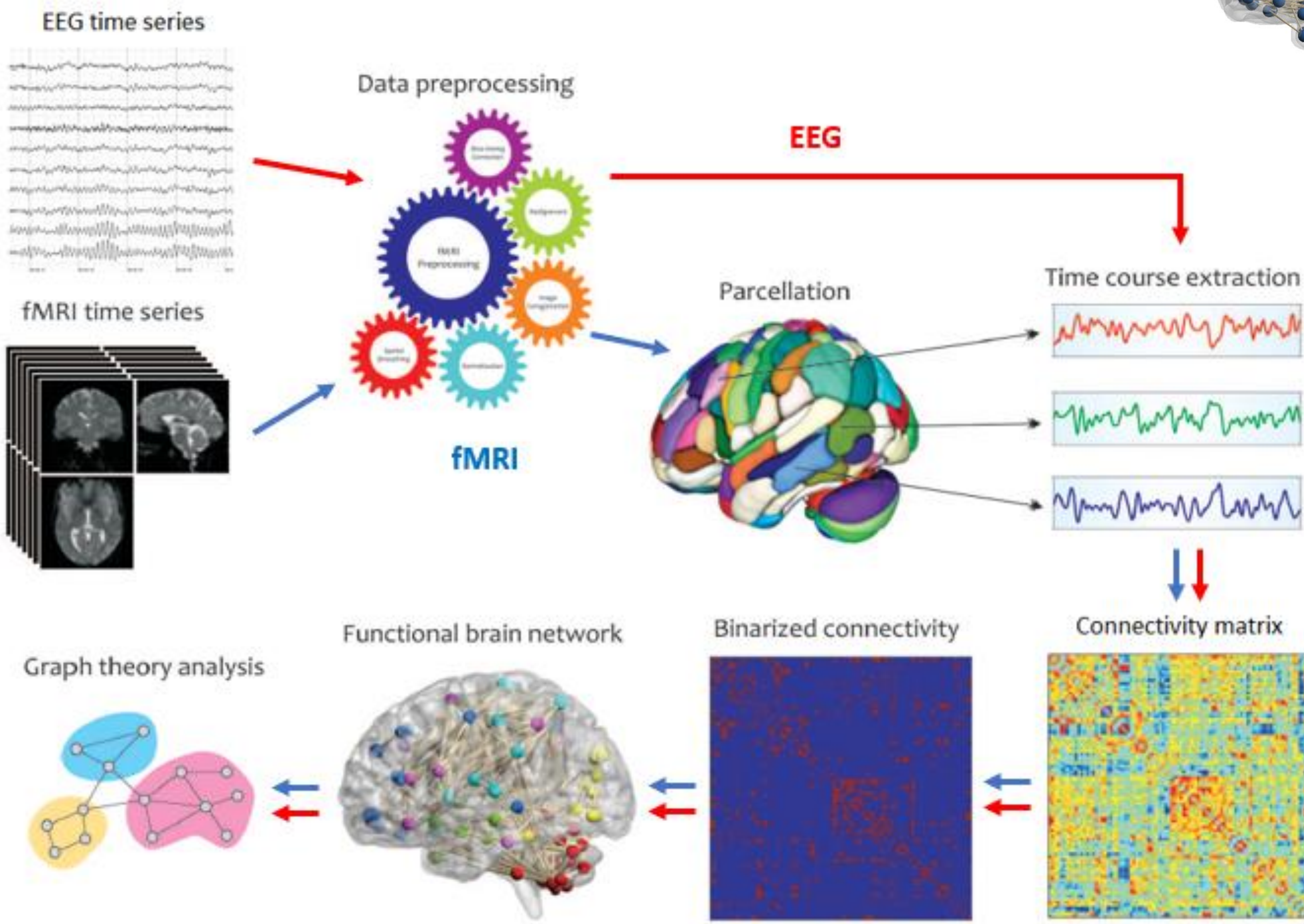


Park & Friston 2013, doi: 10.1126/science.1238411

Graphs



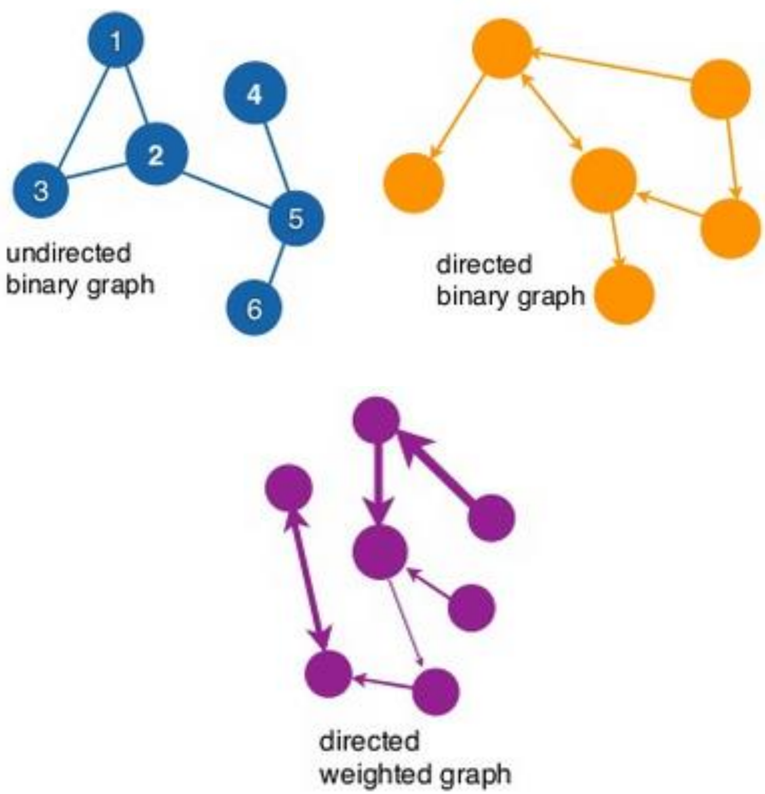
Rafael V. da Silveira 2020



Adapted from Farahani et al. 2019, Front Neurosci doi: 10.3389/fnins.2019.00585

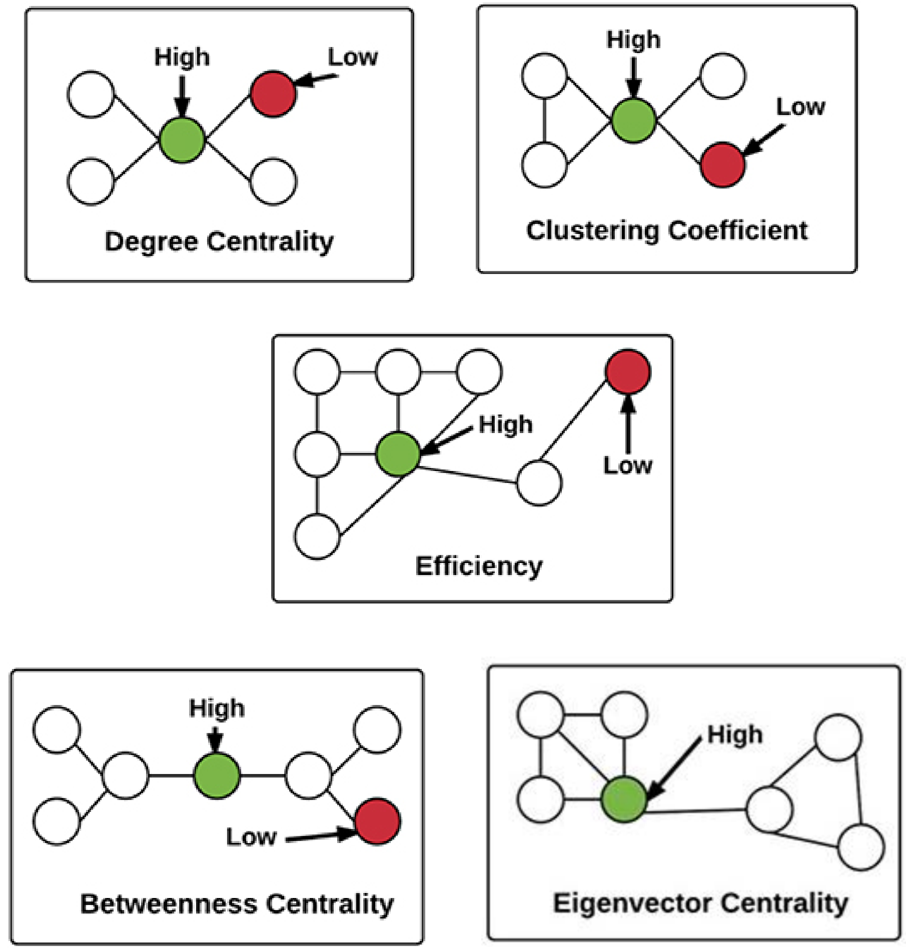
Graphs

Some types



https://www.slideshare.net/paul_kyeong/discovering
-hot-topics-using-twitter-streaming-data

Some measures

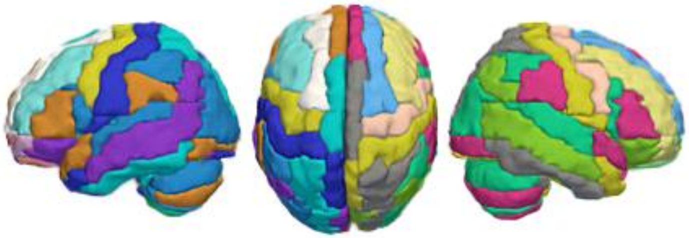


Adapted from Ebadi et al. 2017, doi: 10.3389/fnins.2017.00056

One example with structural data

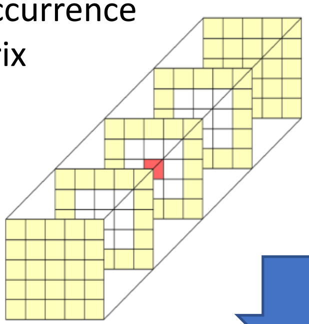
Texture-based brain networks for healthy subjects characterization

Rafael V. da Silveira

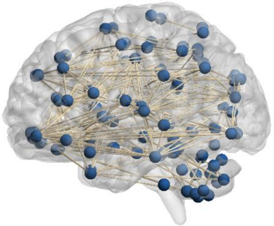


https://www.imn-bordeaux.org/en/news/aal-an-atlas-ranked-second-in-the-top-100-cited-cea-publication/

Cooccurrence matrix



Texture parameters



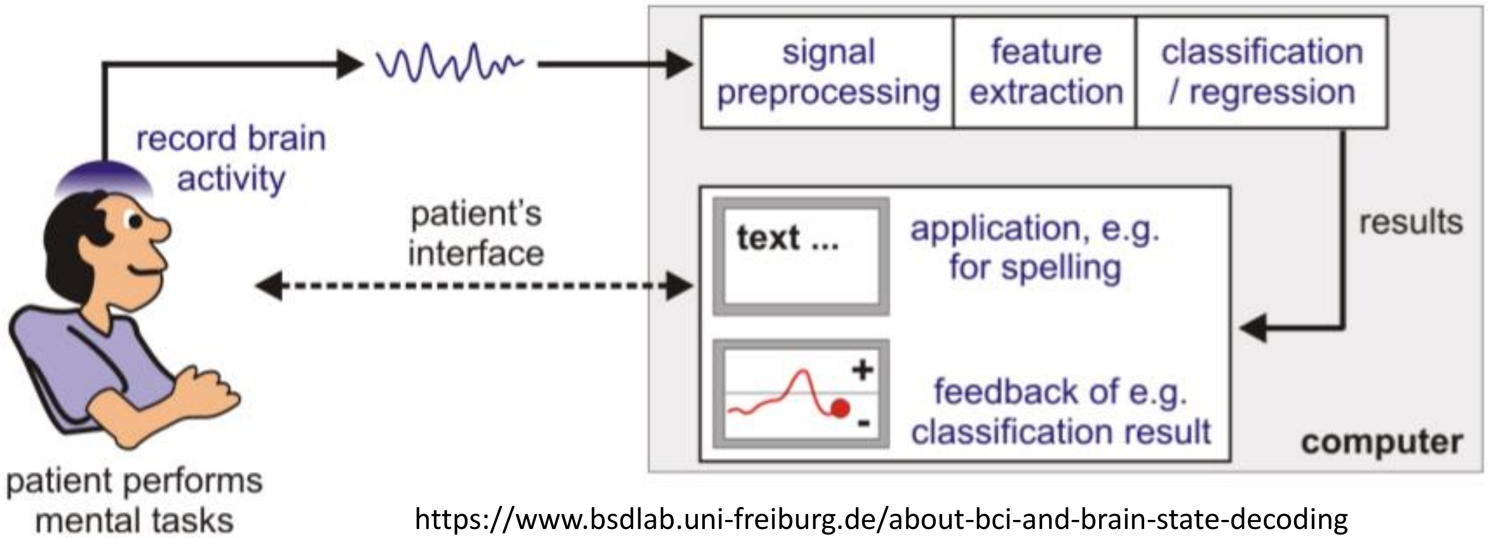
Graph parameters (S, CC, EC, BC)

- Network differences among men and women
  - Women have a hub in the speech area
- Some graph parameters showed dependency with age
- Thalamus and putamen showed a differentiated texture
  - Thalamus – relays signals from sensory to motor areas; regulates consciousness, sleep and alertness
  - Putamen – regulates preparation and execution of movements and influences various types of learning

Silveira et al. 2023, Sci Rep, doi: 10.1038/s41598-023-43544-6

BCIs and neurofeedback

Brain-computer interfaces (BCIs)



https://www.bsdlab.uni-freiburg.de/about-bci-and-brain-state-decoding

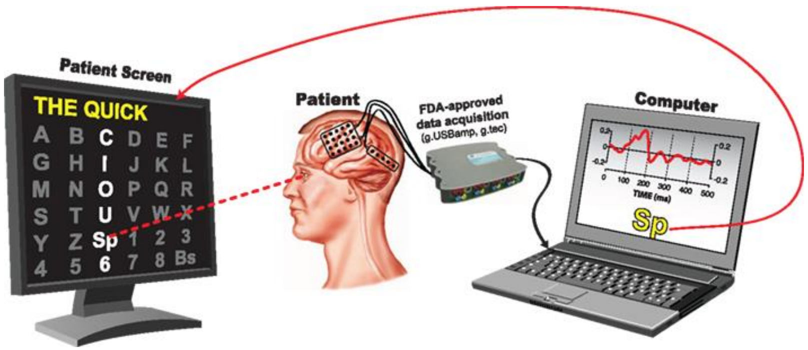
https://news.brown.edu/articles/2012/05/braingate2

https://neurosciencenews.com/locked-in-als-fnirs-6238/

https://www.etpl.sg/innovation-offerings/technologies-for-license/tech-offers/1789

EEG-BCIs' most popular evoking strategies

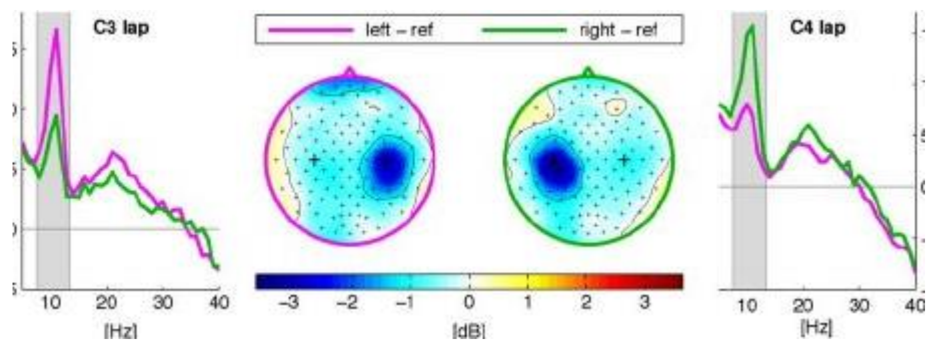
P300



Brunner et al. 2011, Front Neurosci doi: 10.3389/fnins.2011.00005

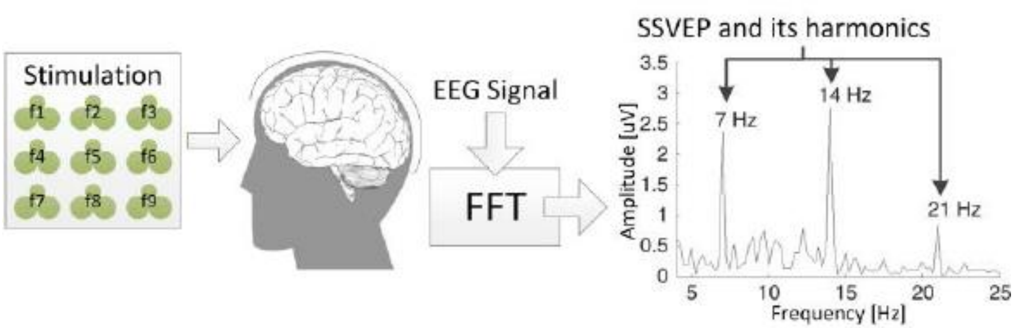
Motor Imagery (MI)

Event-related desynchronization

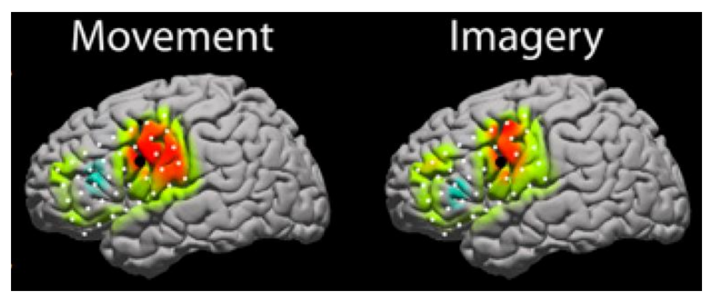


Maeder et al. 2012, IEEE TNSRE
doi: 10.1109/TNSRE.2012.2205707

Steady-state visually evoked potential (SSVEP)



Materka et al. 2014, AISC doi: 10.1007/978-3-319-08491-6_1



Miller et al. 2010, PNAS doi: 10.1073/pnas.0913697107

Motor imagery (MI) strategy

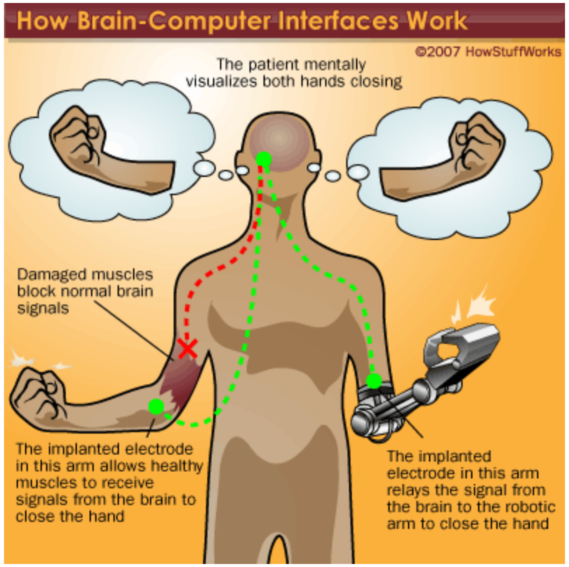
- Does not depend on external device to deliver stimuli (such as P300 and SSVEP)
- Has been successfully used for motor rehabilitation

But

- Presents large inter-subject variability
  - Patterns are very hard to identify

Also, for all EEG-BCIs

- Signal highly affected by noise and artifacts
- Main challenge: to find discriminating and reproducible features



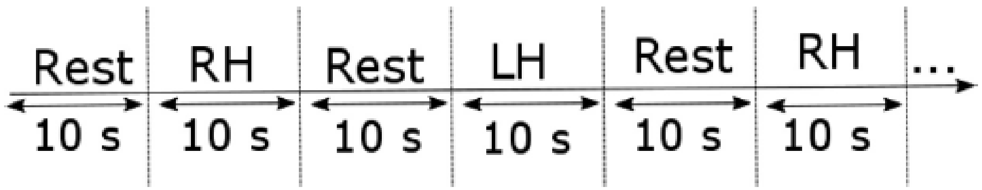
https://computer.howstuffworks.com/brain-computer-interface2.htm

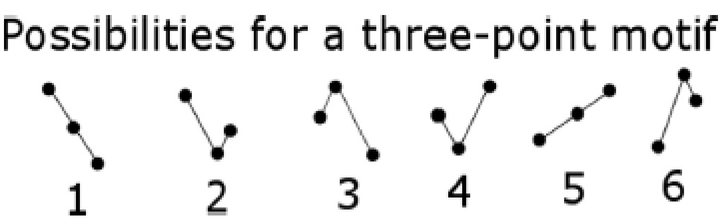
Use of graph measures in MI-BCIs

Carlos Stefano

Romis Attux

- Feasibility of using graph metrics (D, CC, CPL, BC)
- Motif synchronization method
- Comparison between PSD and graph features
- 8 subjects





- Local rather than global graph properties should be used
- PSD features achieved better classification than isolated graph metrics
- Pairwise combined graph metrics + wrappers achieved similar classification rates than PSD (but PSD used more features)

Stefano Filho et al. 2018, BSPC doi: 10.1016/j.bspc.2017.09.026

Relation between ERDs and functional networks


Carlos Stefano


Romis Attux

- Objective: to understand relationship between ERDs and functional networks
- 10 healthy subjects from Physionet's open database
- Significant correlations between PSD variations and functional network alterations for some electrodes, prominently in β band

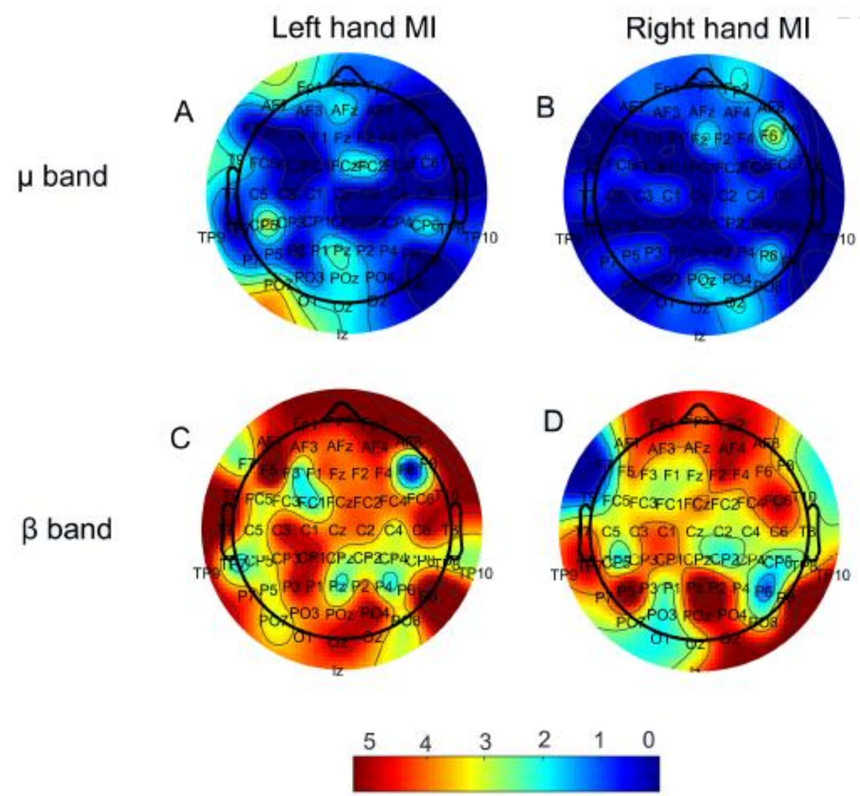


Figure 2 Number of times each electrode showed a significant correlation ($p < 0.05$) between the ERD relative to rest blocks (ΔPSD) and the degree variation on the respective node (ΔW).

Stefano Filho et al. 2017, PeerJ doi: 10.7717/peerj.3983

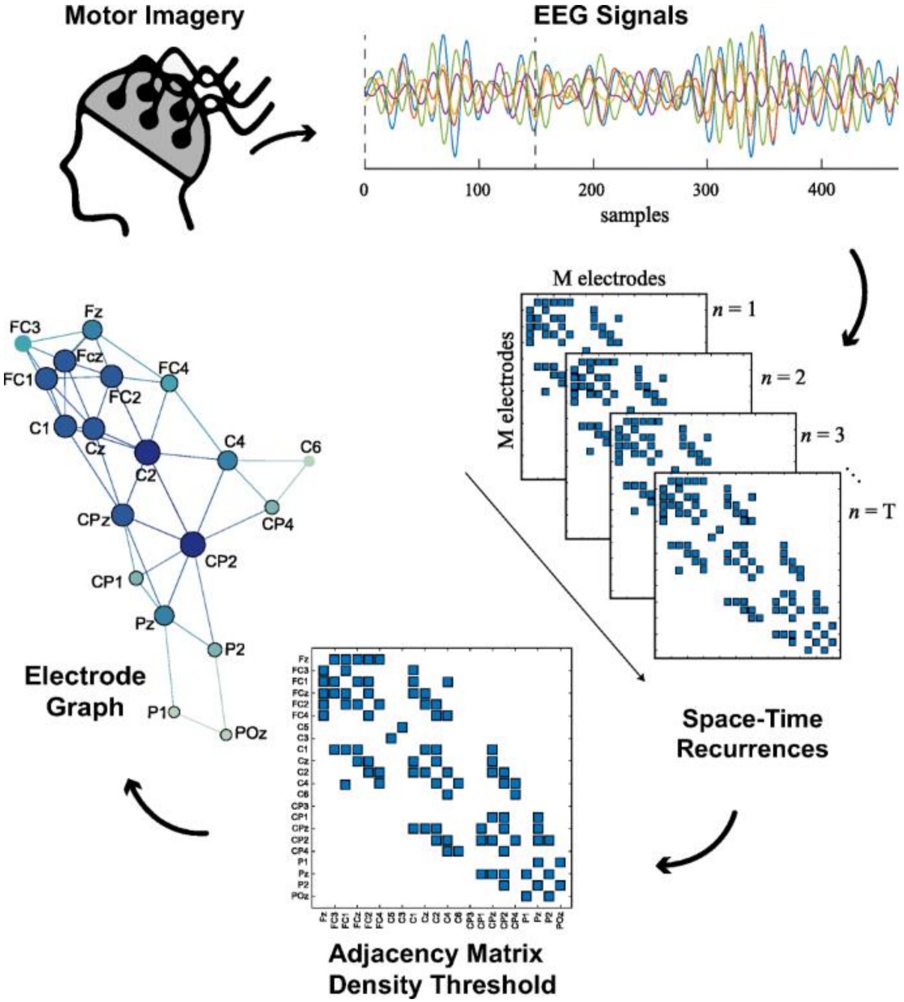
Other FC method: space-time recurrences


Paula Rodrigues


Diogo Soriano

- 4 FC methods: Pearson correlation, Spearman correlation, phase coherence, space-time recurrences
- 2 public datasets:
  - BCI competition IV 2a (9 subjects)
  - Cho et al. 2017 (52 subjects)
- BC, CC, D, EC

- STR significantly better than other frameworks
- EC: best feature regarding processing time
- Attributes found in classical EEG motor cortex positions for subjects with best performances



Rodrigues et al. 2019, Med&Biol Eng Comp doi 10.1007/s11517-019-01989-w

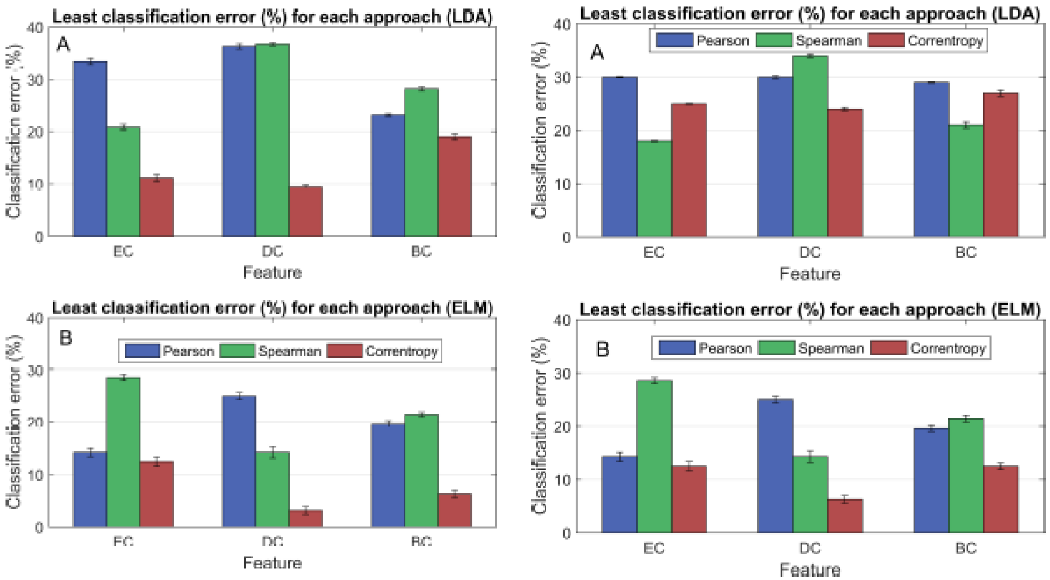
Other FC method: correntropy

Luisa Uribe

Romis Attux

- 3 FC methods: Pearson correlation, Spearman correlation, correntropy
- 2 datasets:
  - Home-acquired dataset (8 subjects)
  - BCI competition IV dataset 2a (9 subjects)
- BC, D, EC

μ band β band

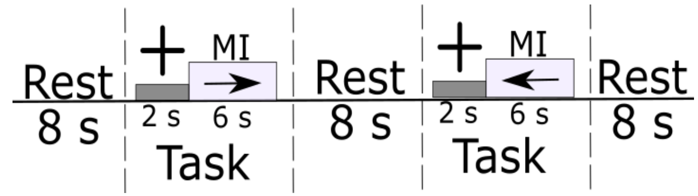


- Our dataset: correntropy + D + ELM was most solid framework
  - Overall classification error ~ 5%
- BCI competition dataset: best correntropy result comparable to top three competitors

Uribe et al. 2019, BPEX doi: 10.1088/2057-1976/ab5145

Graph measures discrimination and stability

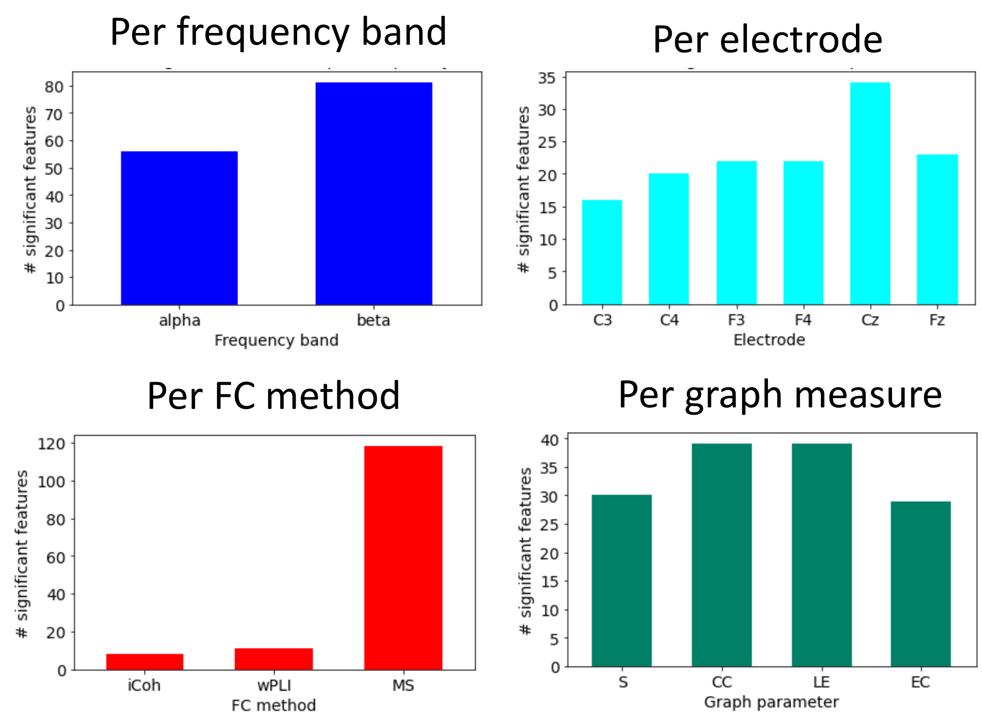
Pedro Vazquez



- 3 FC methods: imaginary coherence, weighted phase-lagged index, motif synchronization
- 10 healthy subjects
- S, CC, LE, EC

- β band and MS method produced most significant metrics
- EC was most stable (8/10) and most discriminating (4/10)
- Only for half the subjects most discriminating metric was most stable metric

Significant metrics

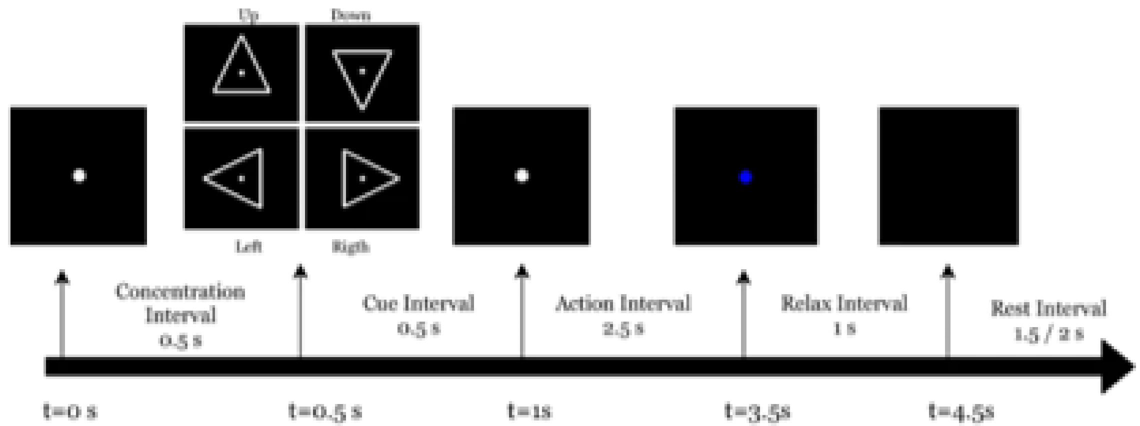


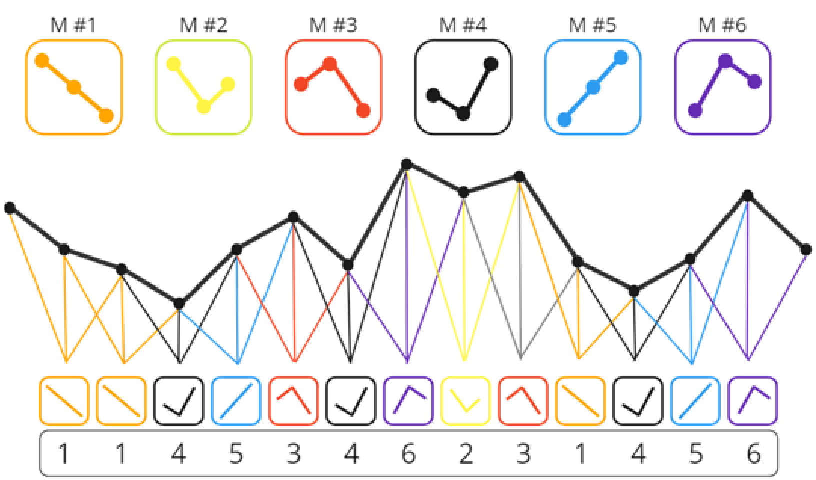
Vazquez et al. 2023, BSPC doi: 10.1016/j.bspc.2023.105061

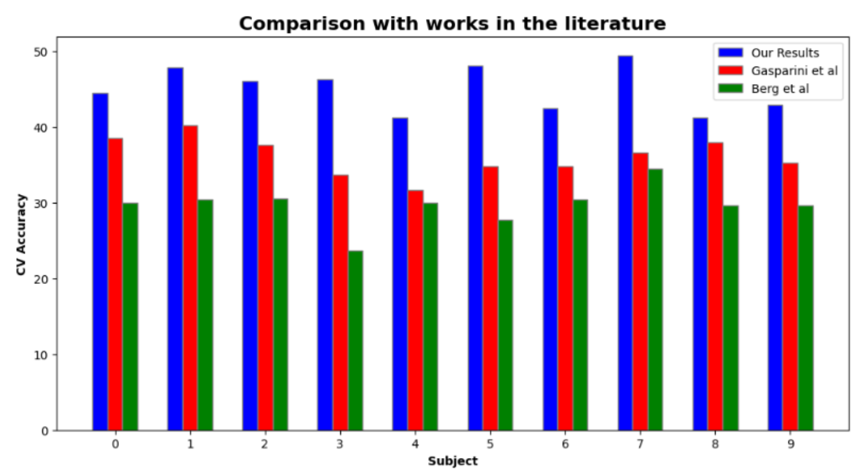
Inner speech paradigm

Eduardo Abreu

- 10 subjects
- Thinking out loud database
- Strength, PageRank
- MS method
- 4 classes



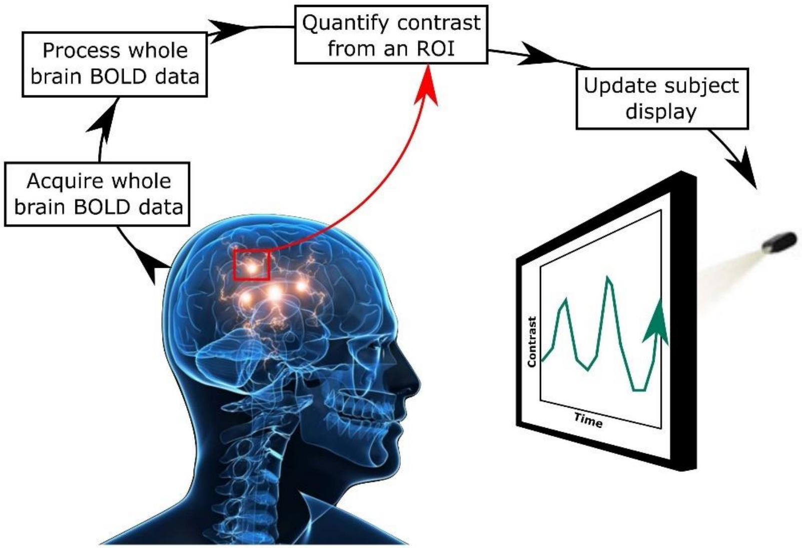




Abreu & Castellano 2024, 10th BRAINN Congress

Neurofeedback (NFB) training

- Self-regulation of brain signals



https://medicalxpress.com/news/2017-11-neurofeedback-tinnitus.html

BCI

- Main goal is the control of an external device
- For the BCI to work:
  - Either signal has to be "improved" by user to be easily recognized (classified) by system
  - Or classifier must be adapted to recognize user's signal

NFB

- Main goal is the brain's autoregulation for improving some characteristic or skill
- For NFB to work:
  - Signal has to be "improved" by user to improve target function

Where is neurofeedback used?

- Cognitive training for several functions and disorders

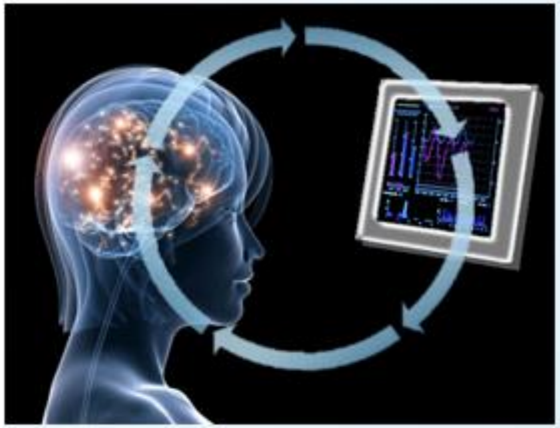
Disorder treatment

- Attention deficit and hyperactivity disorder (ADHD)
- Depression
- Motor disabilities
- Anxiety
- Autism
- Obsessive compulsive disorder (OCD)
- Epilepsy
- Sleep disorders
- …

Controversial results!

Function improvement

- Motor function (athletes' performance)
- Executive function
- Memory
- Attention/focus
- …



http://www.choratech.com/solutions/neurofeedback

Where is neurofeedback used?

- Cognitive training for several functions and disorders

Disorder treatment

- Attention deficit and hyperactivity disorder (ADHD)
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- Sleep disorders
- …

Less controversial!

Function improvement

- Motor function (athletes' performance)
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- Memory
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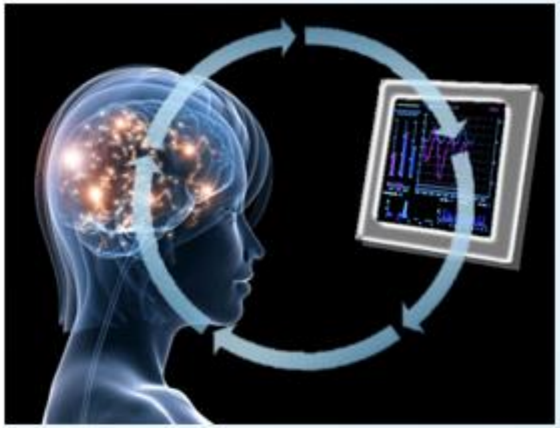
- …



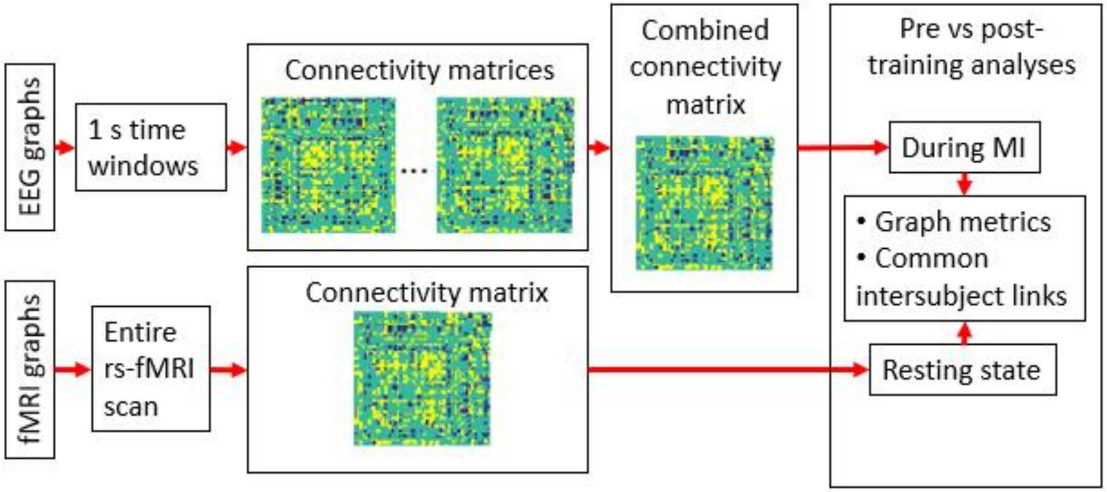
http://www.choratech.com/solutions/neurofeedback

MI practice and feedback effects in functional connectivity

Carlos Stefano

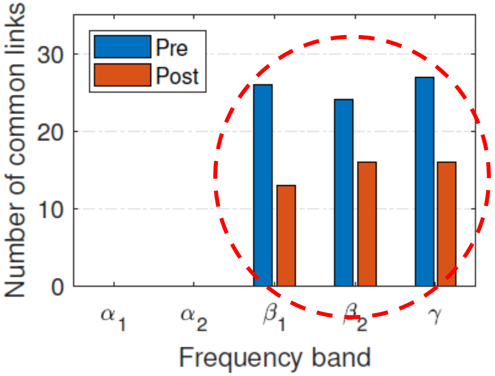
Romis Attux

- 30 healthy subjects, 10 sessions

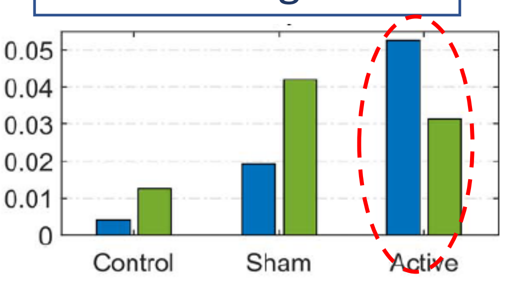


- 5 CP children, 1 session

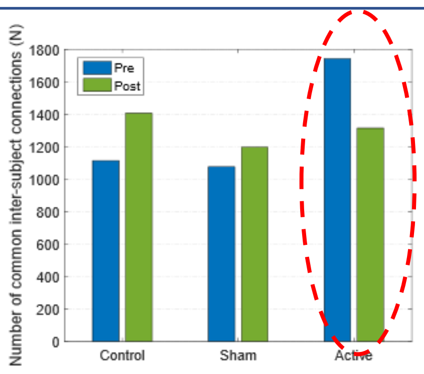
EEG - resting state - CP



EEG - during MI - H



fMRI - resting state - H



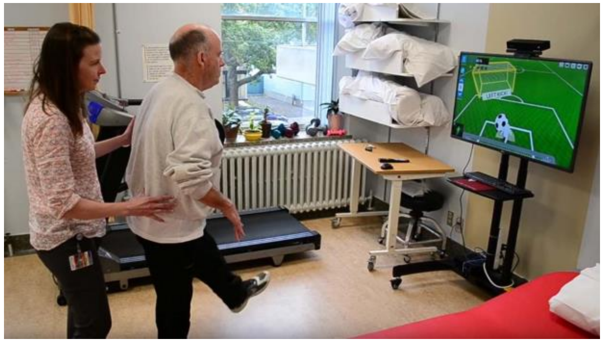
- Consistency of FC patterns decreased for active group
- Similar result obtained for cerebral palsy children

Stefano Filho et al. 2022, JNE doi: 10.1088/1741-2552/ac456d
Stefano Filho et al. 2021, App Sci doi: 10.3390/app11052372

eXtended reality (XR) systems and tDCS for rehabilitation

Why use XR for rehabilitation?

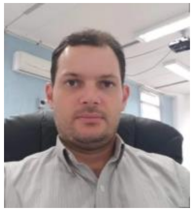
- It promotes neuroplasticity and motor learning
  - XR can trick the brain (false positive feedback)
- More fun
- Can be performed at home with remote supervision



https://www.evolving-science.com/sites/default/files/field/image/Virtual-Reality.jpg

https://cdn.shopify.com/s/files/1/0238/0391/files/013_toyra_rehabilitation_grande.jpg?v=1505765341

https://assets3.thrillist.com/v1/image/2720674/size/sk-2017_04_article_main_mobile.jpg

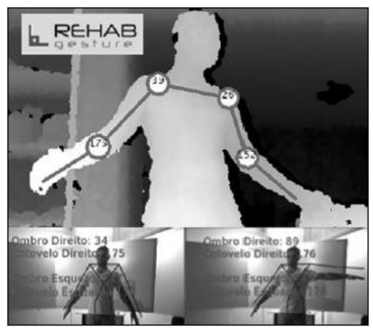

Alexandre Brandão


Diego Dias

XR tools


Gilda de Assis

GestureCollection and KinesiOS



Brandão et al. 2018, JHI https://jhi.sbis.org.br/index.php/jhi-sbis/article/view/544

NeuroR


(a) Posição inicial
(b) Início da flexão
(c) Flexão inferior a 90 graus
(d) Flexão entre 90 e 180 graus

Assis et al. 2014, Dis Rehab doi: 10.3109/17483107.2014.979330

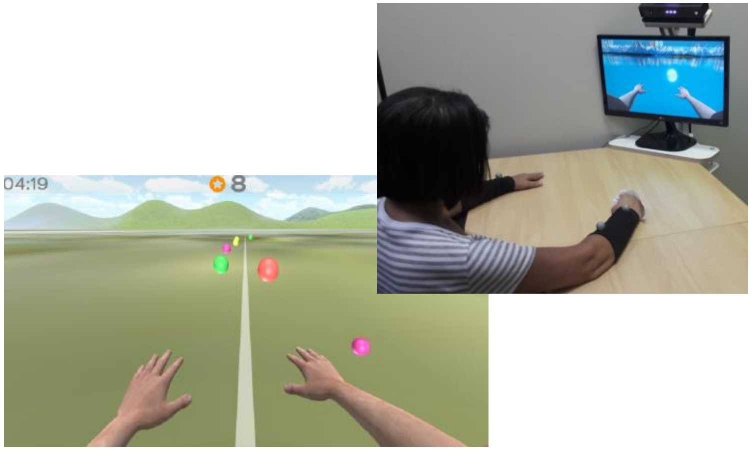
XR tools

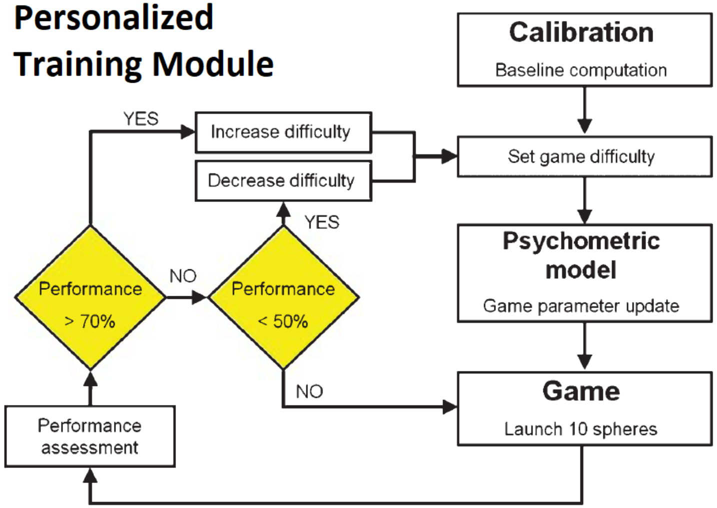
Paul Verschure

Jônatas Manzolli

Elena Partesotti

Rehabilitation Gaming System (RGS)





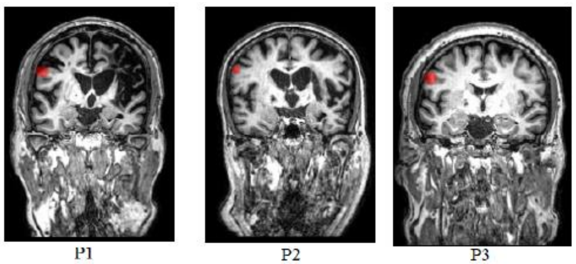
Cameirão et al. 2011, RNN doi: 10.3233/RNN-2011-0599

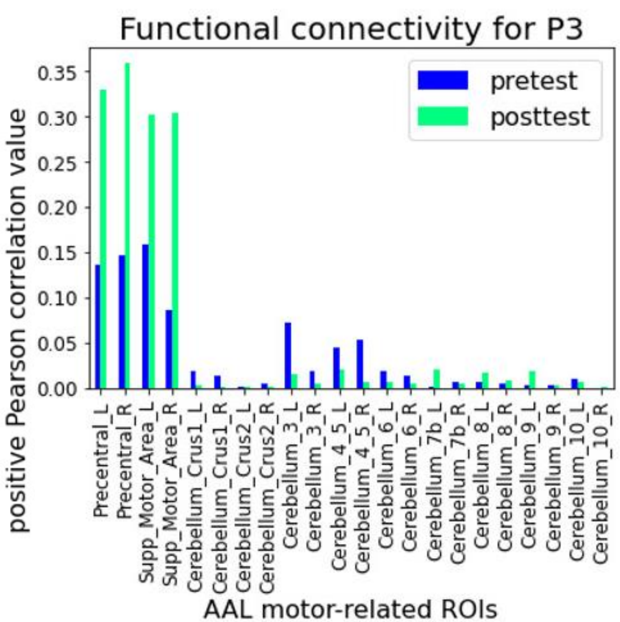
BehCreative

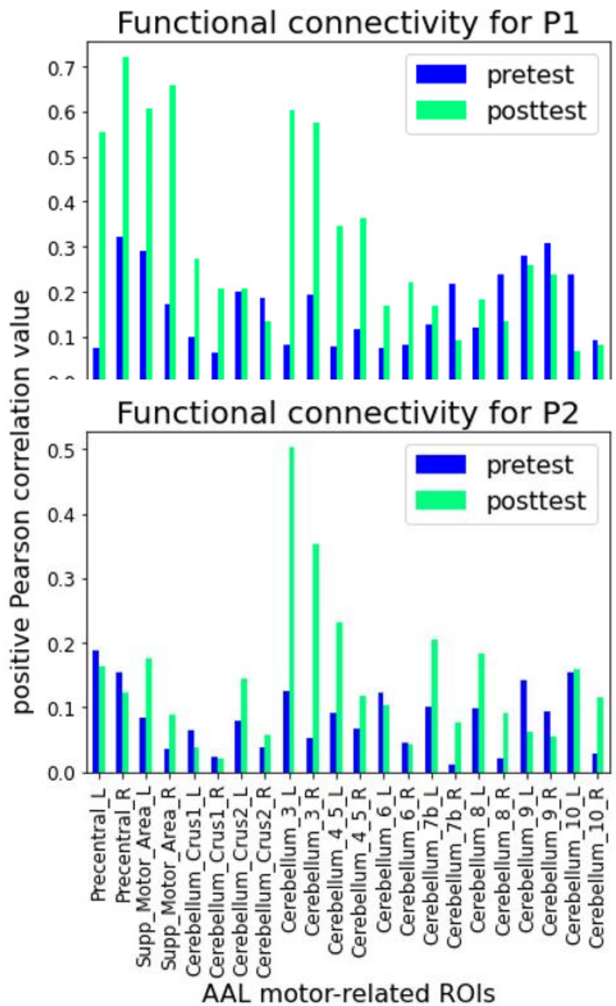
Partesotti et al. 2023, EAI ArtsIT

Functional connectivity changes due to NeuroR therapy

Gilda de Assis







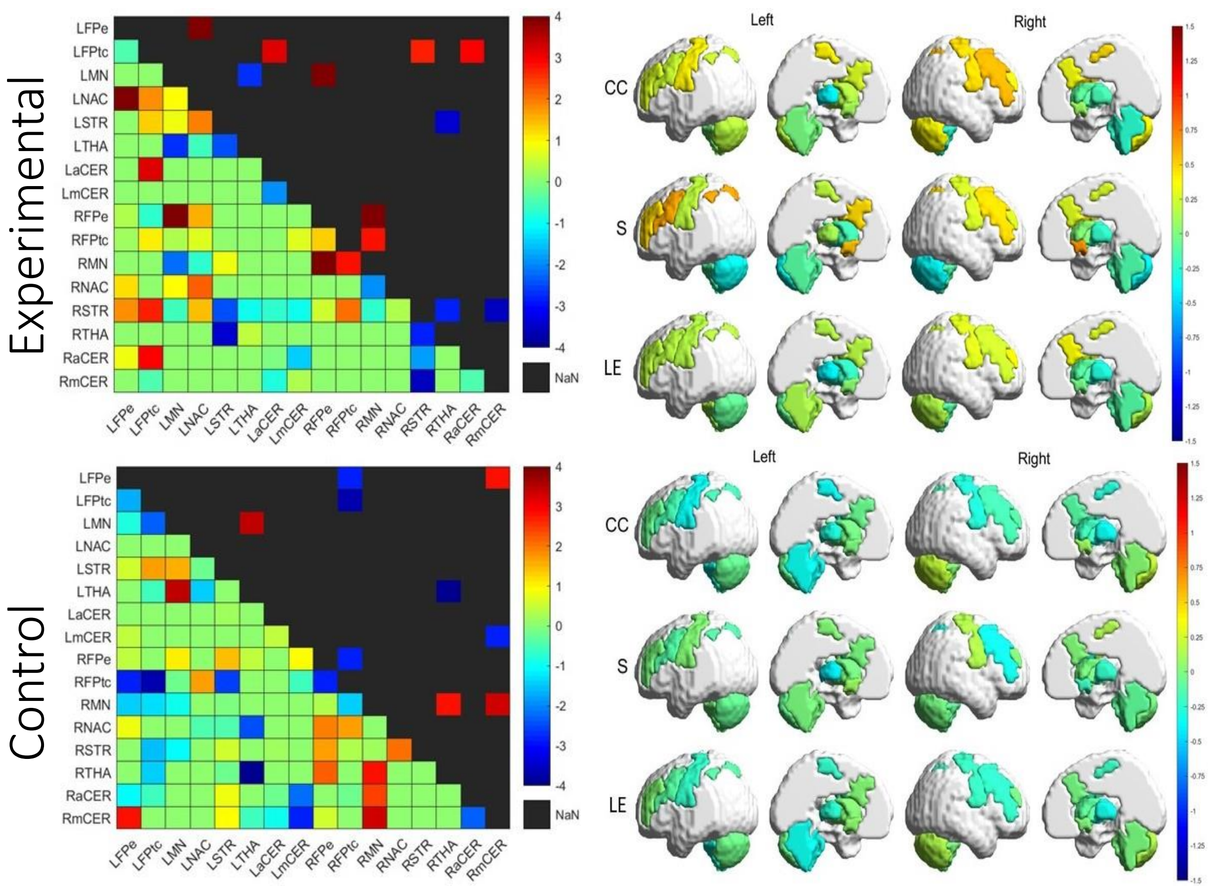
Session	Participant	Abduction		Flexion	
		start	end	start	end
First	P1	60	70	40	40
Last	P1	75	70	50	50
First	P2	0	0	0	0
Last	P2	0	0	0	0
First	P3	60	60	70	40
Last	P3	70	70	80	60

- 3 stroke patients
- 8 rehabilitation sessions
- Significant FC increase of motor areas with seed in ipsilesional motor área for two patients (P1 and P3)
- ROM measurements suggest improvement for two patients (P1 and P3)
- P2 showed signs of post-intervention muscle contraction

Assis et al. 2023, Virt Worlds doi: 10.3390/virtualworlds2010001

Graph changes due to Gesture Collection therapy

- 14 (10) stroke subjects: 7 (5) experimental / 7 (5) control



- Both groups showed improvement in clinical scales
- More increases in FC in the experimental group
- Experimental group had FC changes in regions associated with reward-based motor learning
- Control group had changes in regions more related to a purely mechanical activity
- GestureCollection successfully shown to promote neuroplasticity in several motor-related areas

Feitosa et al. 2023, Front Neurol doi: 10.3389/fneur.2023.1241639

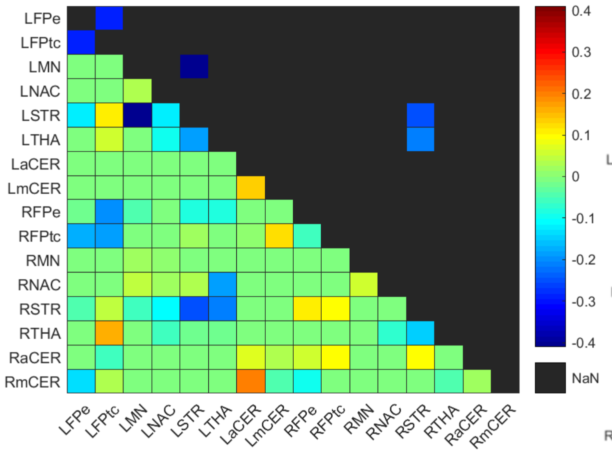
Graph changes due to BehCreative training


Jamille Feitosa

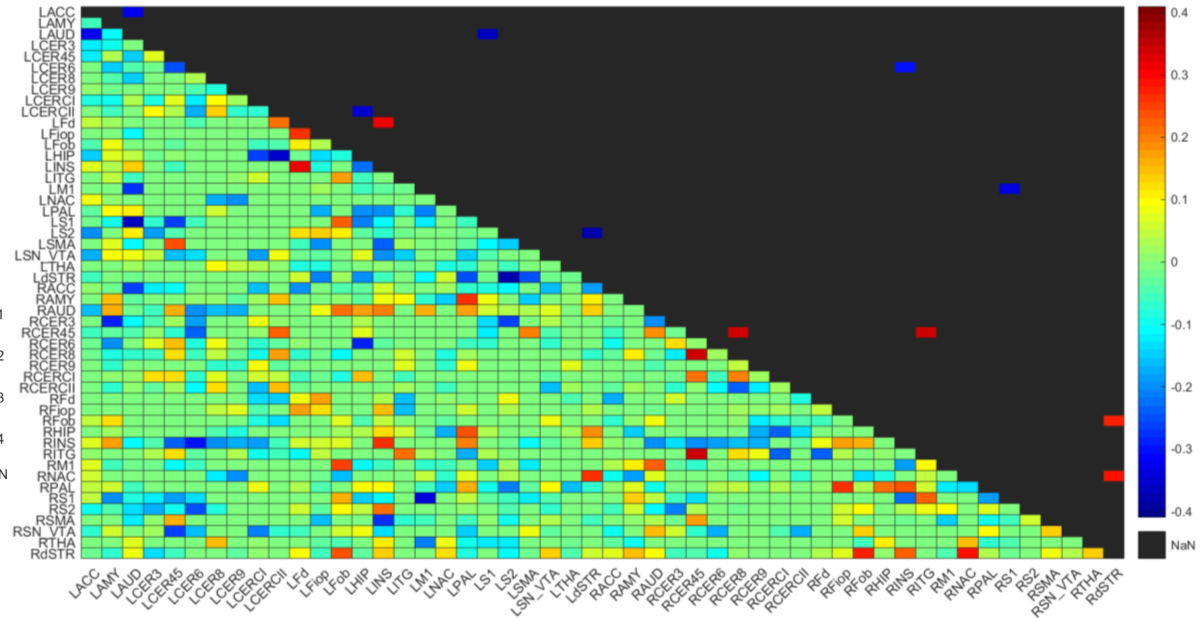

Elena Partesotti

- 11 (5) healthy subjects

Motor-related areas



Motor & emotion-related areas

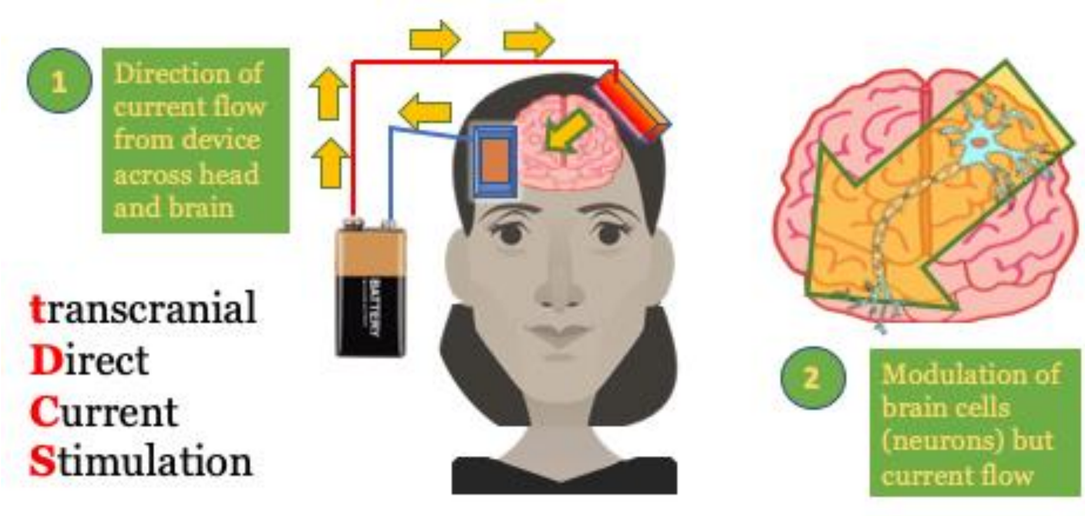


- Different from other XR systems:
  - Subjects showed only significant FC decreases in motor related areas
  - BehCreative promoted an emotional response, possibly associated to visual and auditory stimuli

Partesotti, Feitosa et al., PLOS1, submitted

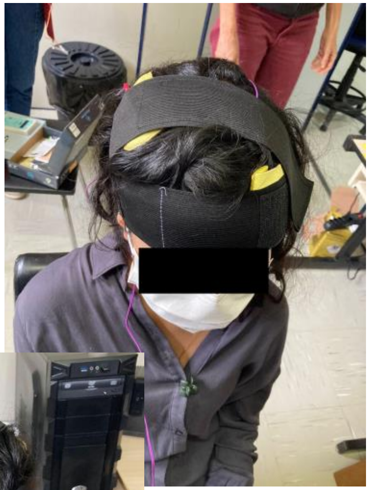
tDCS

- Delivery of low (~1 to 2 mA) electrical current to the scalp
- Limited side-effects, relatively safe and affordable, simple application



https://neuromodec.org/what-is-transcranial-direct-current-stimulation-tdcs/

- Anodal tDCS - resting membrane potential of the tissue depolarizes → increase in neuronal excitability
- Cathodal tDCS - resting membrane potential of the tissue hyperpolarizes → increase in neuronal inhibition
- Motor rehabilitation - excitation of ipsilesional M1 and/or inhibition of contralesional M1 - viable options to enhance motor function



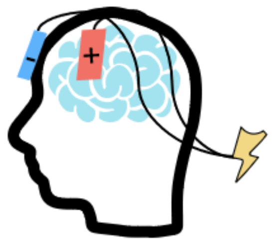
Rehabilitation: BRAINN_XR + tDCS

chronic stroke patients

rehabilitation

XR+atDCS

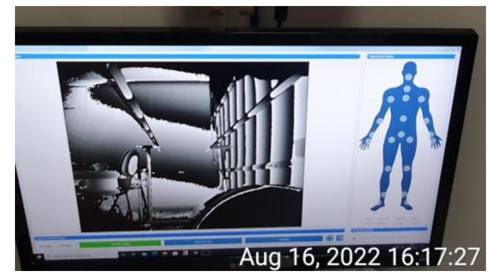
XR+sham



evaluation

clinical / functional scales

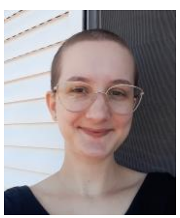
range of motion



EEG

EMG

Cássio Ruas

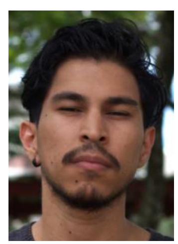


Bruna Carlos

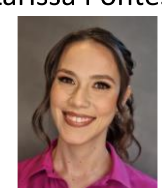
Sara Almeida

Larissa Pontes

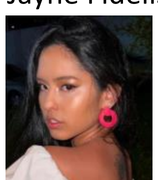
Jayne Fidelis



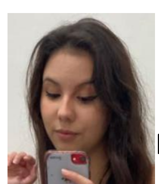
Saulo Feitosa



Júlia Pereira

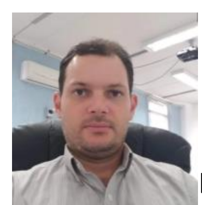


Bruna Furumoto



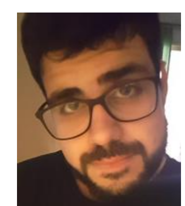
Beatriz Rosa

Márcio Nascimento



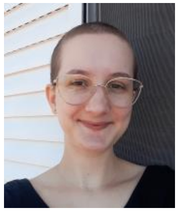
Alexandre Brandão

Lucas Menezes



Pedro Vazquez

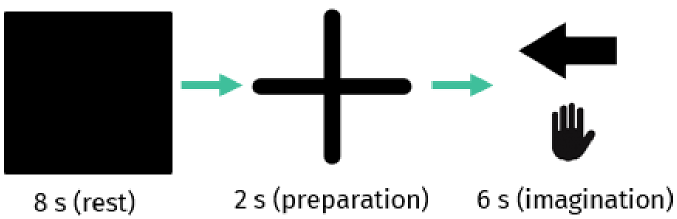
Leonardo Costa

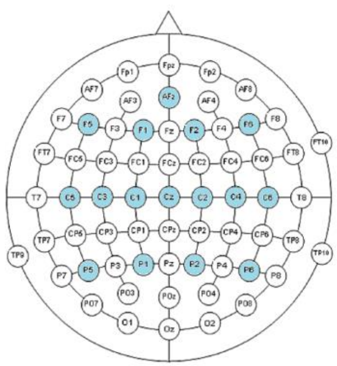


Bruna Carlos

XR+tDCS study

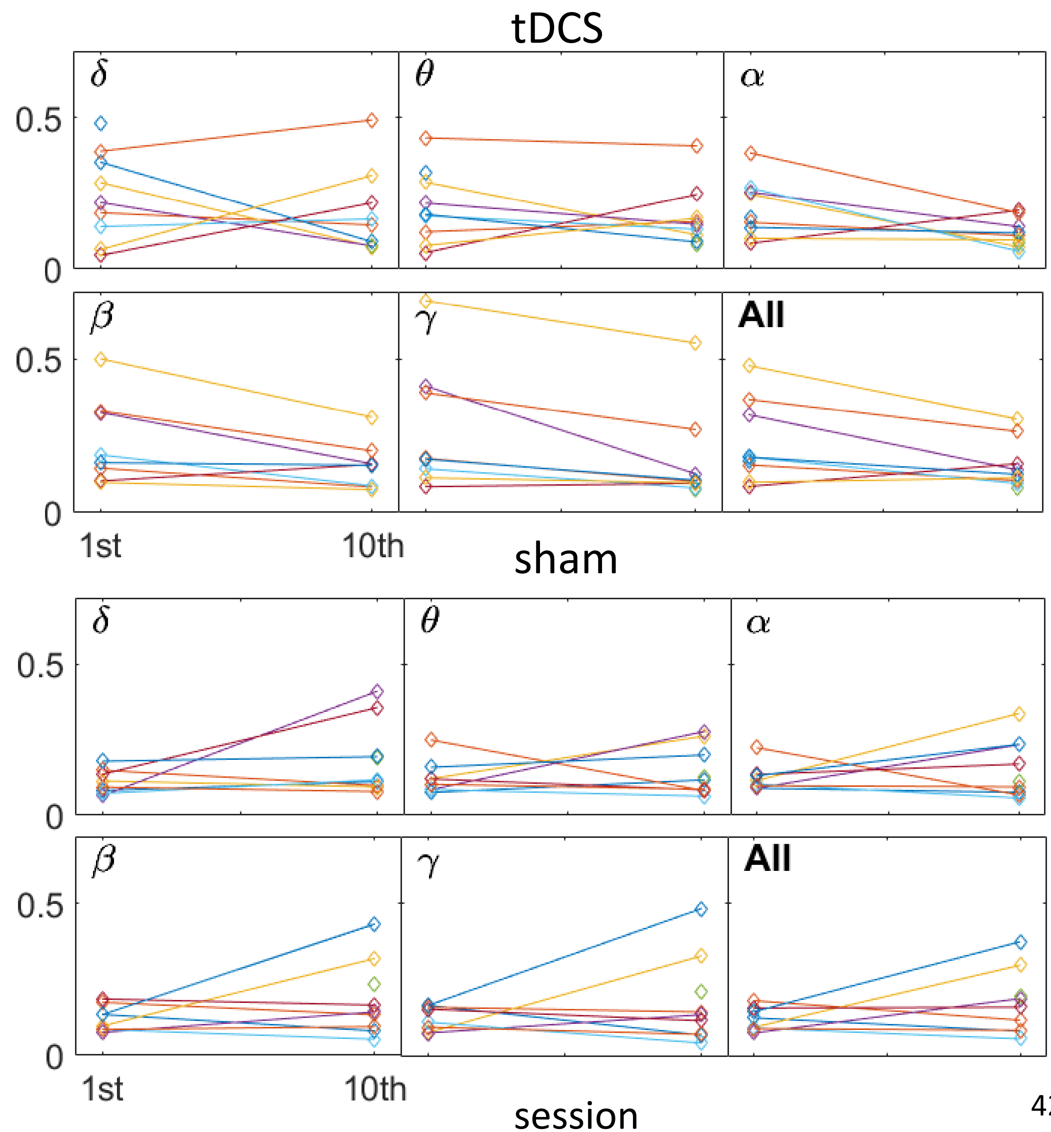
- 19 stroke subjects
- 10 sessions of 30 min
- EEG: resting state (60s) + MI (128s)

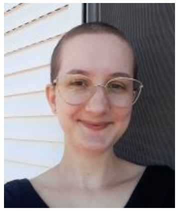




- Comparison between $10^{th}/1^{st}$ and $5^{th}/1^{st}$ sessions

Symmetry evolution (BSI) at rest



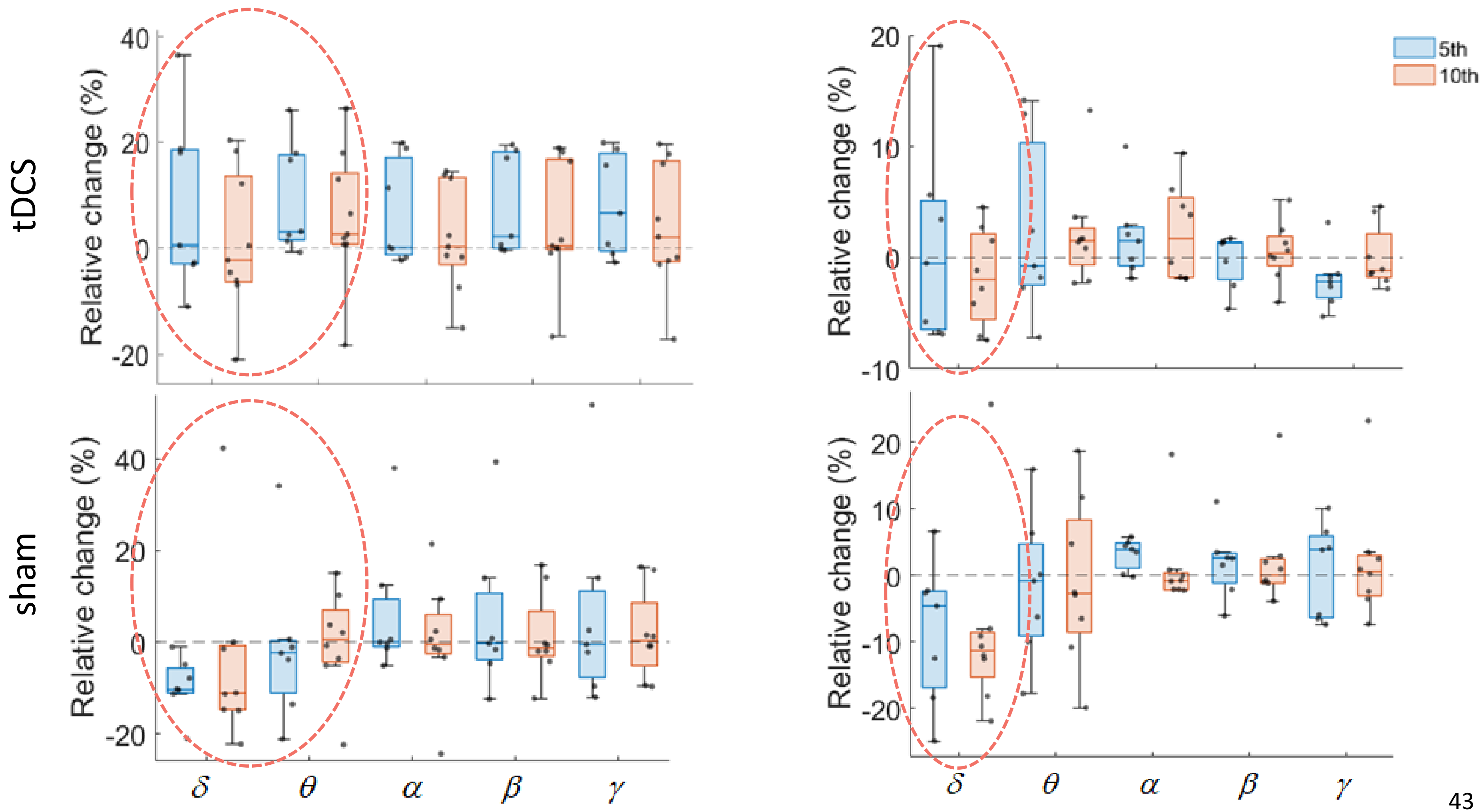


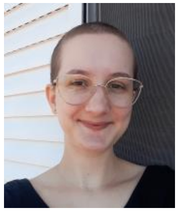
Bruna Carlos

XR+tDCS study

Graph changes – global strength

Rest **MI paretic hand**

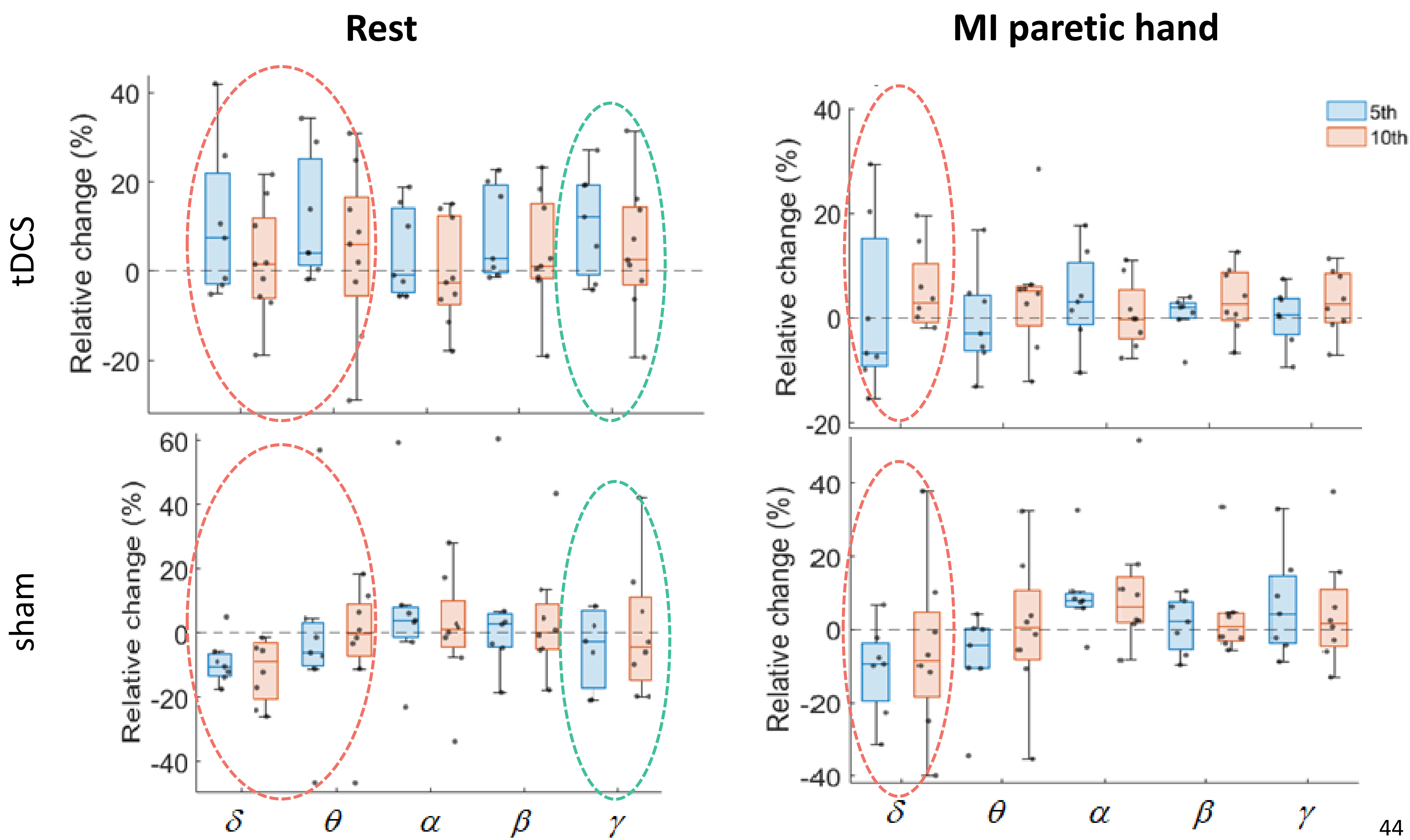




Bruna Carlos

XR+tDCS study

Graph changes - Ipsilateral strength (C3 or C4)



Difficulties / limitations

- The samples used in each study (particularly the XR ones) were small
  - Large number of sessions
  - Patients with limited mobility
  - Data quality due to patients' conditions
  - Covid-19 pandemics
- Heterogeneous samples
  - Hard to find large number of patients with same lesion location and same (exactly) clinical condition
  - Small and heterogeneous populations make it more difficult to find patterns
- Dependence on health professionals (physiotherapists)
  - Difficult to get financial resources

Conclusions

BCI and neurofeedback

- Connectivity measures are related to motor imagery ERDs
- Connectivity measures produce results at least as good as PSD’s for motor imagery paradigm and better results for inner speech paradigm
- Feedback resulted in more different connectivity patterns among subjects, both for healthy subjects and cerebral palsy children

Conclusions

Rehabilitation with XR or XR+tDCS for stroke patients

- Most patients showed improvement in clinical scales
- XR + conventional therapy (GestureCollection study) enhanced the treatment effect
- XR + tDCS
  - Decreased asymmetry for tDCS group in higher frequency bands
  - Increased/decreased connectivity for tDCS/sham group in bands not usually associated to movement execution/imagination
- In general, found brain changes point towards restoration to normal (fMRI/EEG) patterns

Acknowledgements

- All past and present students
- All collaborators
- All subjects (healthy and patients)
- Brazilian Federal and São Paulo State research funding agencies

FAPESP

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