Neurofeedback bimodal EEG-IRM : méthodes et applications

Pierre Maurel, MCF UR1

EMPENN

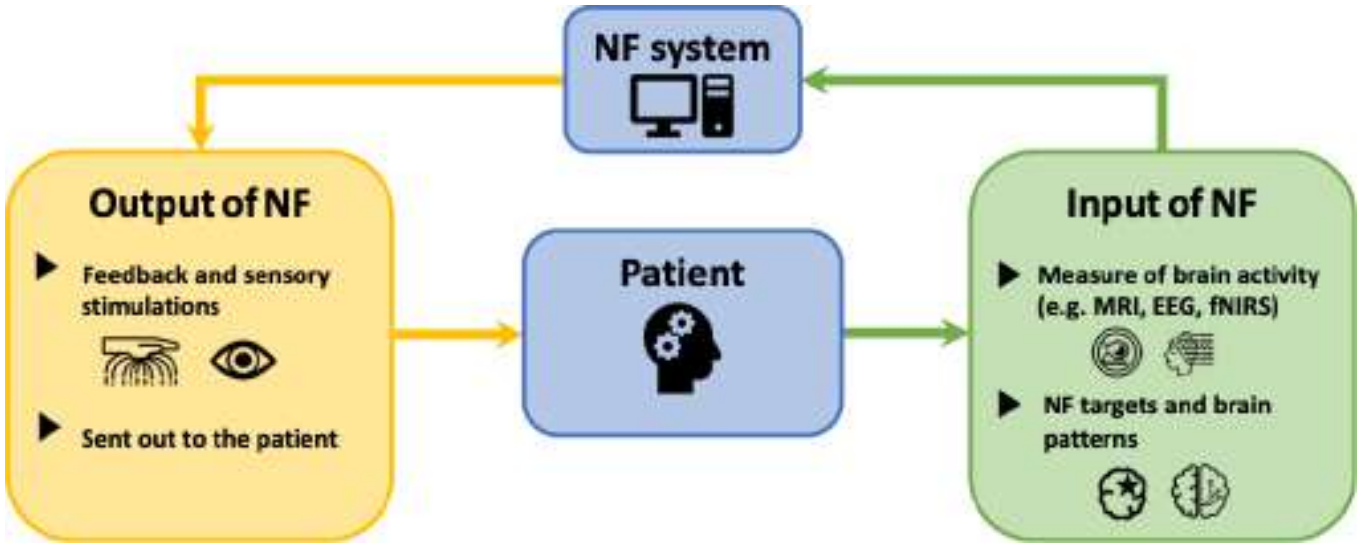
15/12/22

Neurofeedback

Neurofeedback

→ consists in presenting a subject with a stimulus directly related to his/her current brain activity

- can be used to teach subjects to regulate their own brain functions



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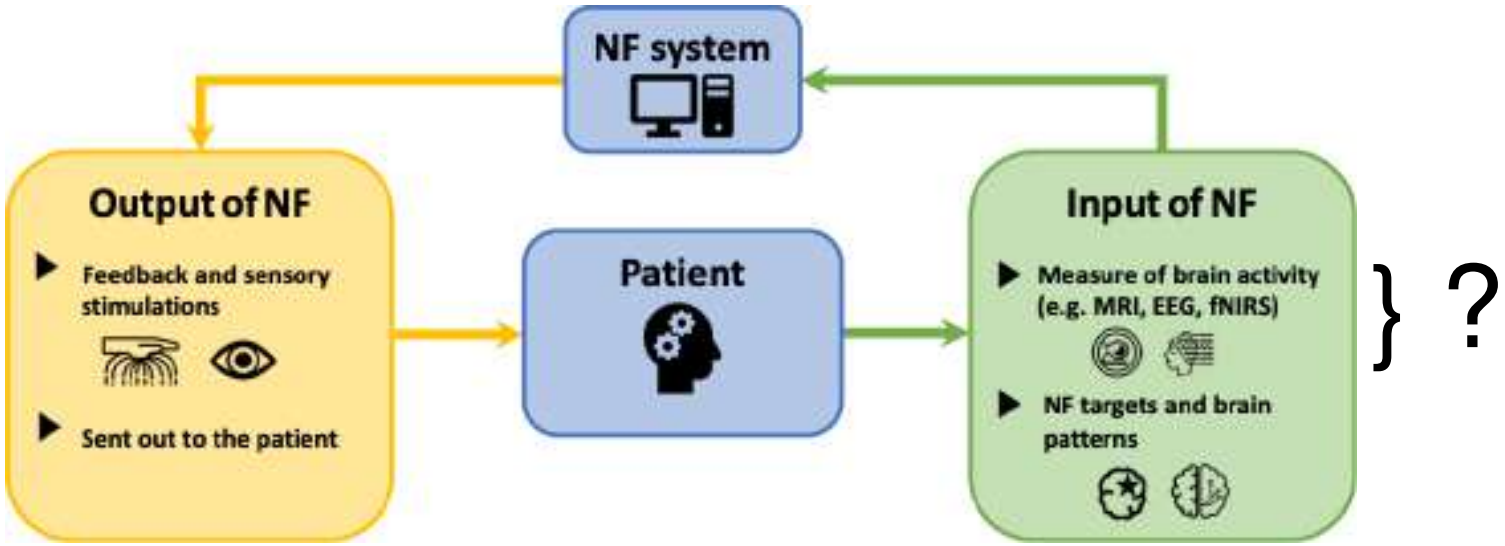
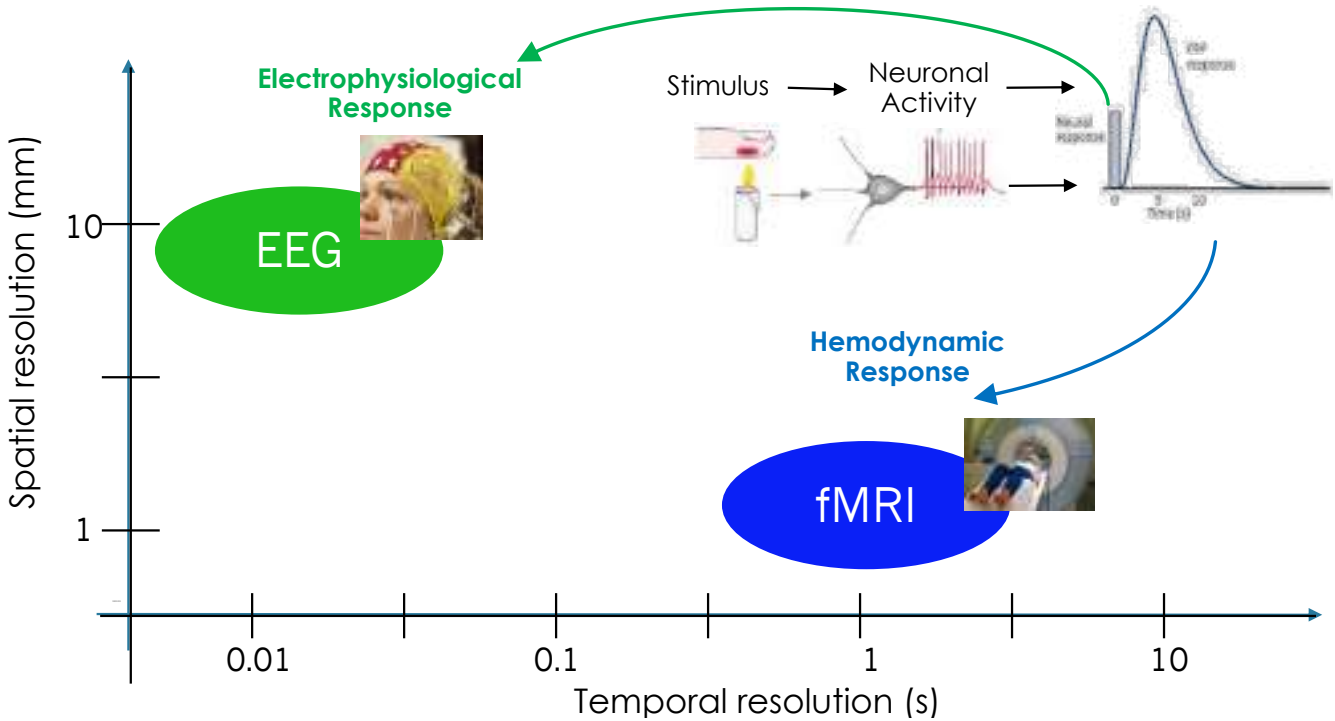


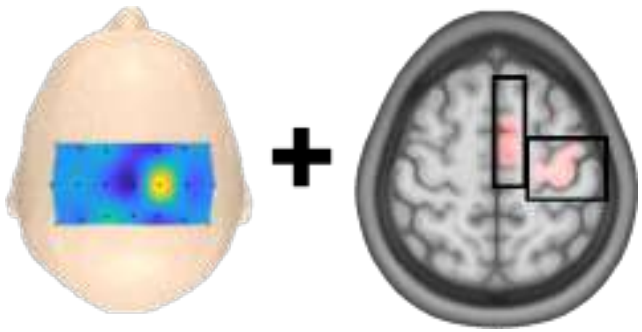
Neurofeedback: Brain Imaging Modalities

- **Electroencephalography (EEG)** → main modality used by clinical practitioners, but low spatial resolution
- **functional MRI** → high spatial resolution & possibility to image deep brain structures, but low temporal resolution and high costs/constraints



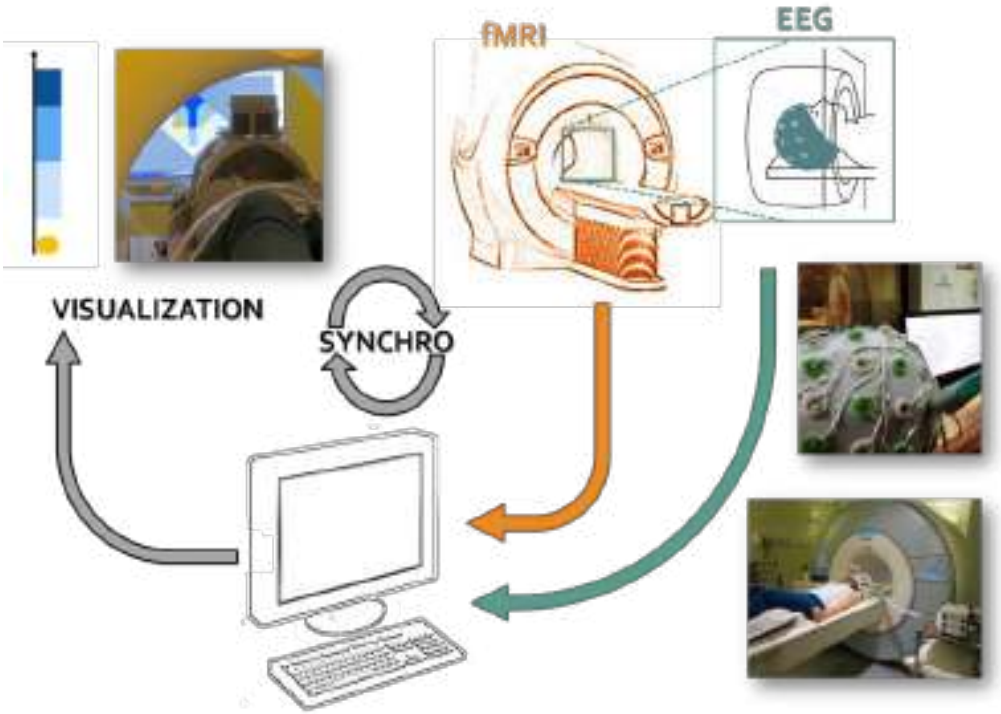
Bimodal Neurofeedback

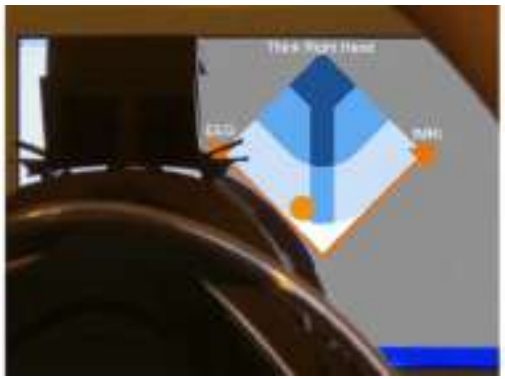
- **Hemisfer project**: hybrid EEG-fMRI and simultaneous neurofeedback for brain rehabilitation



- **Challenges**:
  - → Build a real-time computational platform to integrate EEG and fMRI
  - → Propose new bimodal NF paradigms
  - → Combining bimodal EEG/fMRI NF and unimodal EEG NF for stroke rehabilitation

The Hybrid EEG-fMRI Neurofeedback System





(Mano et al., Frontiers in Neurosciences 2017, Patent 2017)

- Second system worldwide to perform bimodal EEG-fMRI NF
- EEG feedback updated every 250 ms
- fMRI feedback updated every 1 s

The Hybrid EEG-fMRI Neurofeedback System

Setting up the subject

M.Fleury

EEG post-processing

→ **large EEG artifacts induced during fMRI**

(Allen et al., NeuroImage 2020)

A: Raw EEG

EEG post-processing

→ **large EEG artifacts induced during fMRI**

(Allen et al., NeuroImage 2020)

A: Raw EEG

B: Averaged imaging artifact

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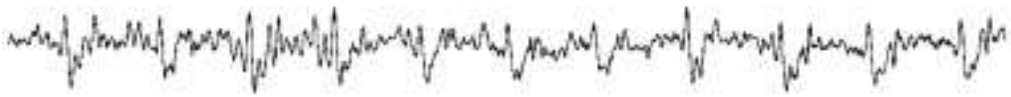
A: Raw EEG

B: Averaged imaging artifact

C: Subtracting B from A



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A: Raw EEG

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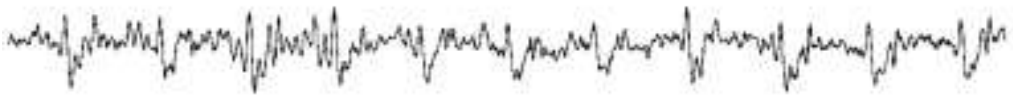


D: averaged pulse artifact from C

EEG post-processing

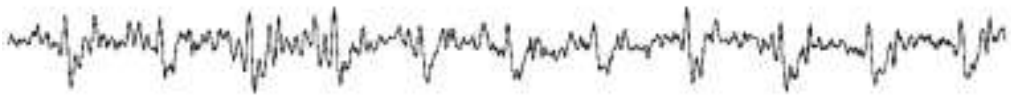
→ **large EEG artifacts induced during fMRI**

(Allen et al., NeuroImage 2020)

A: Raw EEG

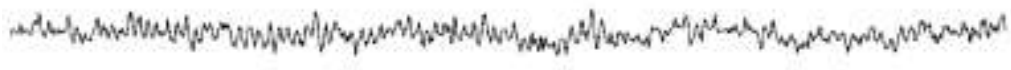
B: Averaged imaging artifact

C: Subtracting B from A



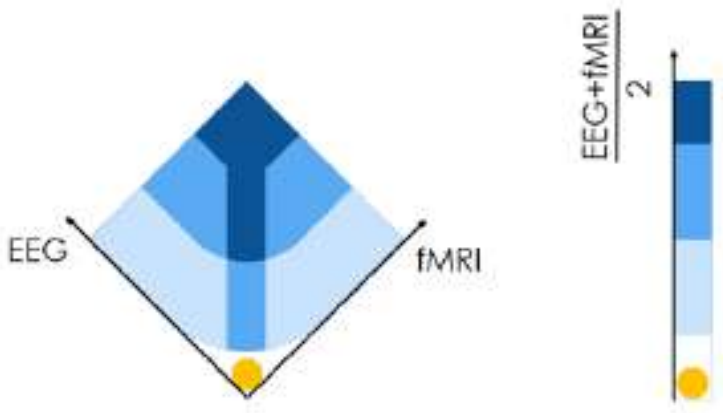
D: averaged pulse artifact from C

E: Subtracting D from C



Proof-of-concept on healthy subjects

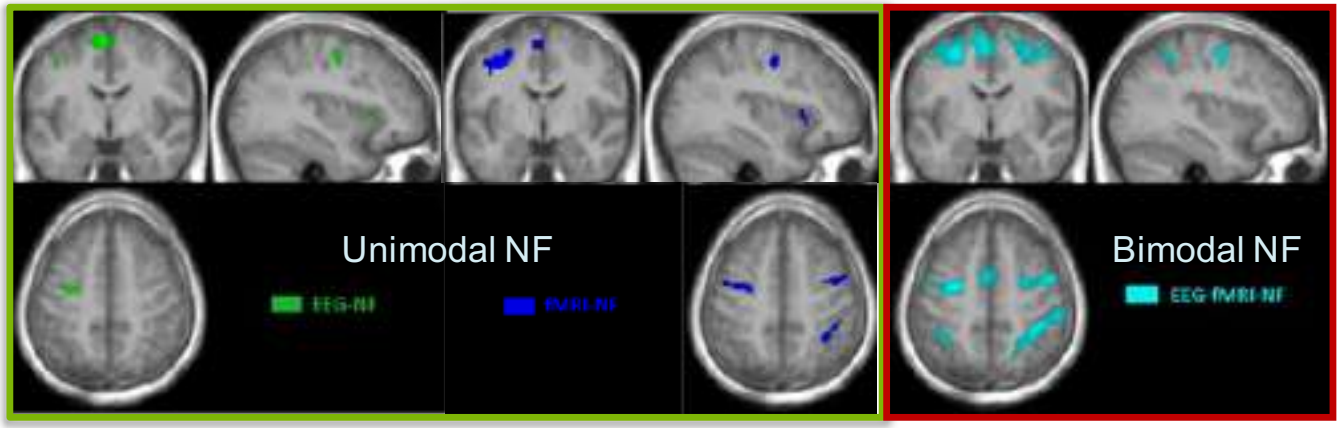
- **Aims**
  - Provide real-time neurofeedback (NF) from simultaneous EEG/fMRI real-time recording on motor imagery
  - Investigate new neurofeedback hybrid paradigms (1D vs 2D)



(Perronnet et al., 2017; Perronnet et al., 2018)

Proof-of-concept on healthy subjects

- **Aims**
  - Provide real-time neurofeedback (NF) from simultaneous EEG/fMRI real-time recording on motor imagery
  - Investigate new neurofeedback hybrid paradigms (1D vs 2D)
- **Results**
  - Simultaneous EEG-fMRI-NF provides stronger, bigger and more widespread activations than EEG or fMRI NF



(Perronnet et al., 2017; Perronnet et al., 2018)

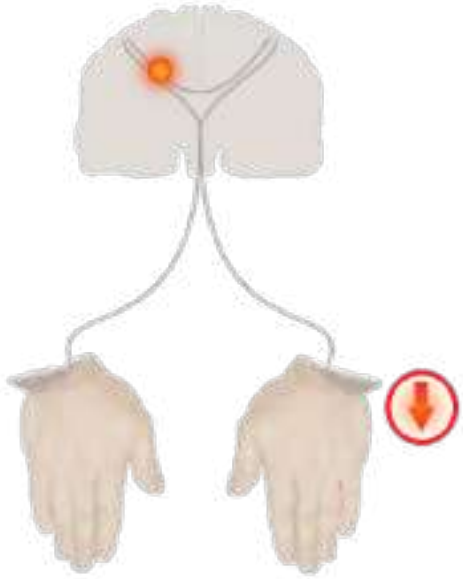
→ public dataset, 27 healthy subjects EEG-fMRI NF (Lioi et al., 2020)

`https://openneuro.org/datasets/ds002336/versions/2.0.0` & `https://openneuro.org/datasets/ds002338/versions/2.0.0`

Neurofeedback for Stroke Rehabilitation

Neurofeedback for Stroke Rehabilitation

- 33 million stroke survivors/year
  $\hookrightarrow$ 80% with motor impairment
- Leading cause of adults acquired disability
- Recovery limited after one year



(Langhorne et al, 2011)

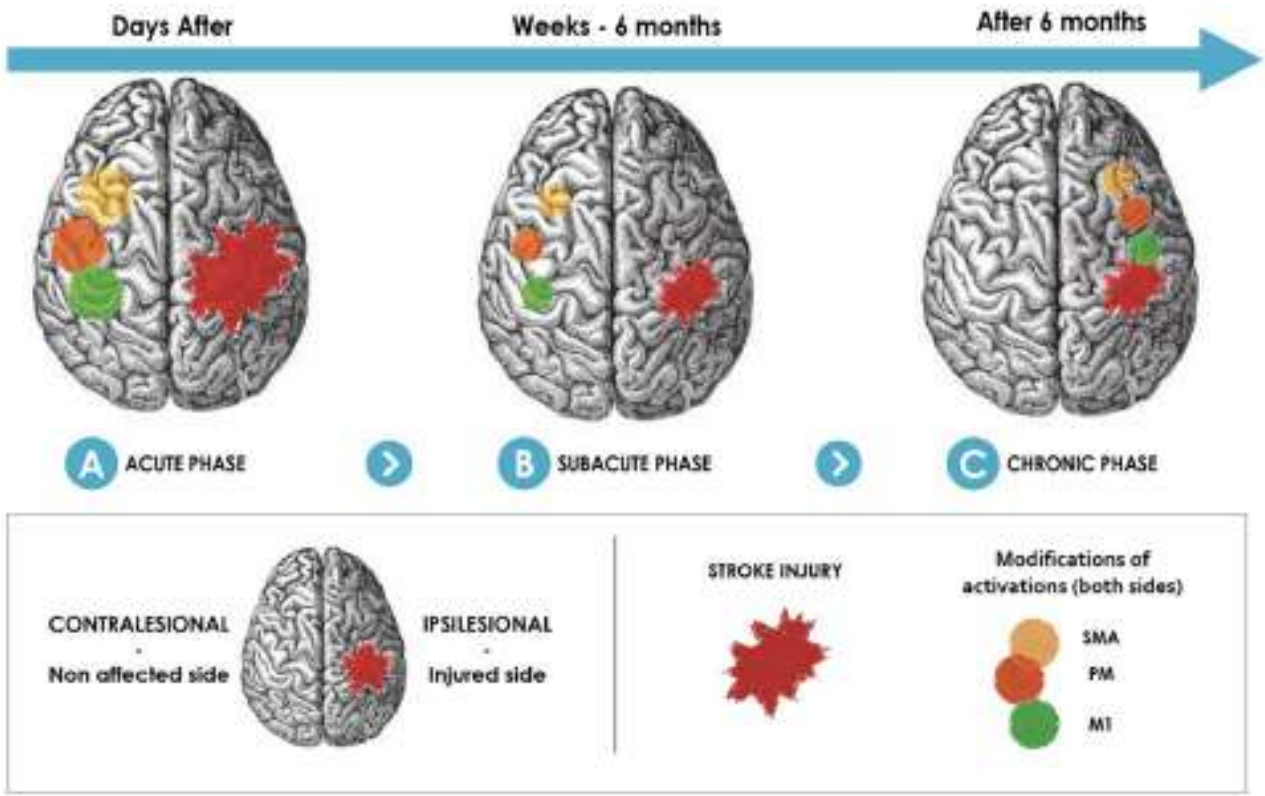
$\rightarrow$ Neurofeedback : potential for stroke rehabilitation, re-education of damaged motor areas by means of Motor Imagery

Isabelle Bonan, Quentin Duché, Giulia Lioi, Mathis Fleury, Emilie Leveque-Le Bars, Simon Butet, Lou Scotto Di Covella, Anatole Lécuyer, Elise Bannier, Pierre Maurel

CHU Rennes, Empenn Team, Hybrid Team

Neurofeedback for Stroke Rehabilitation

Physiological recovery mechanism in brain motor areas after stroke

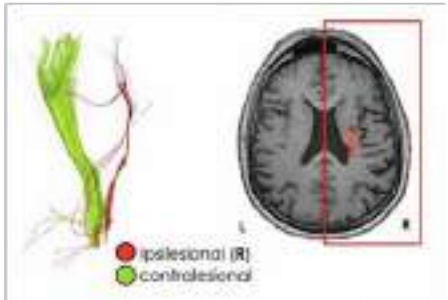


(Le Franc et al. 2022)

→ Neurofeedback to guide brain plasticity by rewarding a recovery of ipsilesional activation

NF for Stroke Rehab. : a Randomized Controlled Trial

- Inclusions Criteria
  - Adults, Unilateral supratentorial stroke
  - More than 6 months post-stroke
  - Motor impairment (22<Fugl-Meyer Motor Score<53)
  - Sufficient integrity of the corticospinal tract ↗



- Interventional group : 14 NF sessions, incl. 5 bimodal

- Control group : 14 motor imagery sessions (without NF)

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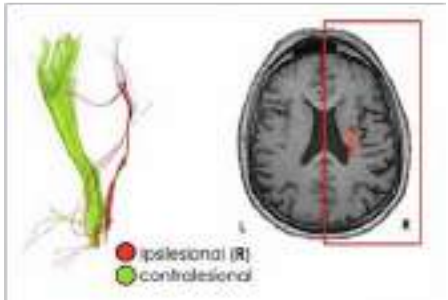

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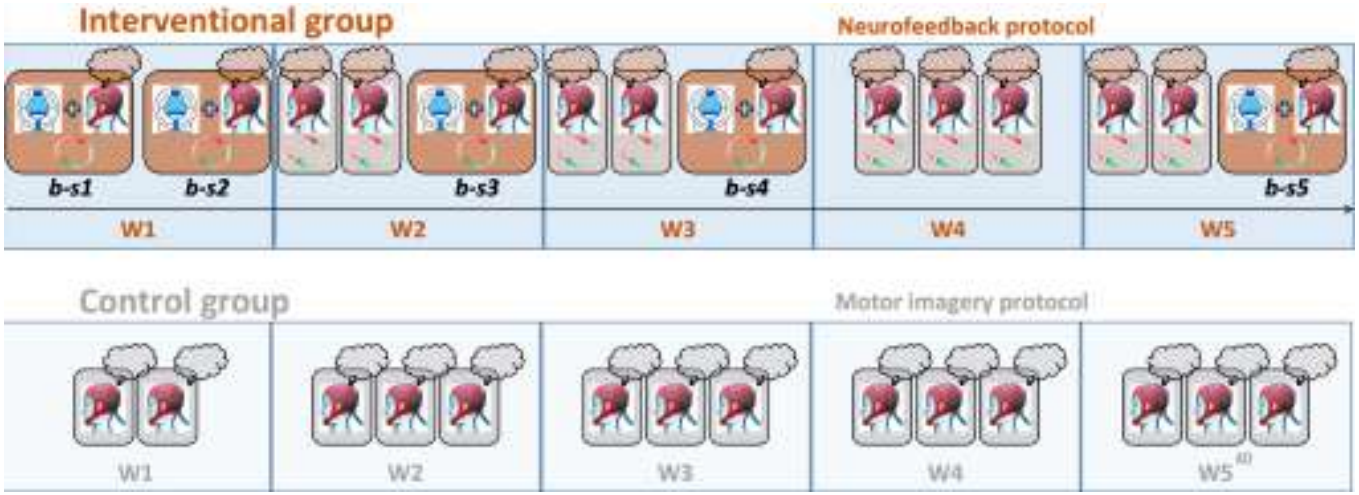
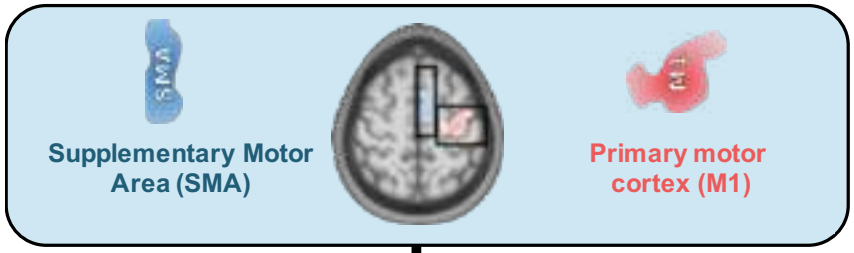


Q.Duché

NF for Stroke Rehab. : a Randomized Controlled Trial

Choice of NF score

Trained and rewarded brain targets



« easy » activation in motor imagery
(Mehler et al. 2019)

Activation associated with good motor recovery
(Favre et al. 2014)

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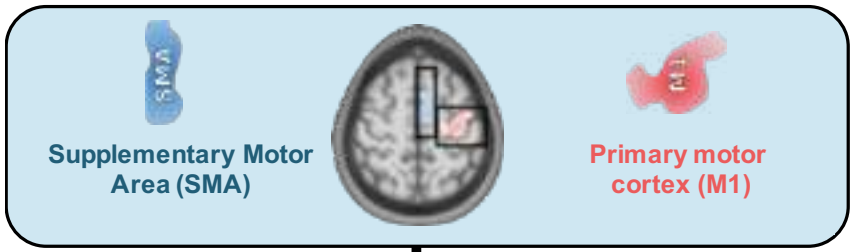

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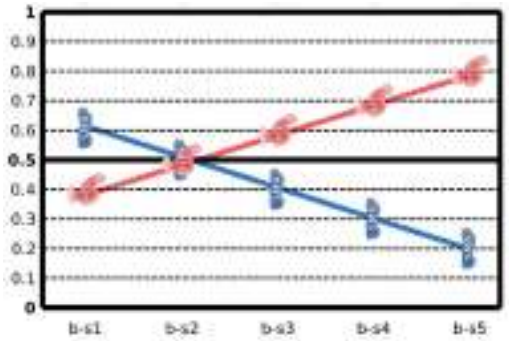

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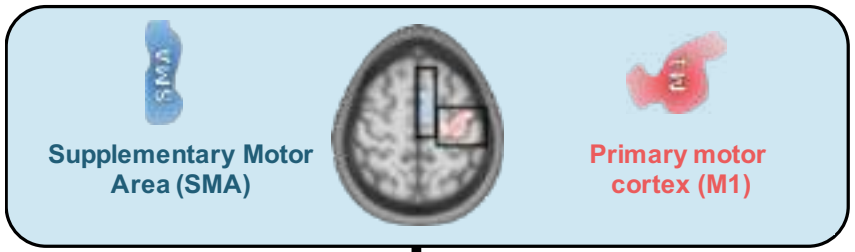

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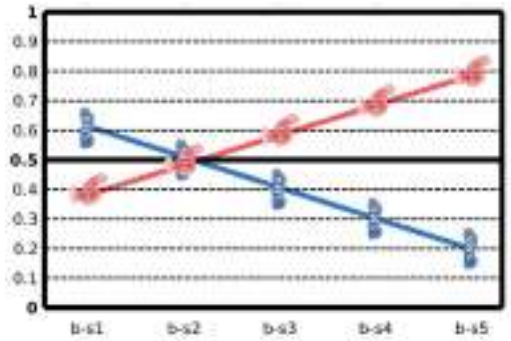
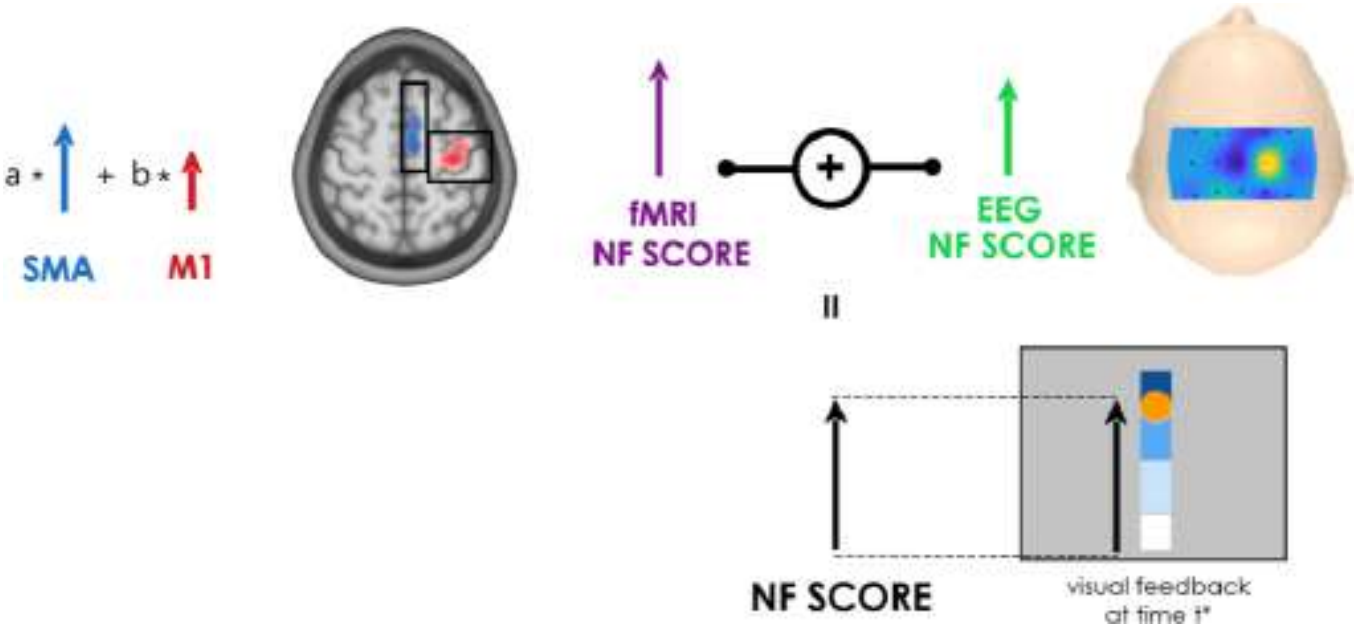
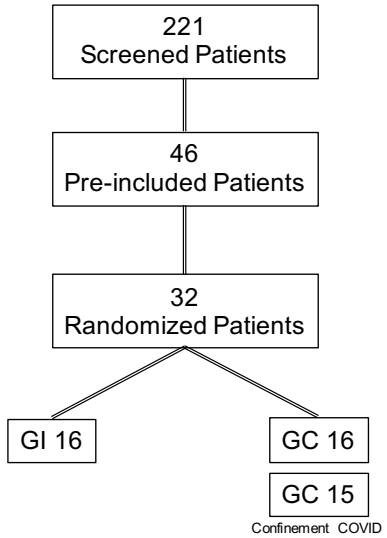




NF for Stroke Rehab. : a Randomized Controlled Trial

- end of inclusions in July 2022 $\longrightarrow$
- **Demonstrated feasibility, no dropouts**



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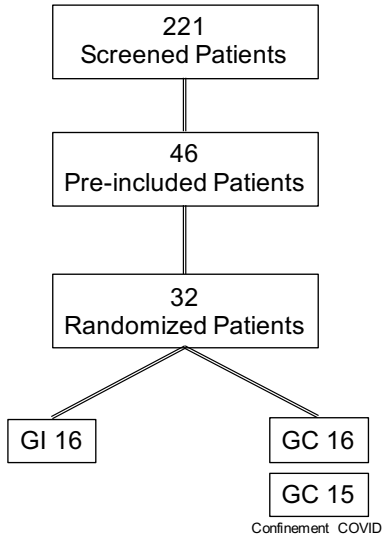


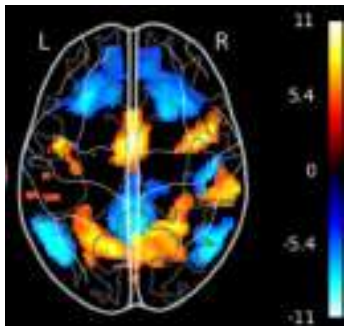
- **Demonstrated feasibility, no dropouts**
- Ongoing analyses, but first results :
  - No statistically significant results at the group level . . .
  - . . . but some patients do improve

	GI	GC
Amélioration sur FMA > 4 points = « répondeurs »	8 patients / 16 Soit 50 %	3 patients / 16 Soit 18,75 %

$\rightarrow$ correlation with cerebral relateralisation ?
with neurofeedback quality/success ?
with lesion localization/nature ?

Preliminary fMRI analyses

- All IG patients, all sessions, NF vs rest



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→ A focal activity is observed in perilesional M1

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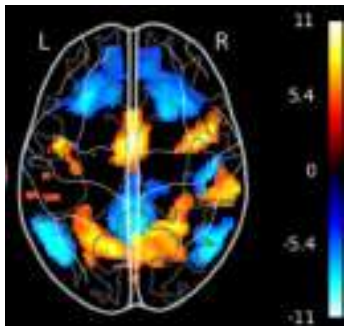

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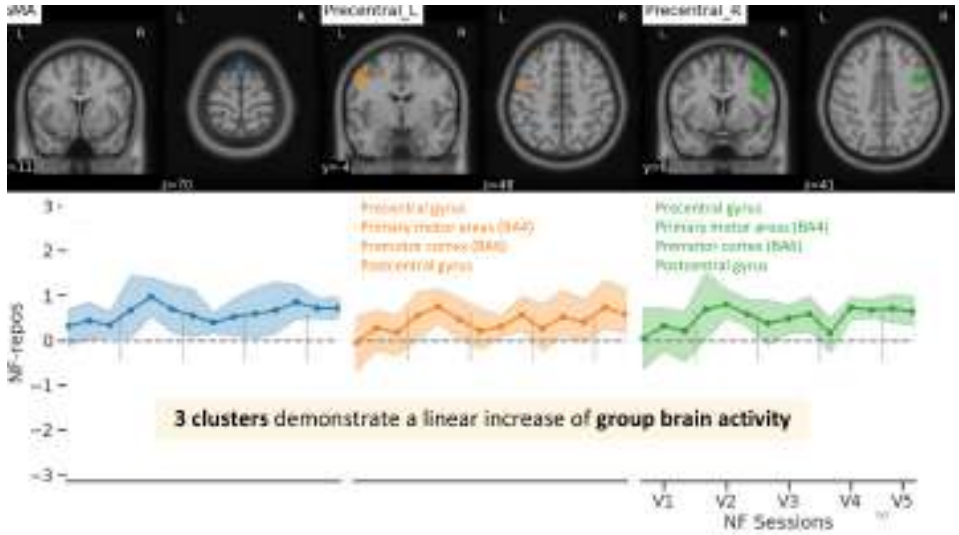

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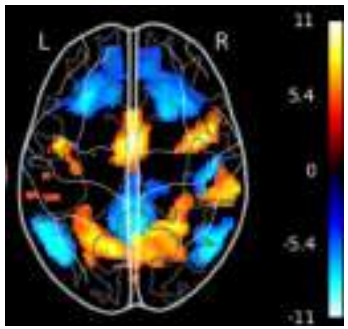

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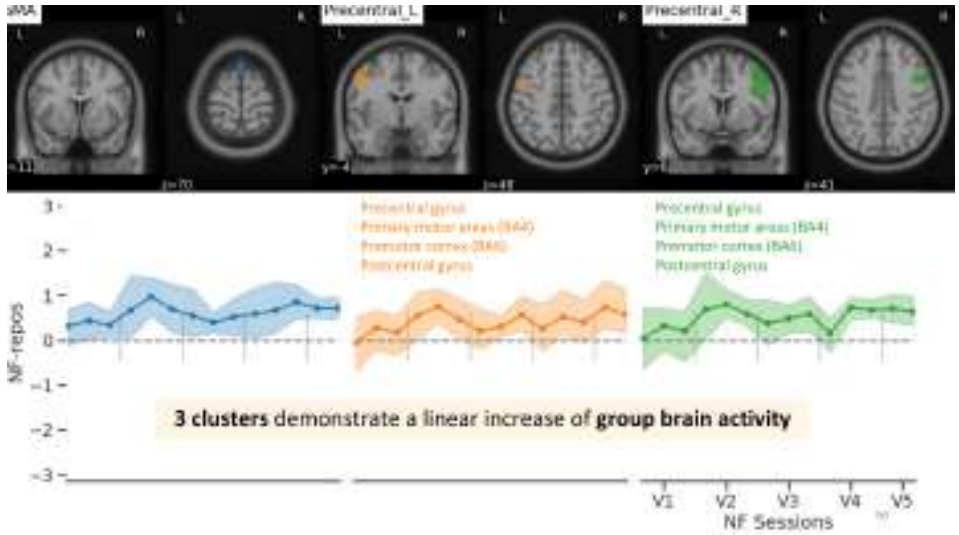
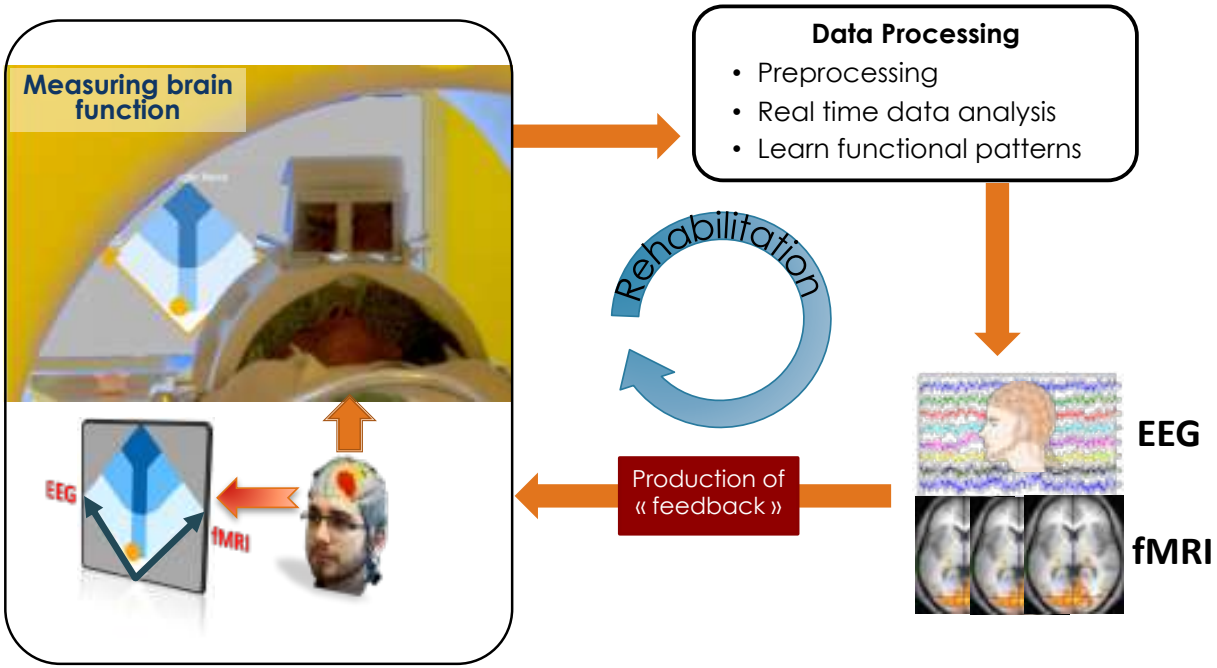


→ high interindividual variability in the response to the NF protocol : some patients change their M1 hemispheric dominance from neutral or contralesional side at the beginning of the protocol to ipsilesional side in the end.

Methodological contributions

Joint EEG-fMRI Neurofeedback: Spatial Registration



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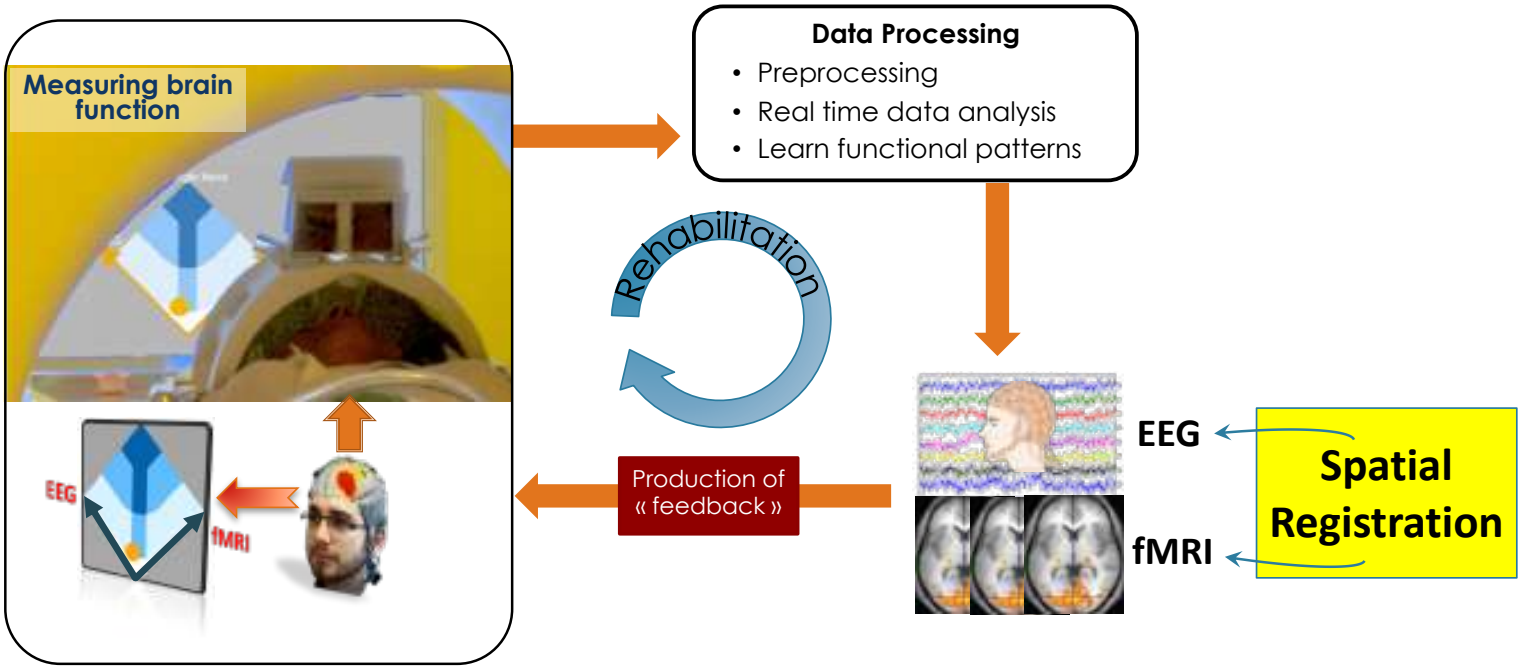

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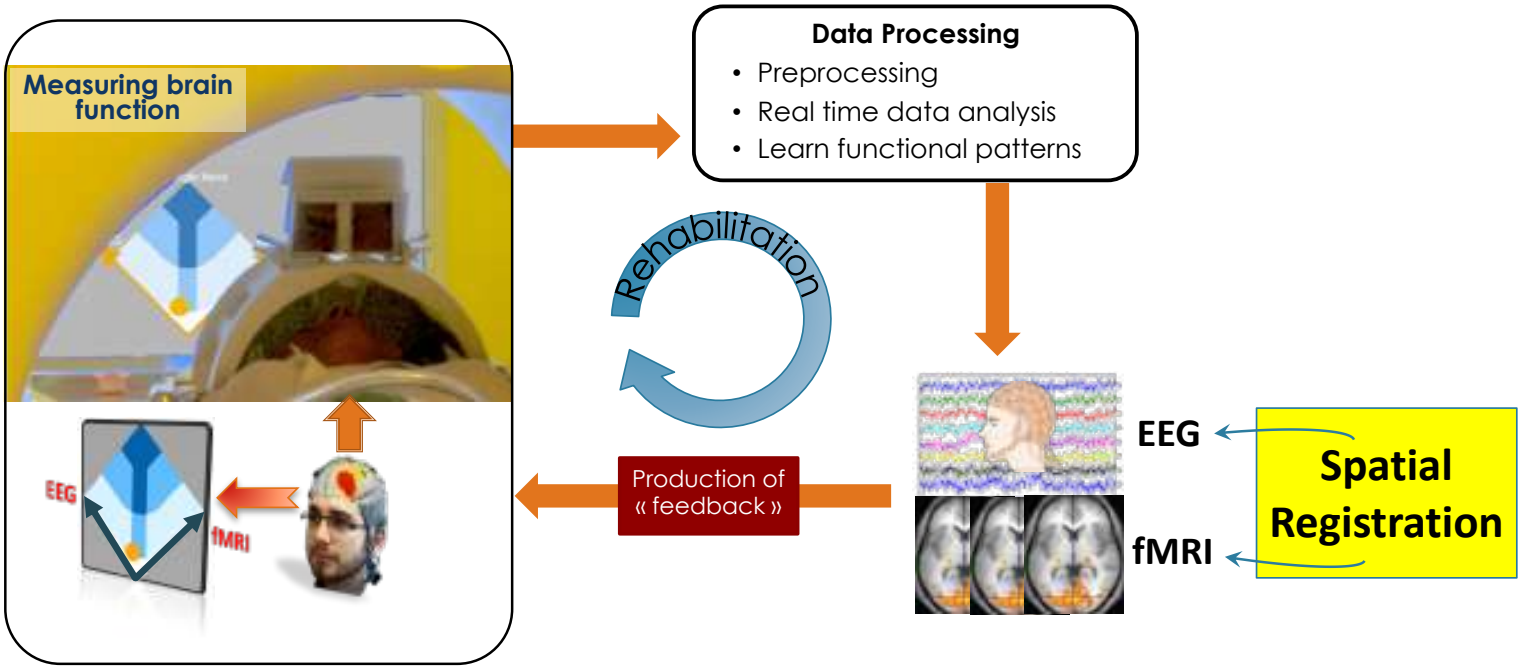


Context

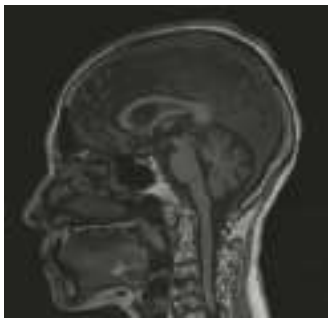
- EEG source localization ↔ spatial electrodes position
- Often : approximate, using fiducial points, or external equipment
- Here : MRI = external measurement instrument ?

Electrodes Detection During Simultaneous EEG/fMRI

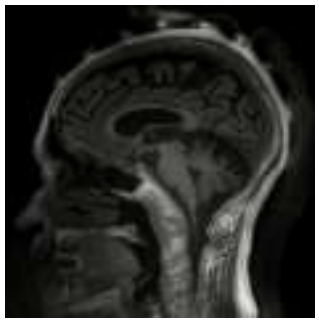
Contribution

(Fleury et al., 2018)
(Pinte et al., 2021)

- But MRI-compatible EEG cap → designed to be as invisible as possible on most MRI sequences
- Ultra-short echo-time (UTE) sequence



T1



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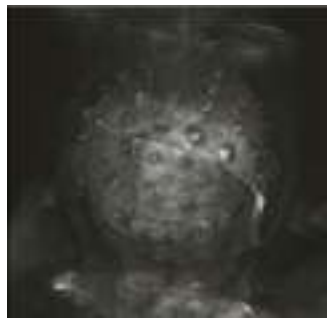
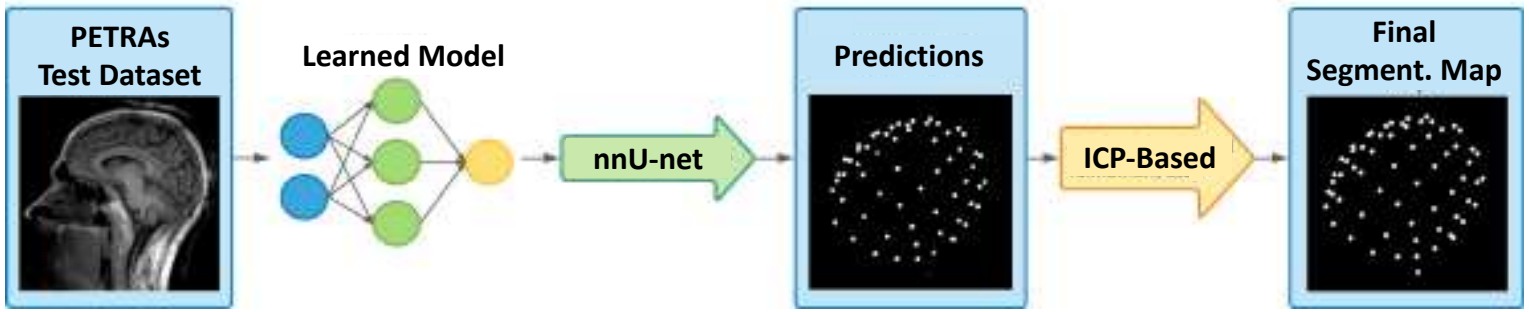


Volume Rendering of UTE

- → Deep learning detection step, followed by a registration-based phase



Electrodes Detection During Simultaneous EEG/fMRI

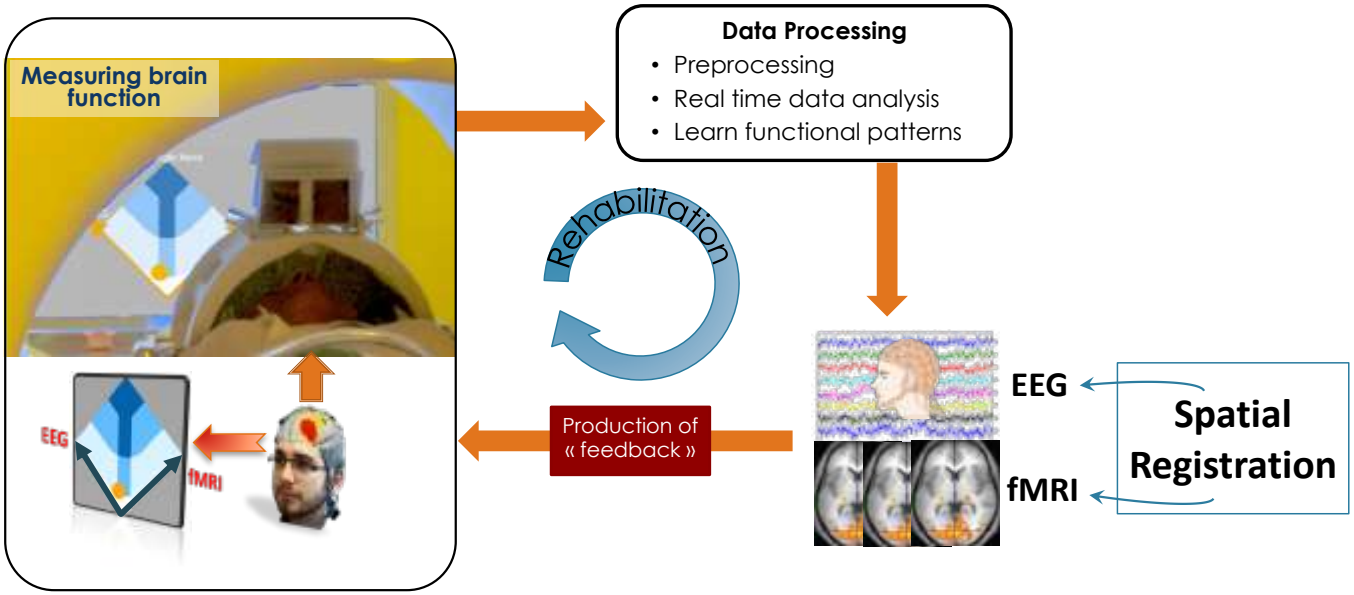
Validation

	Deep learning detection	Final results
Position Error (mean ± std in mm)	6.78 ± 25.4	2.23 ± 1.4
PPV (%)	96.3	99.8
# Detections	67.7	65
# Labeling Errors mean (max)	3.2 (13)	0 (0)

+ same model (learned on the PETRA sequence) / test on an other UTE sequence → **worse detections from NN but corrected after ICP**

→ ICP step brings important **robustness** (faster machine learning step, different UTE sequences)

Joint EEG-fMRI Neurofeedback : Source Estimation



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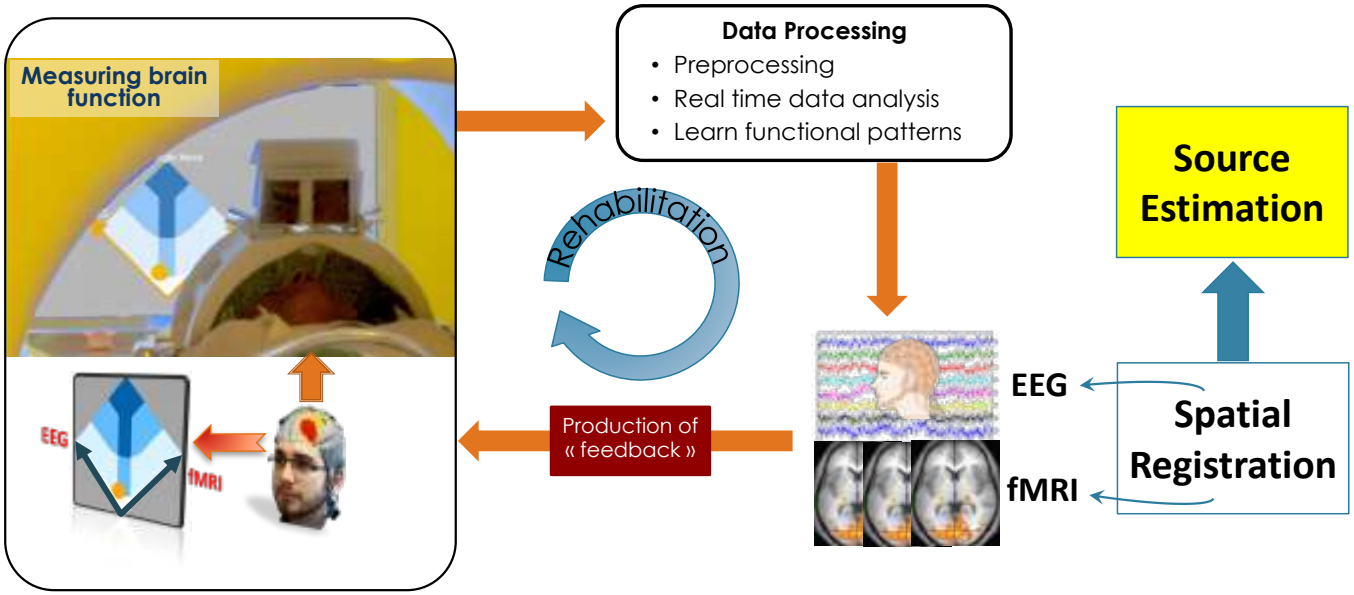

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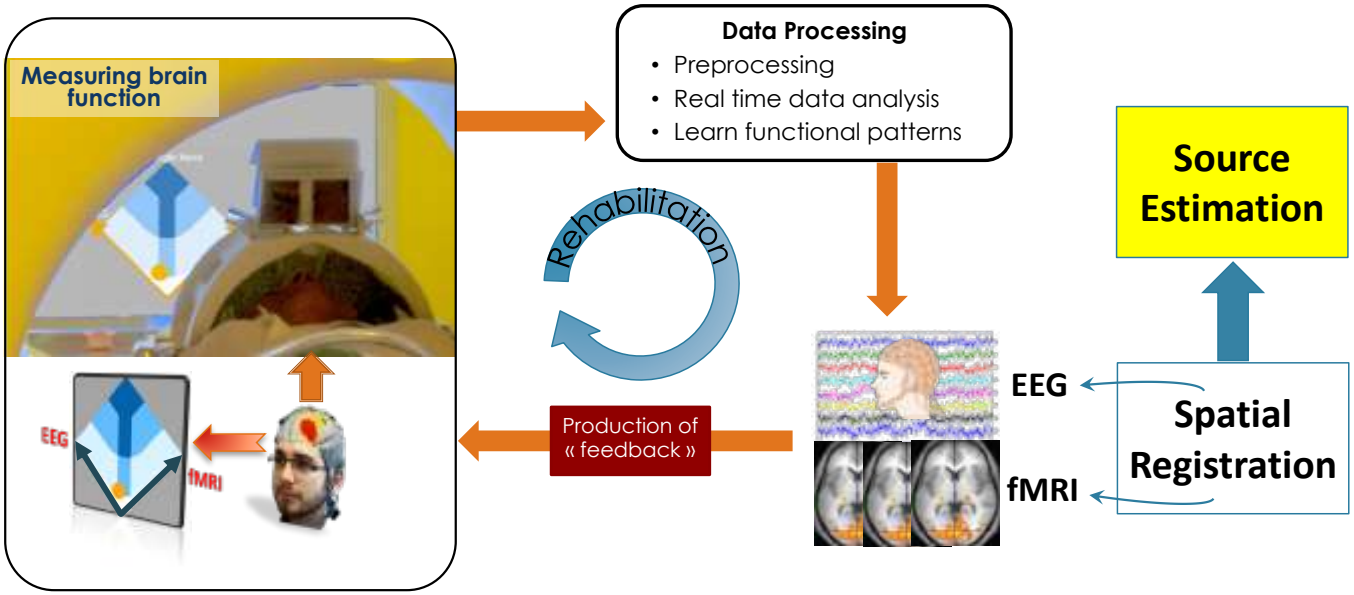


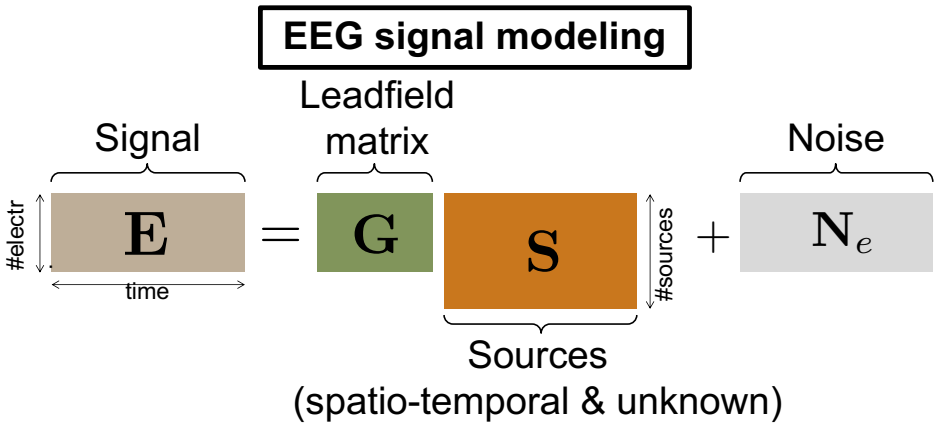
Context

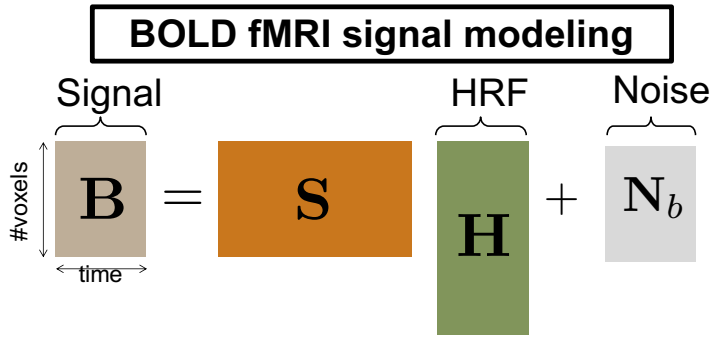
- During neurofeedback sessions : real-time constraint → no source reconstruction
- What about *a posteriori* analyses ?
- Ideally : EEG+fMRI → high spatial **and** temporal resolution

Joint EEG-fMRI Neurofeedback : Source Estimation

Contribution (Noorzadeh et al., 2017; Oberlin et al., 2015)

- Combining EEG and fMRI to spatio-temporal source estimation





- Estimating $\mathbf{S}$ is an ill-posed inverse problem in each case

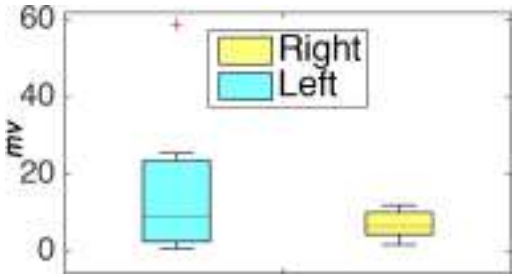
→ Joint linear model with sparse constraint

$$\hat{\mathbf{S}} = \arg\min_{\mathbf{S}} \left\{ \alpha \left\| \mathbf{GS} - \mathbf{E} \right\|_{\mathscr{L}_2}^2 + (1-\alpha) \left\| \mathbf{SH} - \mathbf{B} \right\|_{\mathscr{L}_2}^2 + \lambda \left\| \mathbf{S} \right\|_{\mathscr{L}_1} \right\}$$

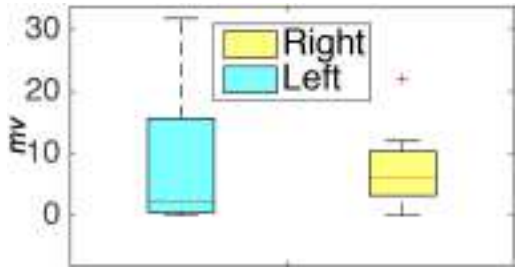
Joint EEG-fMRI Neurofeedback : Source Estimation

Validation

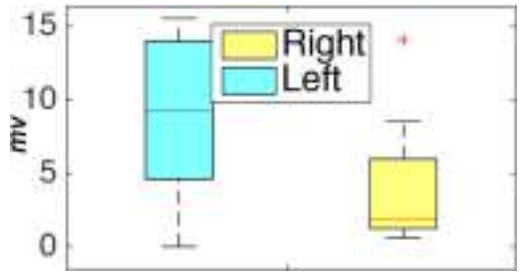
- 8 healthy subjects, right hand motor task, simultaneous EEG-fMRI



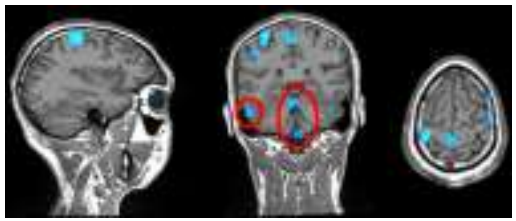
fMRI only



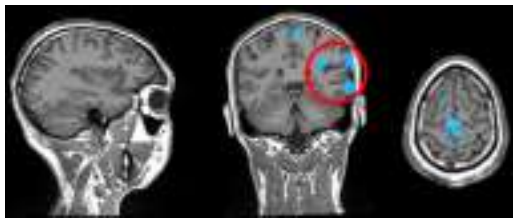
EEG only



joint EEG-fMRI



fMRI only

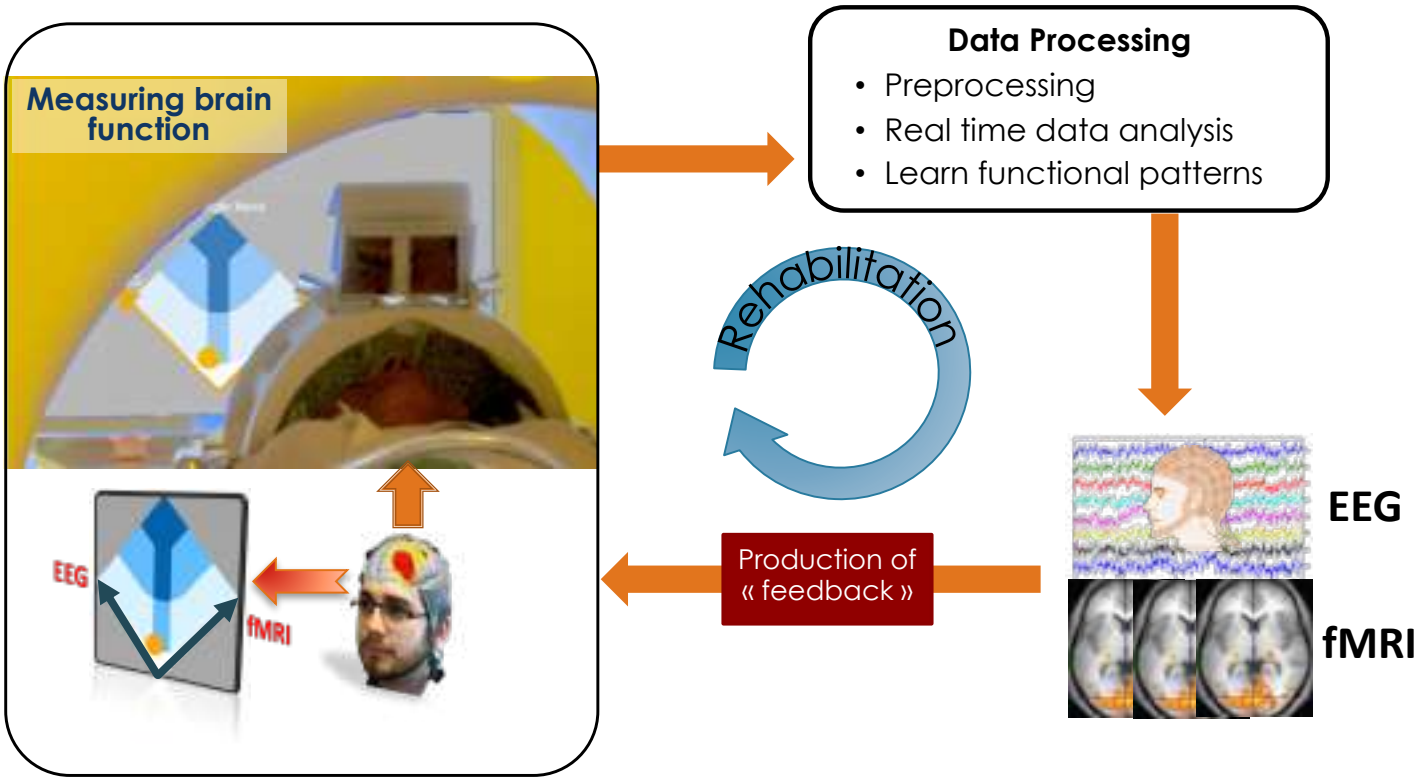


EEG only

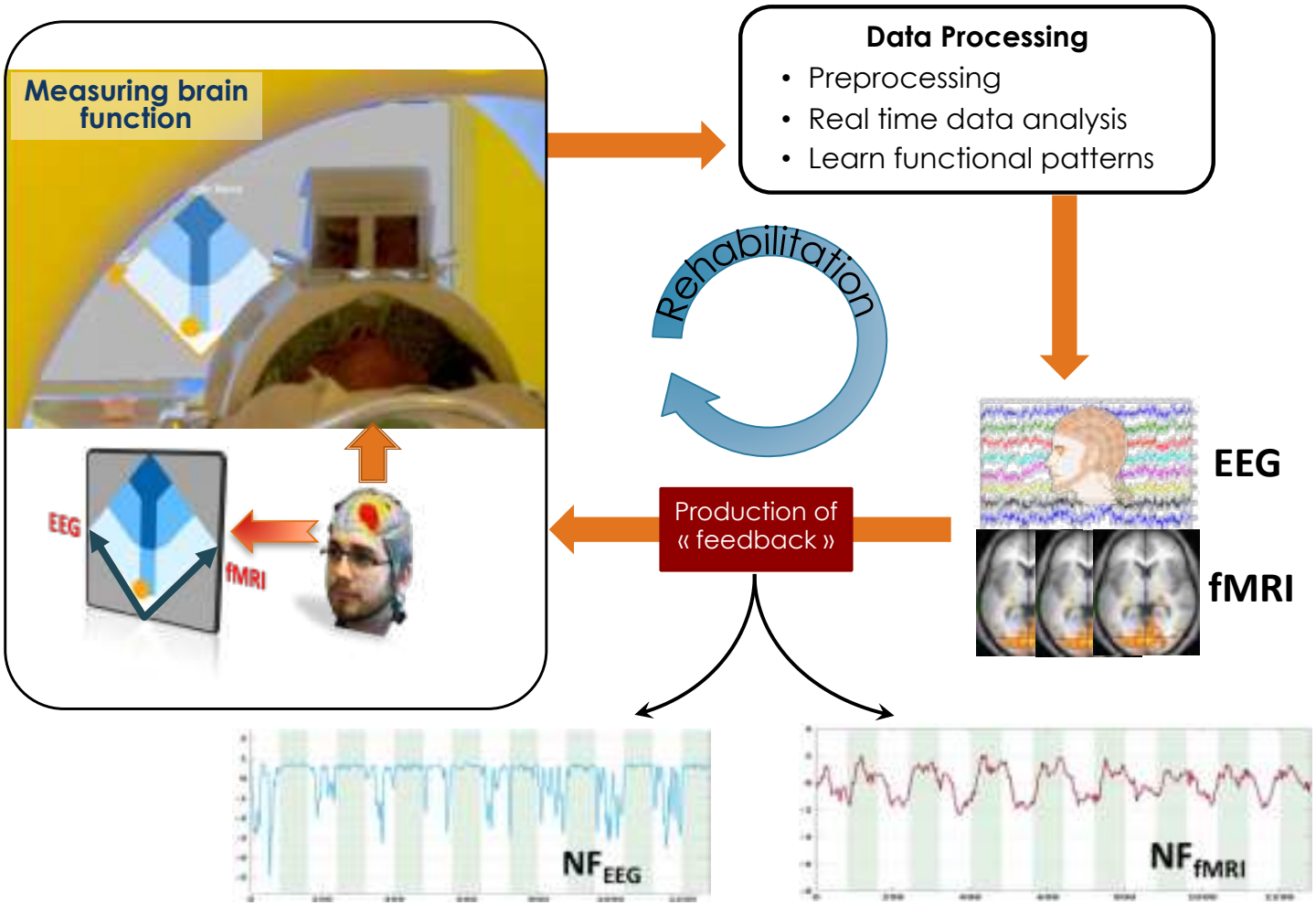
joint EEG-fMRI

→ High-resolution temporal reconstruction, but not validated on real data

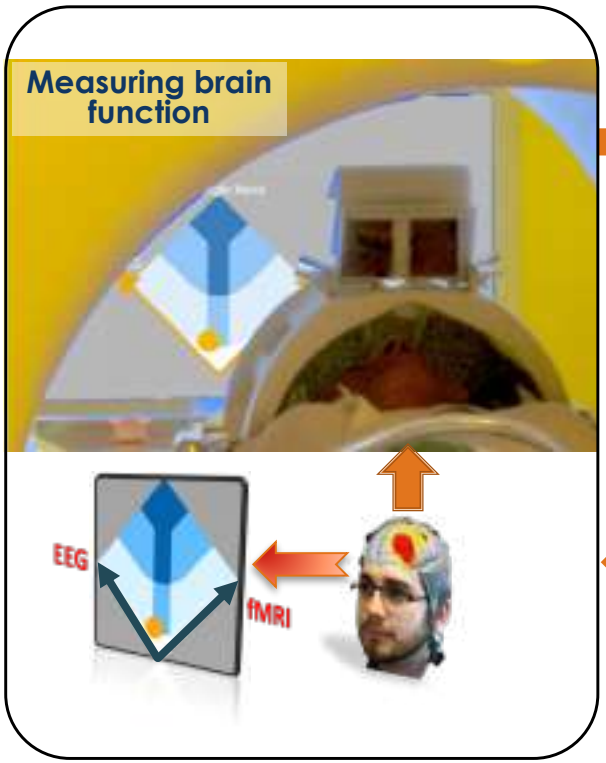
Joint EEG-fMRI Neurofeedback



Joint EEG-fMRI Neurofeedback



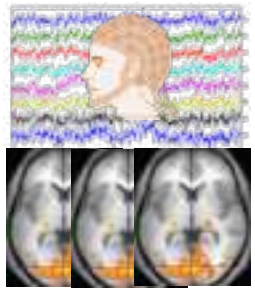
Joint EEG-fMRI Neurofeedback



Data Processing

- Preprocessing
- Real time data analysis
- Learn functional patterns

Rehabilitation

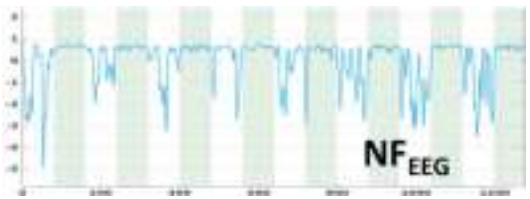


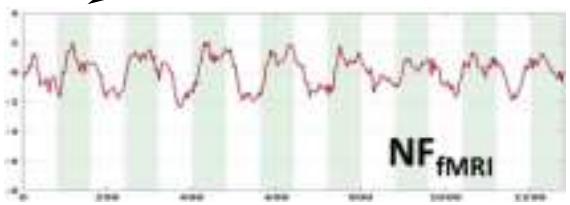
EEG

fMRI

Production of « feedback »

Predict NF_{fMRI} from EEG ?





Prediction of Neurofeedback Scores from EEG

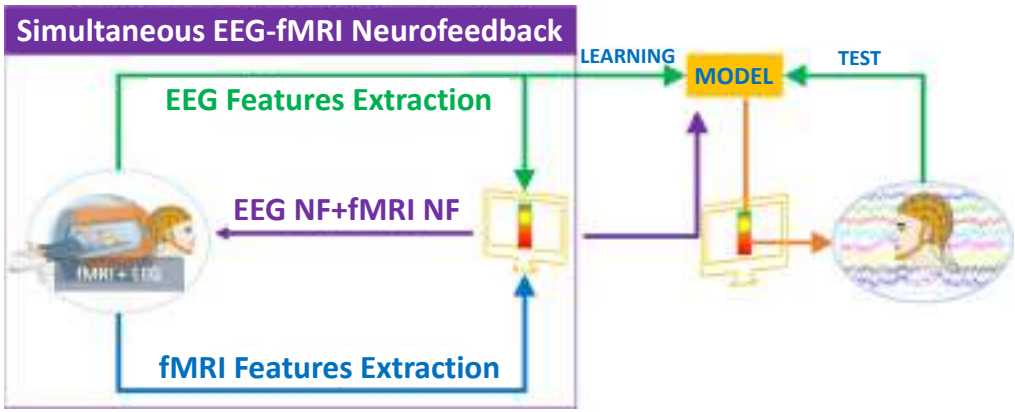
Context

- EEG-fMRI joint neurofeedback: promising for brain rehabilitation
- But MRI $\rightarrow$ costly, exhausting, time-consuming
- Hemisfer stroke rehabilitation protocol: alternates between EEG-fMRI and EEG-only sessions

Contribution (Cury et al., 2020)

- Is it possible to enhance EEG-only neurofeedback sessions ? using information from joint EEG-fMRI sessions ?

$\rightarrow$



Prediction of Neurofeedback Scores from EEG

Transformed EEG signal

$$\hat{\boldsymbol{\alpha}} = \arg\min_{\boldsymbol{\alpha}} \left[\sum_{t=1}^{T} \frac{1}{2} \left(\mathbf{NF_{fMRI}}(t) - \langle \mathbf{X}(t), \boldsymbol{\alpha} \rangle \right)^2 + \varphi(\boldsymbol{\alpha}) \right]$$

Actual $\mathbf{NF_{fMRI}}(t)$

Predicted $\mathbf{NF_{fMRI}}(t)$

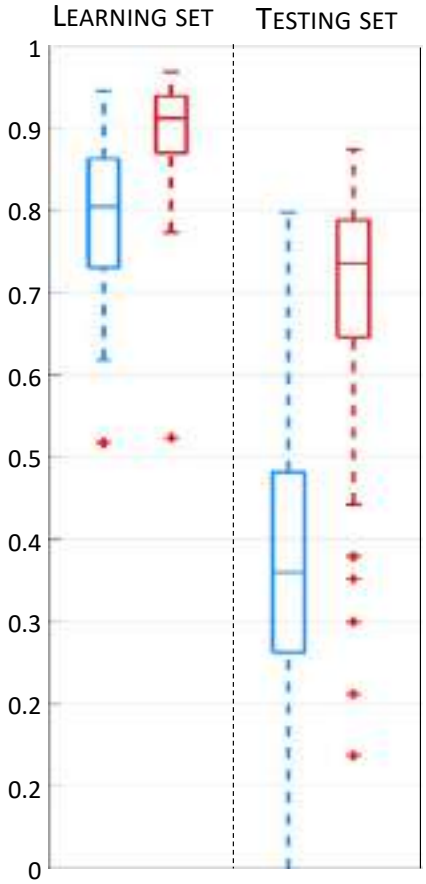
regularization : $\varphi(\boldsymbol{\alpha}) = \lambda \|\boldsymbol{\alpha}\|_{2,1} + \rho \|\boldsymbol{\alpha}\|_1$

$$= \lambda \underbrace{\sum_m \sqrt{\sum_b \alpha_{m,b}^2}}_{\text{spatial sparsity frequency smoothness}} + \rho \underbrace{\sum_{m,b} |\alpha_{m,b}|}_{\text{Group sparsity on freq.}}$$

Prediction of Neurofeedback Scores from EEG

Validation

Pearson Correlations



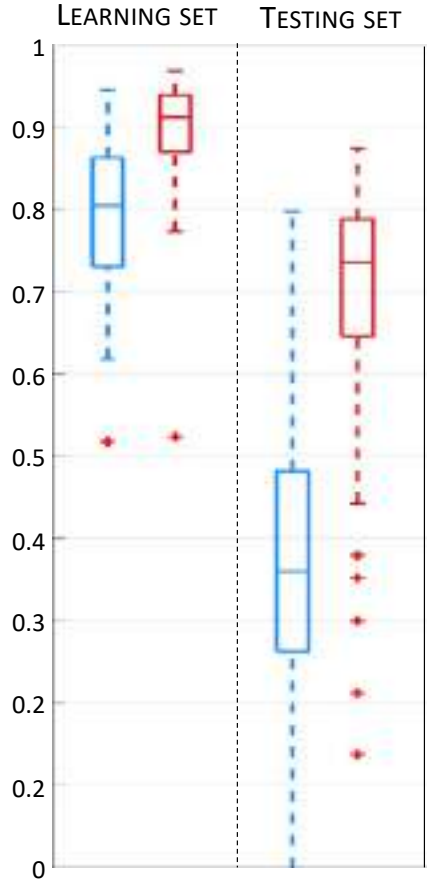
actual NF_{fMRI}
vs
predicted NF_{fMRI}

actual bimodal **score**
vs
predicted bimodal **score**

Prediction of Neurofeedback Scores from EEG

Validation

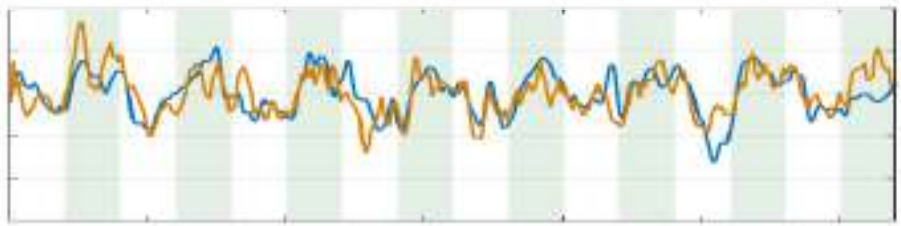
Pearson Correlations



actual NF_{fMRI} vs predicted NF_{fMRI}

actual bimodal **score** vs predicted bimodal **score**

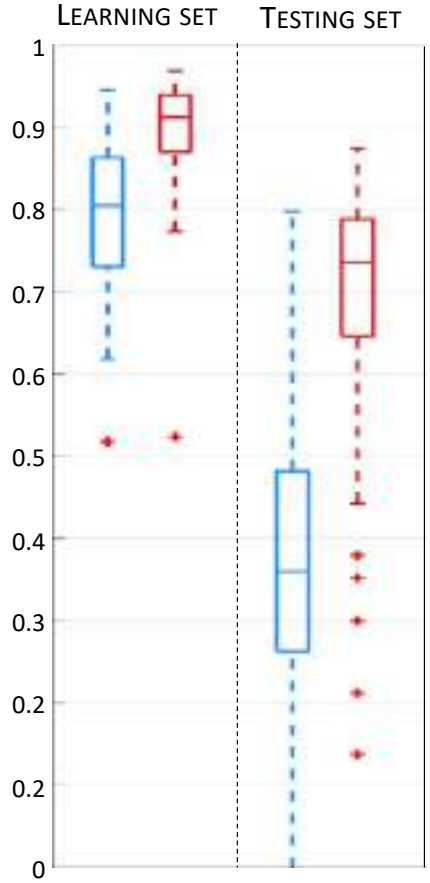
Actual NF_{fMRI}
Predicted NF_{fMRI}
r = 0.64



Prediction of Neurofeedback Scores from EEG

Validation

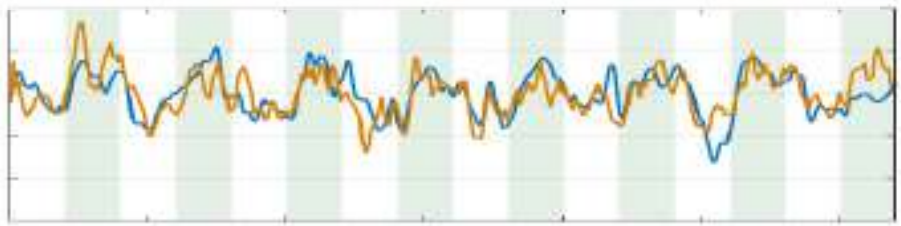
Pearson Correlations



actual NF_{fMRI} vs predicted NF_{fMRI}

actual bimodal **score** vs predicted bimodal **score**

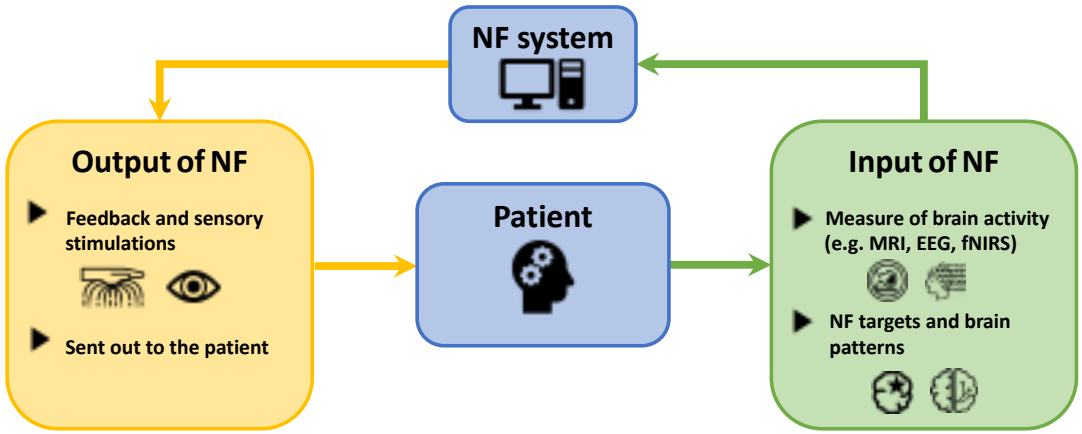
Actual NF_{fMRI}
Predicted NF_{fMRI}
r = 0.64



Only on healthy subjects and not always that good
$\rightarrow$ ongoing work (C.Pinte's PhD) on Recurrent Neural Network

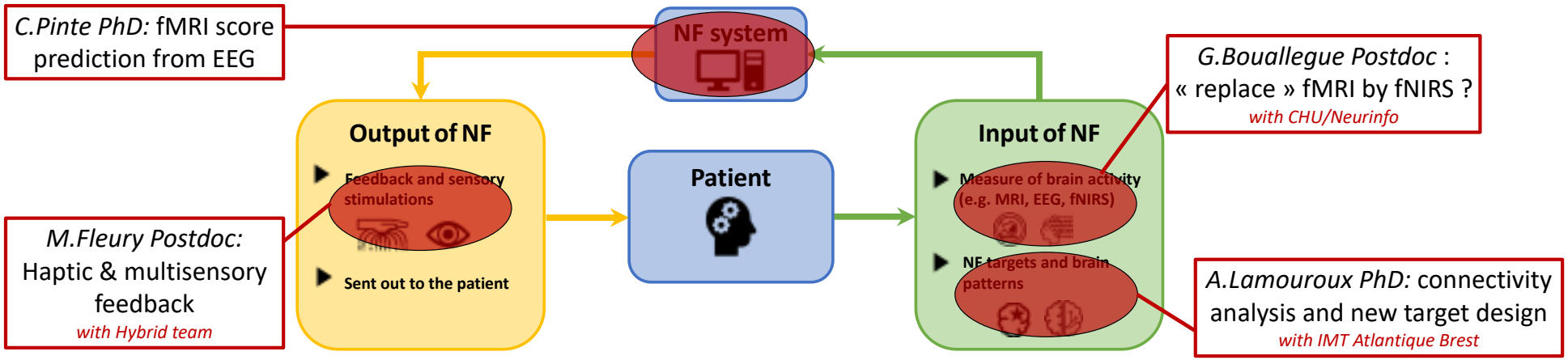
Perspectives

PEPERONI : Portable and Personalized Neurofeedback for Stroke Rehabilitation



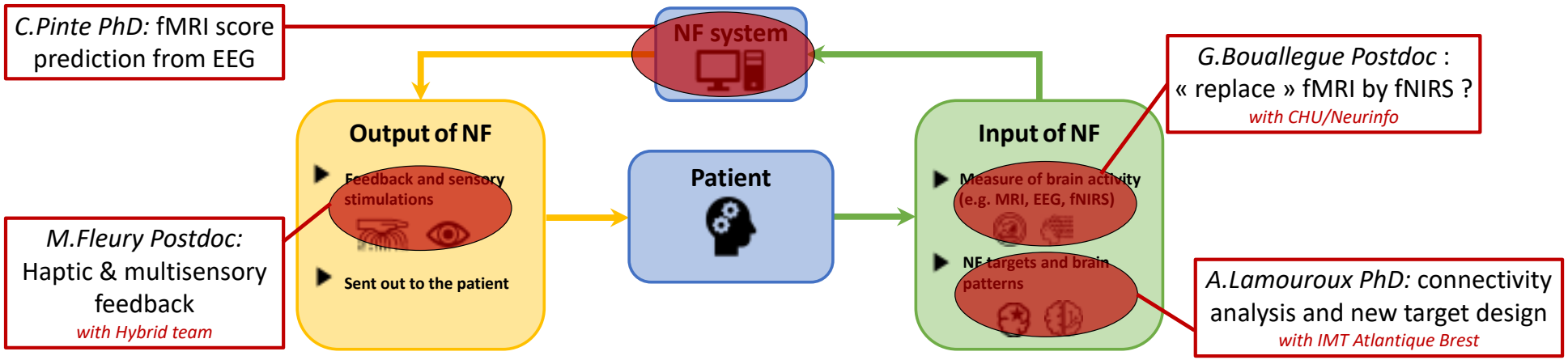
Perspectives

PEPERONI : Portable and Personalized Neurofeedback for Stroke Rehabilitation



Perspectives

PEPERONI : Portable and Personalized Neurofeedback for Stroke Rehabilitation



→ and also, EyeSking-NF : Eye-tracking and skin conductance measures for neurofeedback analysis and validation.

Thank you for your attention