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Combining EEG And fMRI for Neurofeedback

PhD defense of **Lorraine Perronnet**

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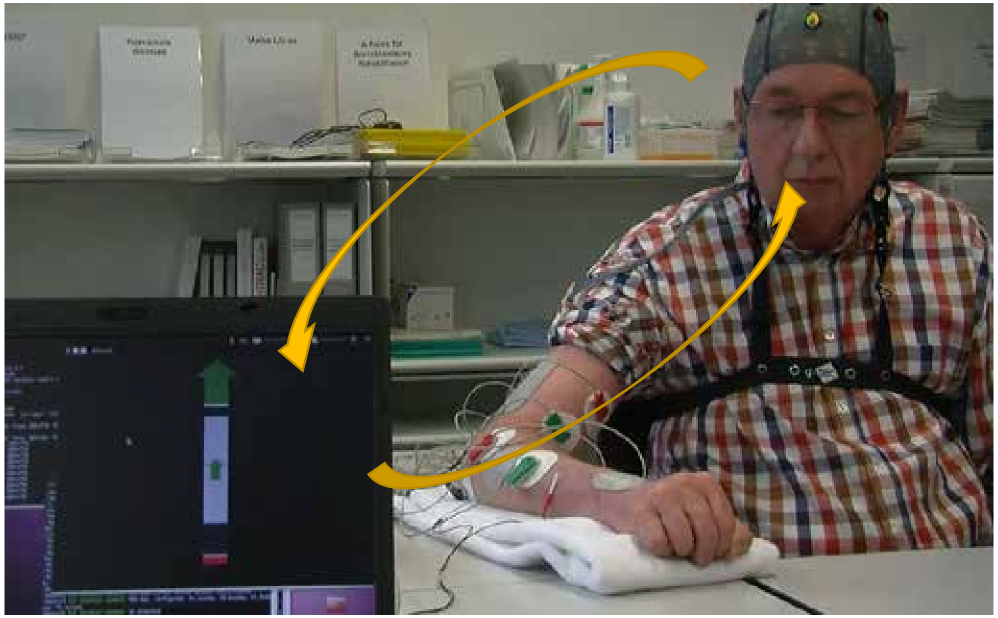
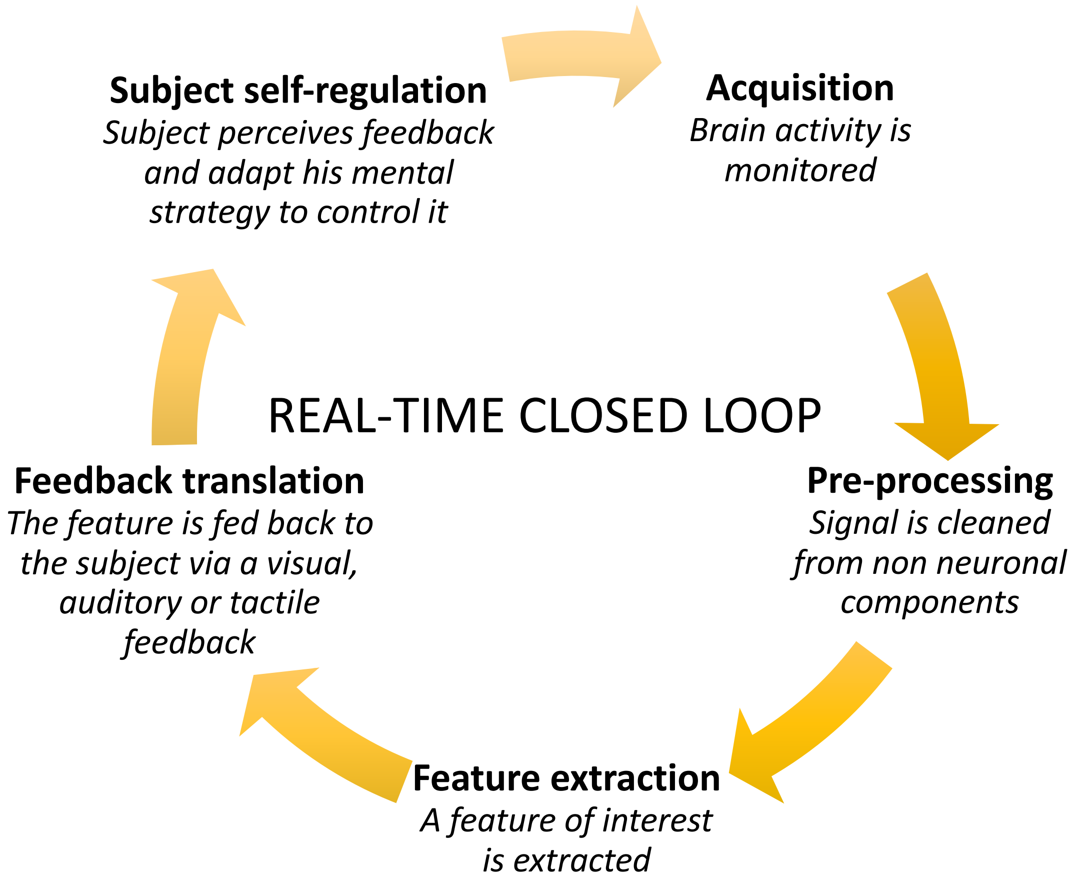
Neurofeedback (NF)

Definition: *"Neurofeedback is a type of biofeedback in which neural activity is measured, and a visual, an auditory or another representation of this activity is presented to the participant in real time to facilitate self-regulation of the putative neural substrates that underlie a specific behaviour or pathology"* *[Sitaram et al. 2016]*

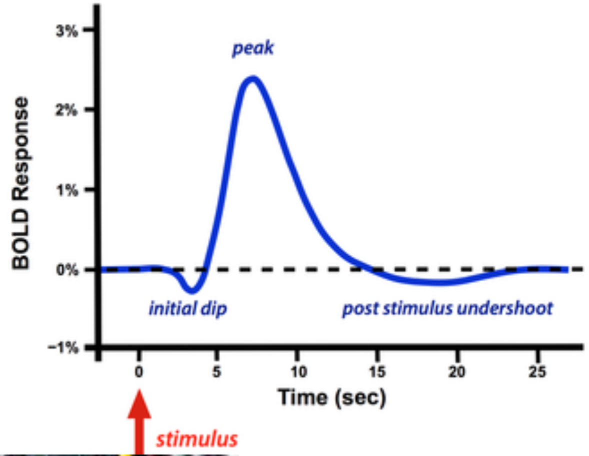


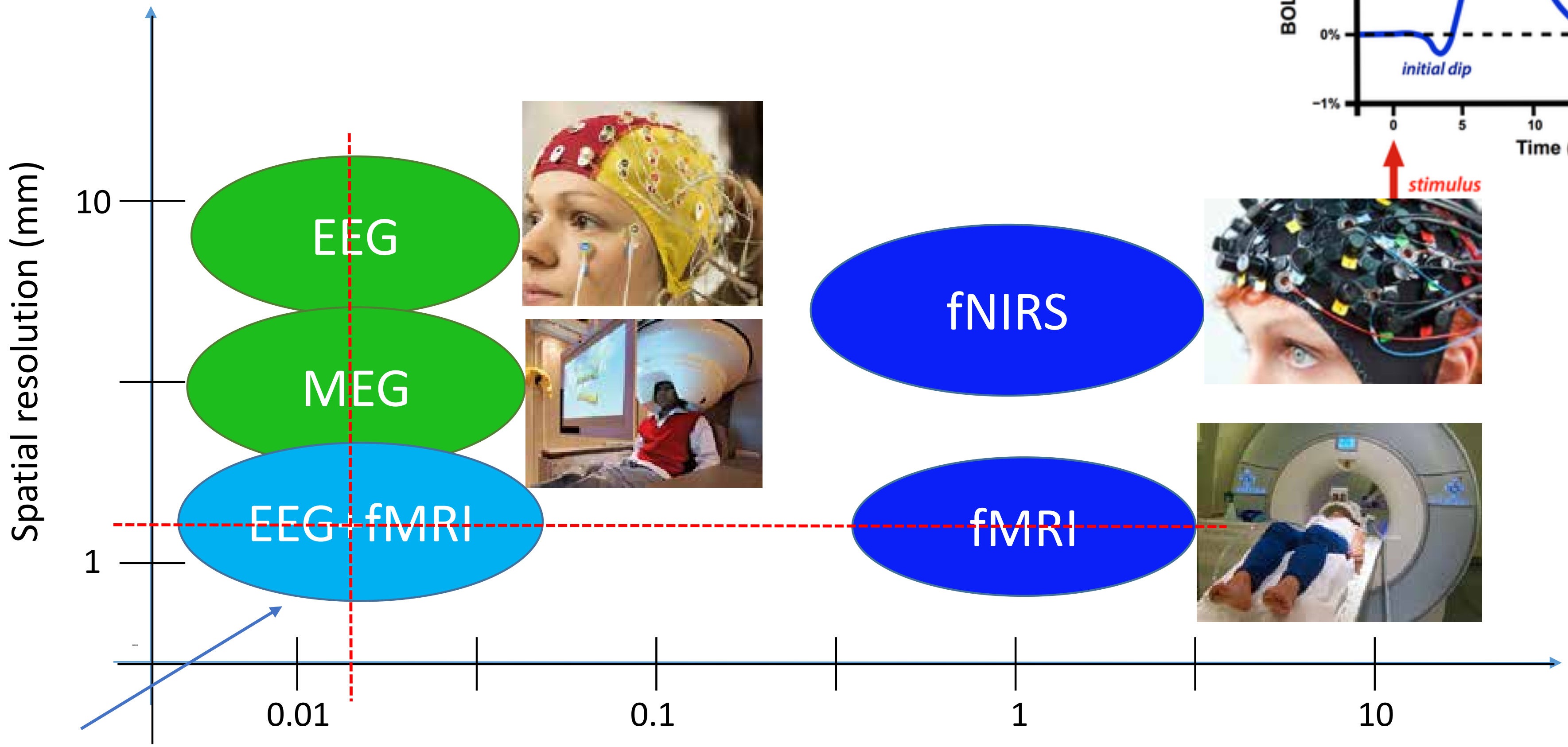
Motor rehabilitation of stroke patients

Neurofeedback (NF)



NF modalities



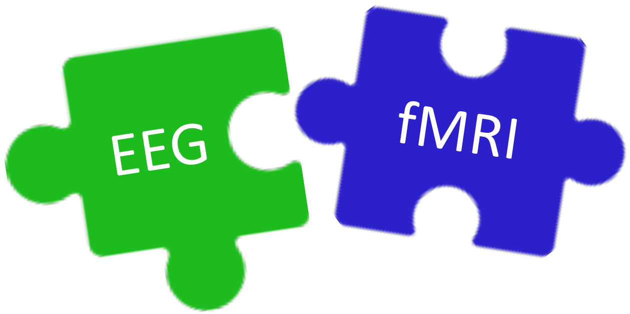


High spatial (mm) and high temporal (ms) resolution

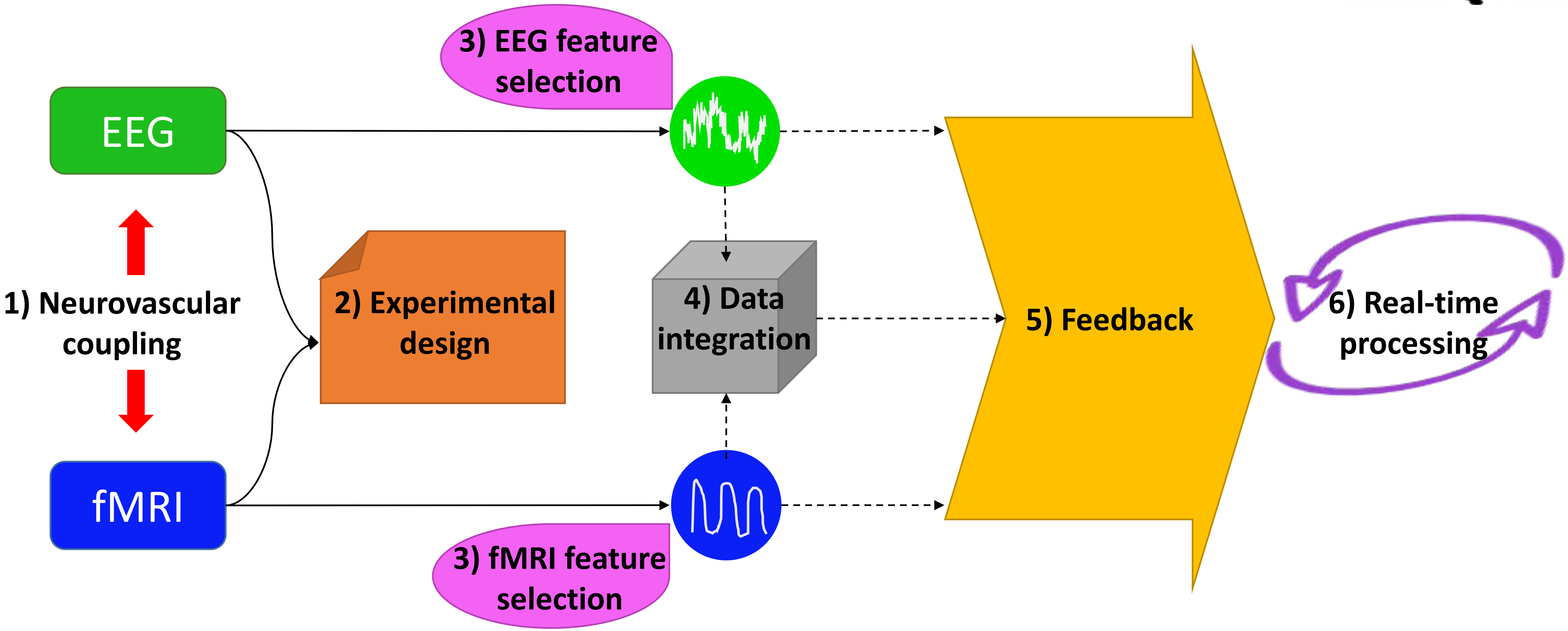
Problem and motivation

Limited efficiency/efficacy of *unimodal* NF approaches

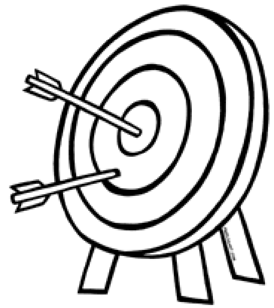
Design novel **NF approaches combining EEG and fMRI** that could be more effective than unimodal approaches



Challenges of combined EEG/fMRI for NF



Thesis objectives



1. Identify critical methodological aspects that differ between EEG-nf and fMRI-nf *(Related works> EEG-nf vs fMRI-nf)*
2. Explore how to combine EEG and fMRI for NF *(Related works> Contribution 1)*
3. Develop an experimental EEG/fMRI NF platform *(Contribution 2)*
4. Evaluate added value of bimodal EEG-fMRI-nf over unimodal NF *(Contribution 3)*
5. Propose and evaluate strategies to represent EEG and fMRI simultaneously *(Contribution 4)*

Outline

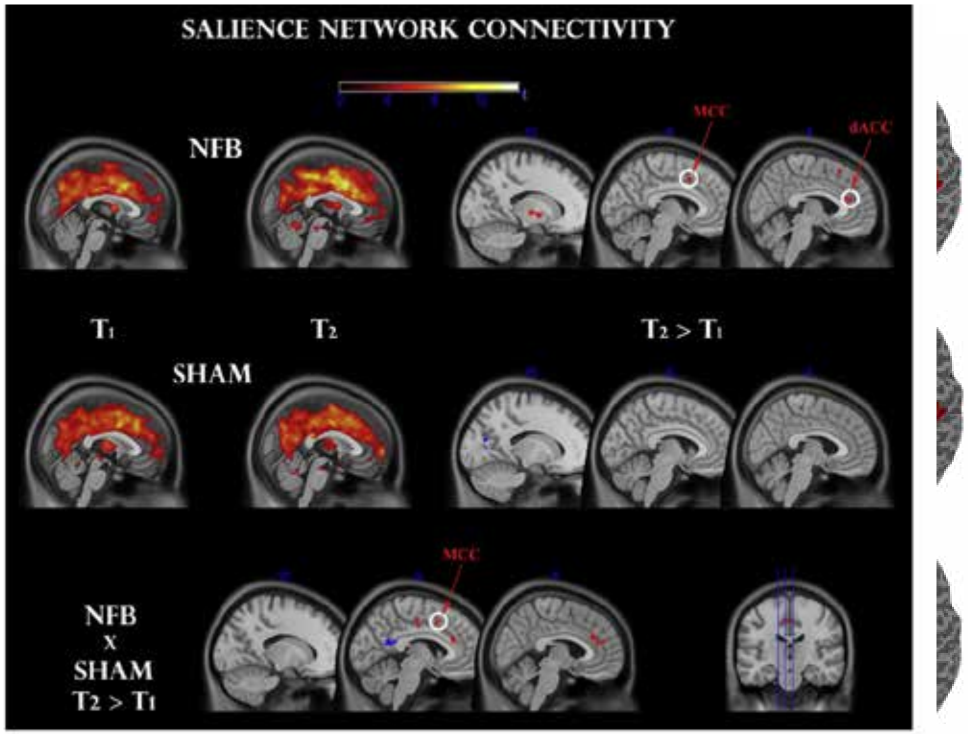
- Related works
  - Contribution 1 (*methodo*.) : Taxonomy of EEG/fMRI NF studies
- Contribution 2 (*techno.*) : EEG/fMRI NF platform
- Contribution 3 (*study*): Unimodal vs bimodal NF
- Contribution 4 (*methodo. + study*): Towards integrated feedback
- Conclusion
- Perspectives

EEG-nf vs fMRI-nf

	EEG-nf	fMRI-nf
NF signal	• Amplitude of specific frequency bands at one, two electrode sites • Slow cortical potentials *[Rockstroh et al. 1990]* • Z-score NF *[Thatcher et al., 1998]* • Source-based (Loreta-NF, BSS-NF) *[Cannon et al. 2009, White et al. 2014]*	• Average percent signal change in ROI • Differential signal between two regions • MVPA, Effective connectivity *[Sulzer et al., 2013]*
Task design	Block, continuous/self-paced	Block
Task duration	Flexible: usually 2-5 minutes, few seconds for MI, tens of minutes for deep state NF	15 - 45 seconds
Nb of sessions	20 - 40	5 - 10

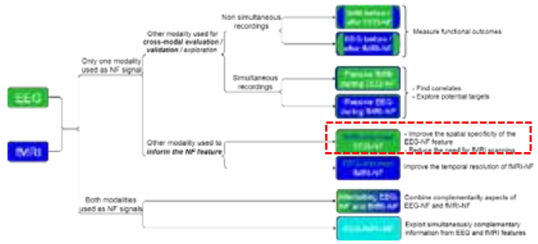
Cross-modal evaluation / validation

- fMRI before/after EEG-nf
  - Plasticity induced by a single alpha down EEG-NF session *[Ros et al., 2012]*
    - After 30 minutes of NF, increase of connectivity within regions of the salience network involved in intrinsic alertness (dACC)
- Passive fMRI during EEG-nf
  - fMRI signature of MI-based EEG-nf *[Zich et al., 2015]*
    - EEG and BOLD contralateral activity is correlated
    - EEG and BOLD lateralization patterns are not always correlated
- Passive EEG during fMRI-nf
  - Correlation between amygdala BOLD activity and frontal EEG asymmetry during fMRI-nf in MDD patients *[Zotev et al., 2016]*
    - Average frontal alpha asymmetry changes significantly correlated with the amygdala BOLD laterality

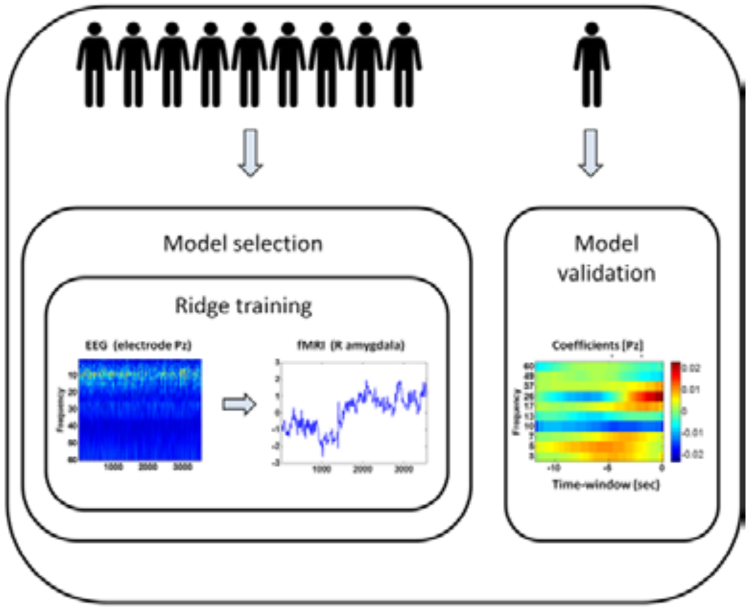


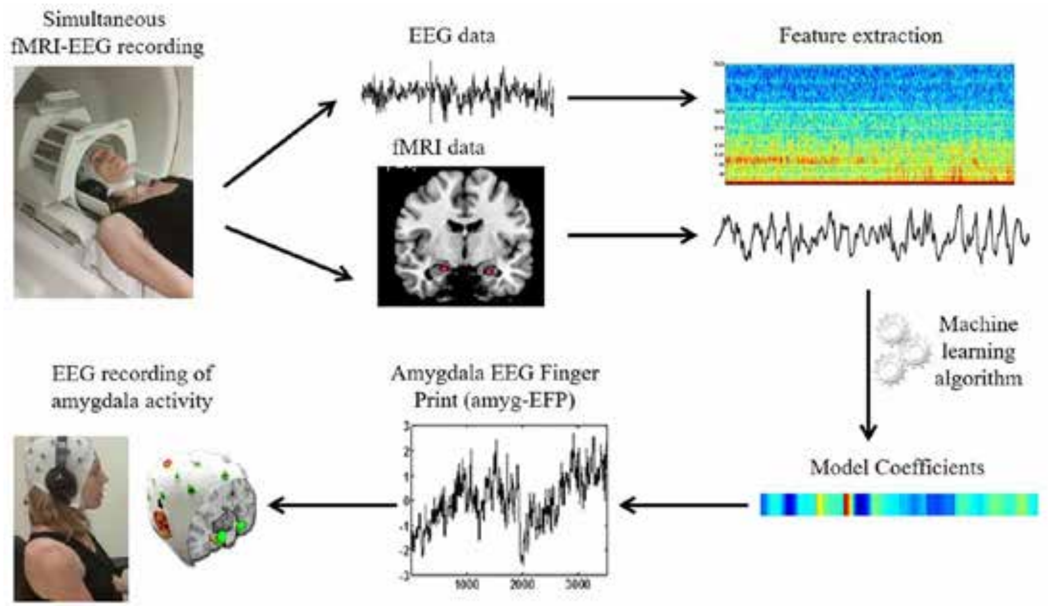
4. Functional connectivity change within the salience network, before (T1) and after (T2) feedback, for NFB (top panel) and SHAM (middle panel) groups. Clusters surviving the ily-wise error (FWE<0.05) correction are circled in white. Other clusters were thresholded at P<0.001 uncorrected. A Time × Group interaction (bottom panel) reveals a signif- t modulation in comparable regions. dACC: dorsal anterior cingulate cortex; MCC: mid-cingulate cortex.

fMRI-informed EEG-nf



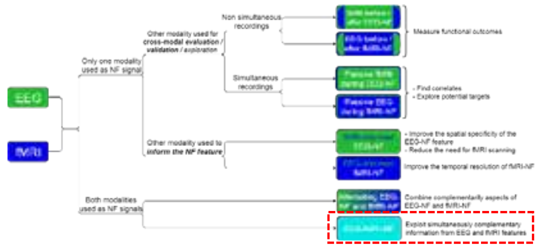
EEG finger-print (EFP) *{electrode, frequency}* of fMRI deep regional activation [*Meir-Hasson et al., 2014*], [*Lin et al. 2017*]: *time-frequency decomposition of EEG, ridge regression*

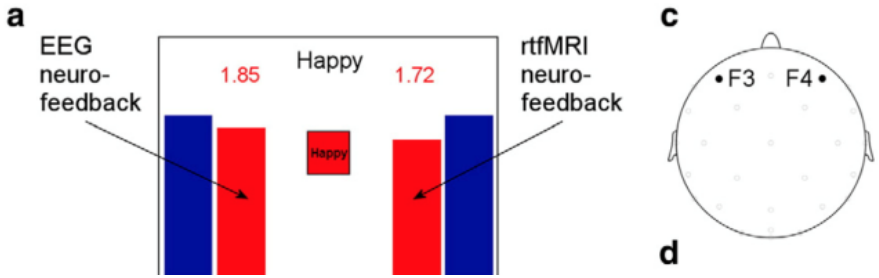




Common EFP model (valid across subjects and sessions) [*Meir-Hasson et al., 2016*] : *one class classification, hierarchical clustering algorithm applied to the estimated EFP models' coefficients*

EEG-fMRI-nf
[Zotev et al., 2013]





- Methods
  - Participants: 6 healthy subjects
  - Task: emotional self-regulation
  - EEG feature: frontal high-beta (21-30 Hz) asymmetry
  - fMRI feature: left amygdala
- Authors hypothesized that: *EEG-fMRI-nf > EEG-nf | fMRI-nf*
- Limitations
  - 2 separate feedback gauges
  - No evaluation against unimodal NF

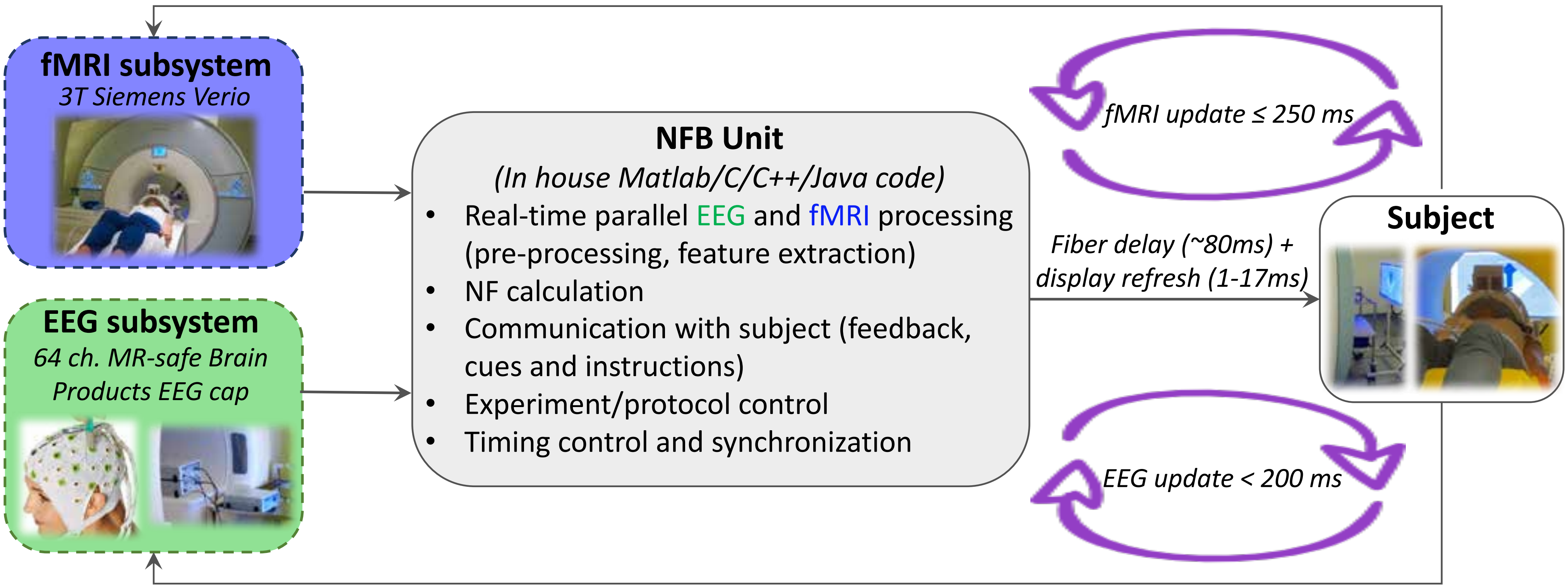
Outline

- Related works
  - Contribution 1 (*methodo*.) : Taxonomy of EEG/fMRI NF studies
- Contribution 2 (*techno.*) : EEG/fMRI NF platform
- Contribution 3 (*study*): Unimodal vs bimodal NF
- Contribution 4 (*methodo. + study*): Towards integrated feedback
- Conclusion
- Perspectives

System description (1)

- Goal
  - Develop a platform able to do **simultaneous acquisition and real-time processing of EEG and fMRI** to provide **unimodal and bimodal NF**
- Challenges
  - Multimodal
  - Real-time performance
  - Artifacts (gradient, pulse, helium pump, ventilation)
  - Novel approach, no comprehensive solution available

System description (2)



Published in : M Mano, A Lécuyer, E Bannier, **L Perronnet**, S Noorzadeh, C Barillot (2017). How to build a hybrid neurofeedback platform combining EEG and fMRI. *Frontiers in Neuroscience, 11,* 140.

My role

- State-of-the-art and specifications
- Issue detection and resolution
- Recruiting volunteers
- Running the experiments and analyzing the data

Outline

- Related works
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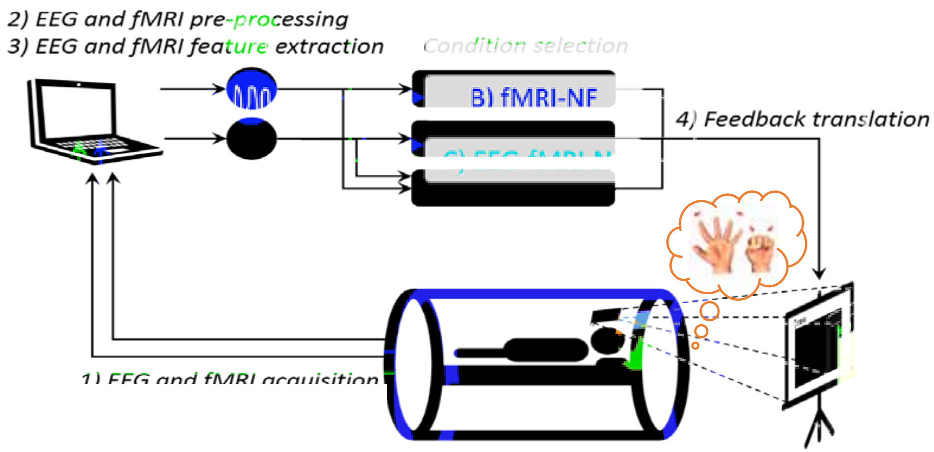
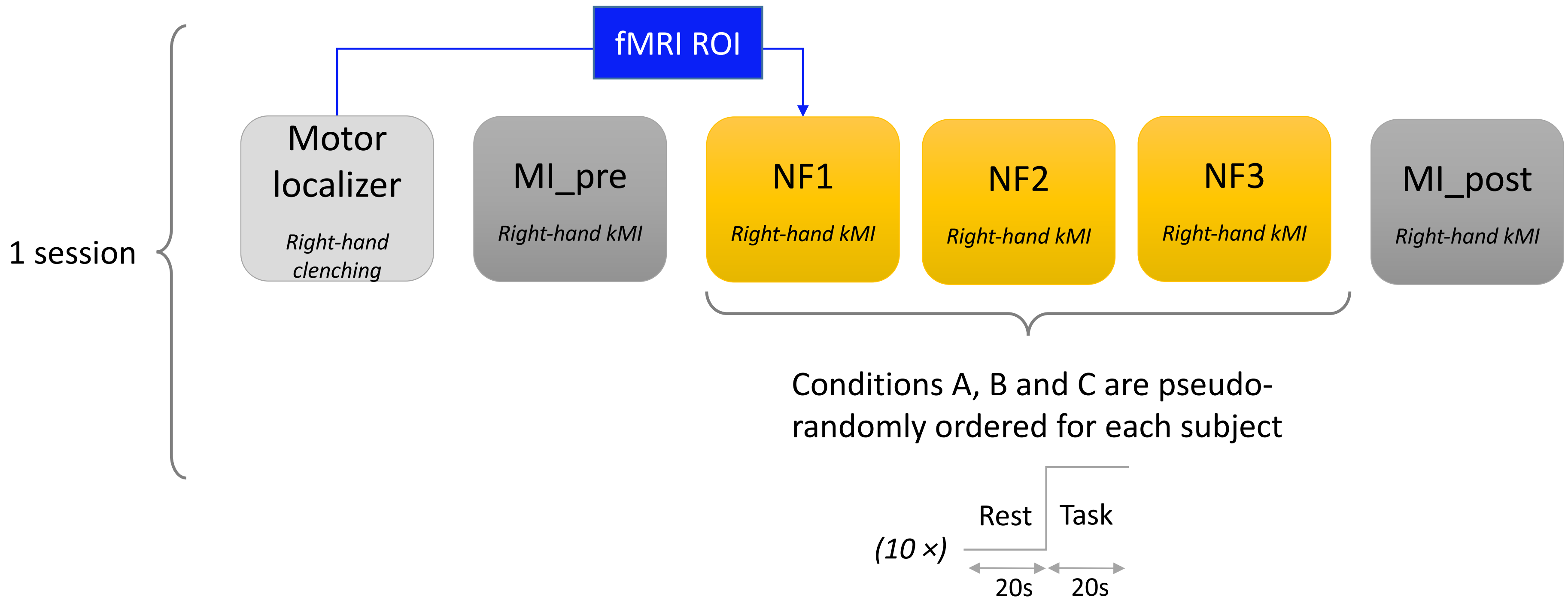
Goal and methods

- <u>**Goal**</u>: *evaluate the added value of EEG-fMRI-nf compared to unimodal EEG-nf and fMRI-nf*
- **Participants**: 10 healthy subjects(28 +/- 5.7 y, 2 females)
- **Design**: within-subject
- **Collected data**: EEG + fMRI
- **Task**: kinesthetic motor-imagery (kMI) of the right hand under unimodal/bimodal NF conditions
- **Evaluation criteria**:
  - EEG and fMRI activation levels
  - fMRI activation maps
  - Questionnaires



Experimental protocol

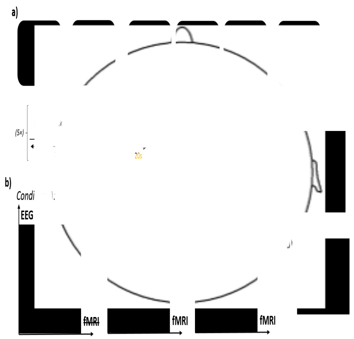


Features

Features: laterality indices between left and right motor area

EEG feature: $eeg_{lat}(t) = \frac{nLbp(t) - nRbp(t)}{nLbp(t) + nRbp(t)}$

- **Electrodes**: C1 and C2
- **Frequency band**: μ (8-12 Hz)
- **Baseline**: from previous rest block
- **NF rate**: 8 Hz



fMRI feature: $fmri_{lat}(t) = \frac{B_{left}(v)}{B_{left}(previous\_rest)} - \frac{B_{right}(v)}{B_{right}(previous\_rest)}$

- **ROI**: 9×9×3 box over left and right M1 *[Chiew et al., 2012]*
- **Baseline**: from previous rest block
- **NF rate**: 0.5 Hz (= TR)

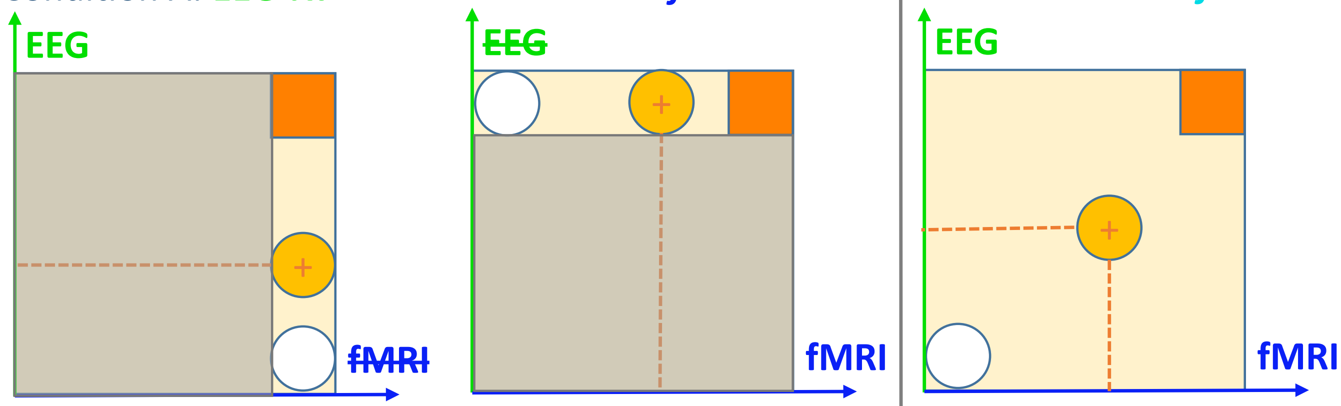
Experimental conditions

Unimodal | Bimodal

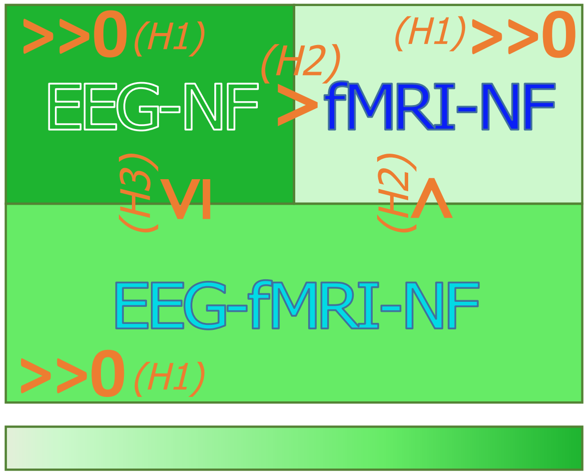
Condition A: ***EEG-NF***

Condition B: ***fMRI-NF***

Condition C: ***EEG-fMRI-NF***



Hypotheses



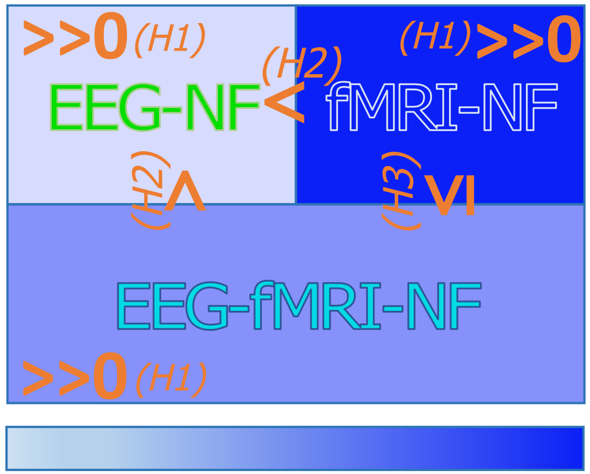
Level of NF-related EEG activity

Hypotheses

H1: Generalized NF effect

H2: Direct NF effect

H3: Compromise effect

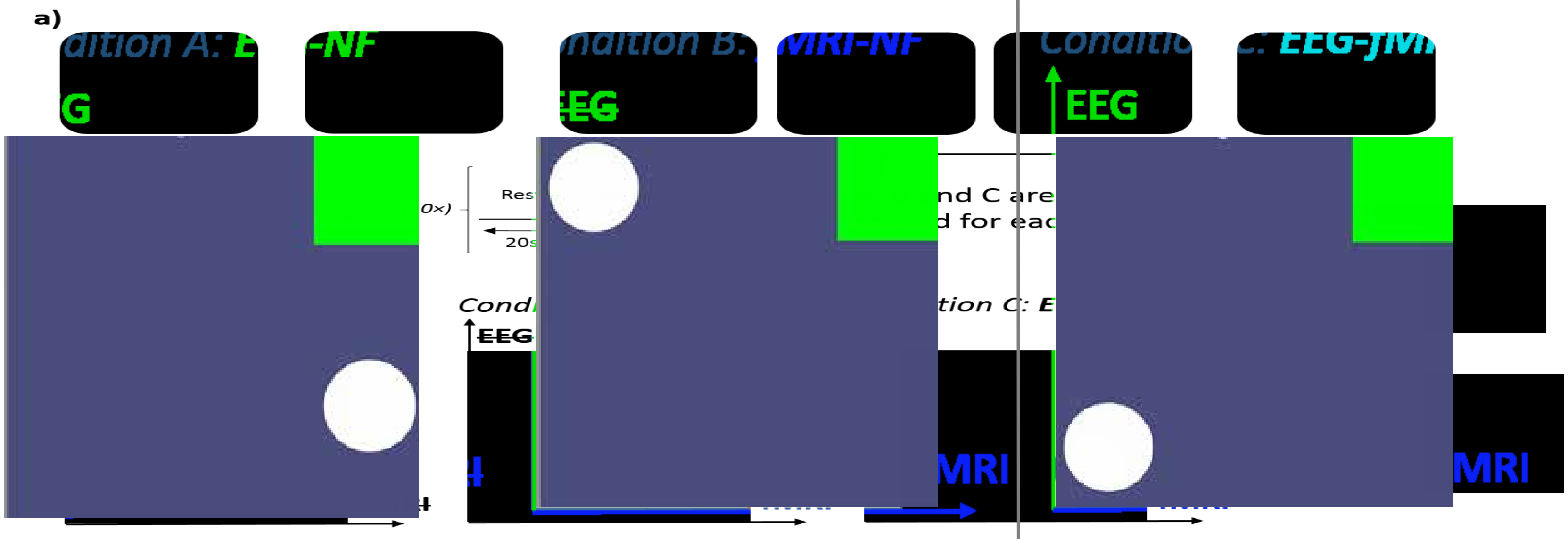


Level of NF-related fMRI activity

Demo

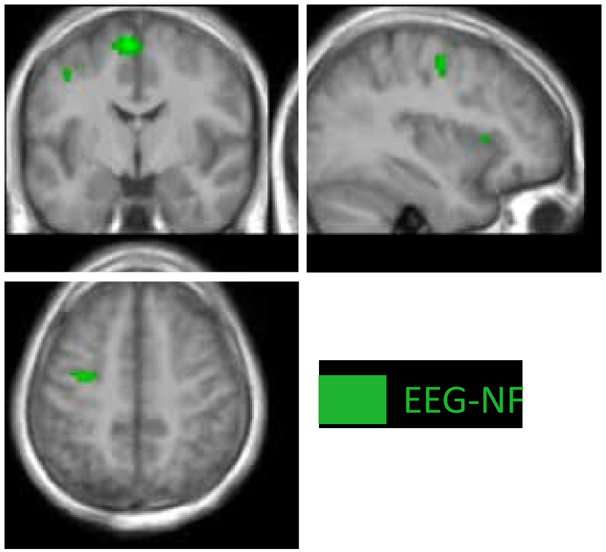
Unimodal

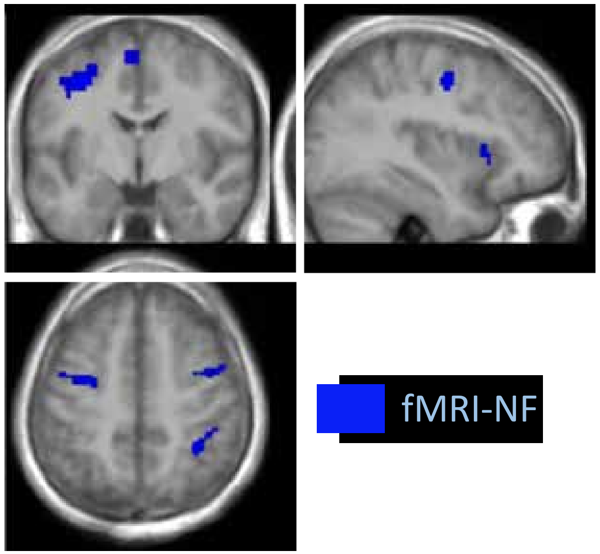
Bimodal



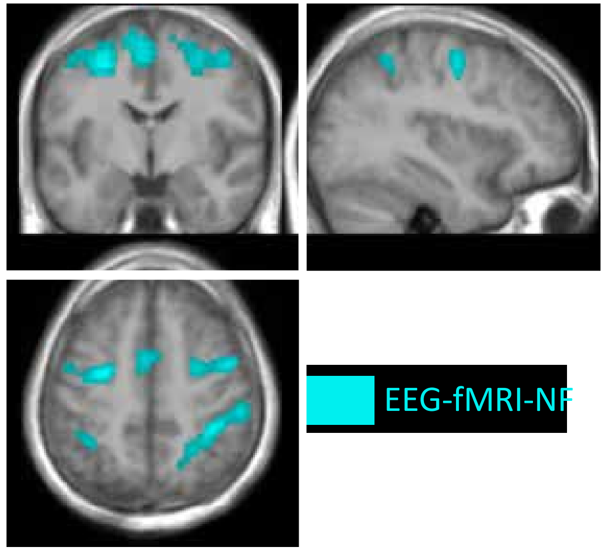
Results > BOLD activation maps

Unimodal





Bimodal

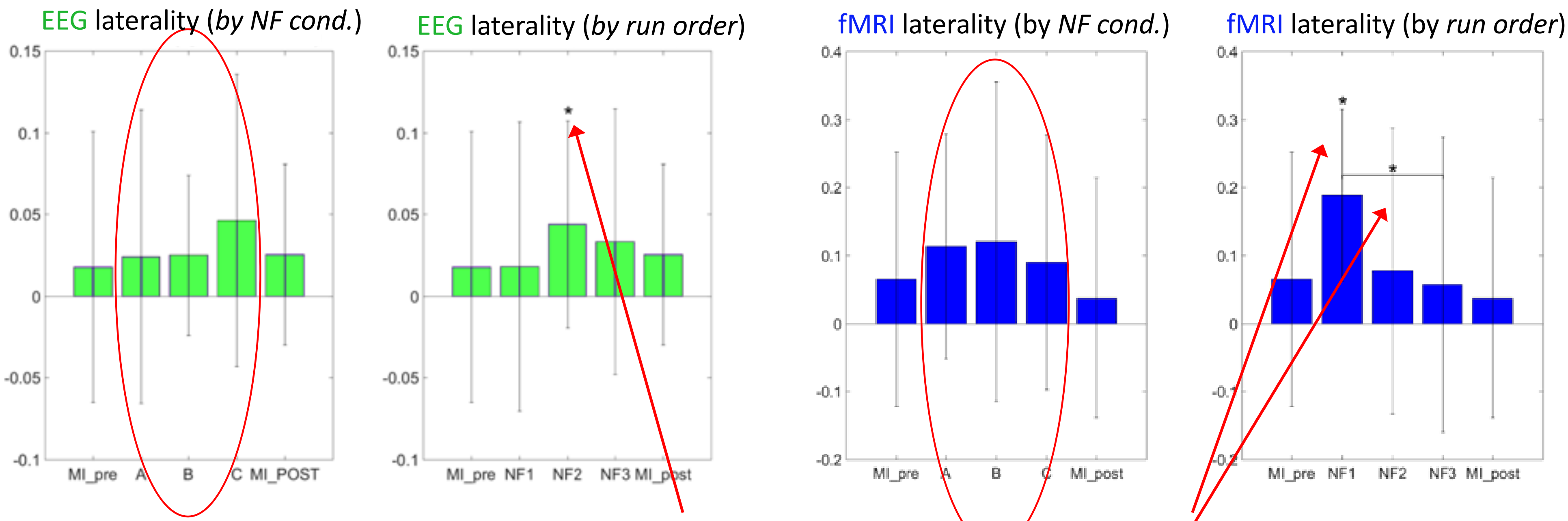


- Stronger, bigger and more widespread activations during EEG-fMRI-NF

=> higher level of engagement or higher level of self-regulation ?

(TASK > REST; p > 0.05 FWE corrected; k > 10 voxels)

Results > NF performance (online)

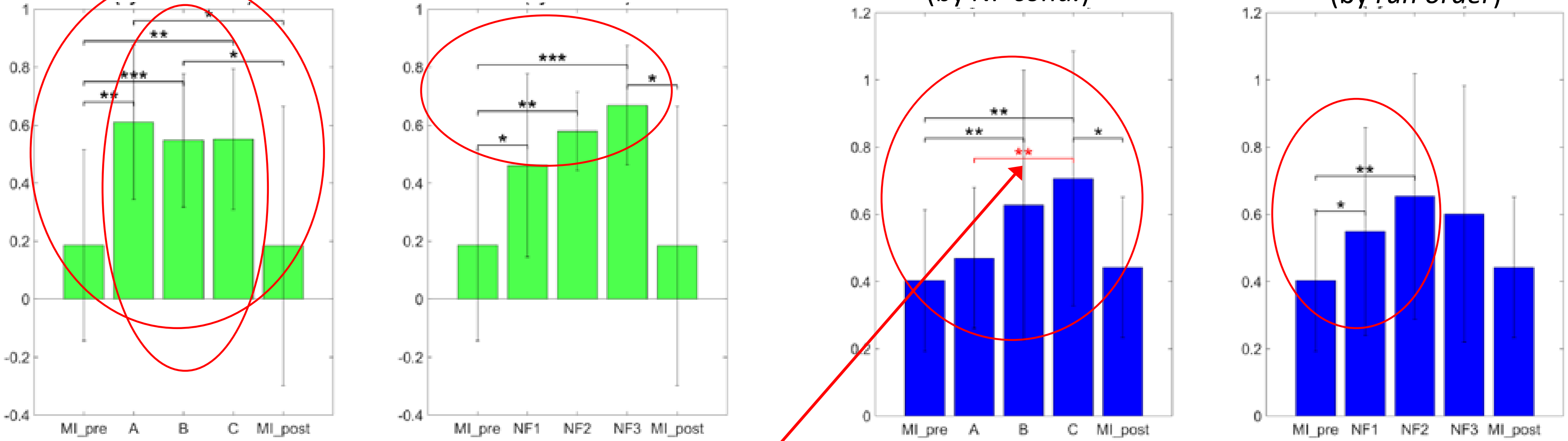


- EEG laterality significant in NF2, fMRI laterality significant in NF1
- High inter and intra subject variability
- Loss of performance on online fMRI laterality between NF1 and NF3
- No significant difference between NF conditions
- Laterality indices might have been too hard to regulate in one session

A: EEG-nf
B: fMRI-nf
C: EEG-fMRI-nf

Results > NF performance (posthoc)

EEG ERD on CSP filtered data (*by NF cond.*) — EEG ERD on CSP filtered data (*by run order*) — fMRI PSC in posthoc ROI (by *NF cond.*) — fMRI PSC in posthoc ROI (by *run order*)

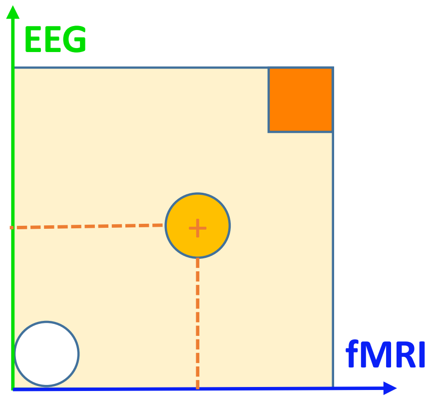


- EEG and BOLD activity significantly higher during NF than during MI_pre => H1
- BOLD activity significantly higher during EEG-fMRI-nf than during EEG-nf => H2
- No significant difference on EEG between NF conditions

A: EEG-nf
B: fMRI-nf
C: EEG-fMRI-nf

Results > Questionnaire

During EEG-fMRI-NF:



fMRI was easier to control than EEG	6/10
EEG was easier to control than fMRI	3/10
EEG and fMRI were as difficult to control	1/10
Same attention given to both feedback dimensions	8/10
More attention given to the dimension that was harder to control	2/10

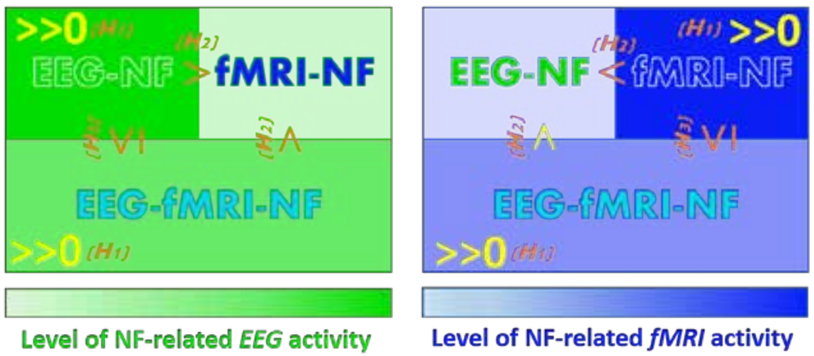
Discussion

- Need further studies to reinforce our results and evaluate the rest of the hypotheses
- Opposite tendency of online EEG and fMRI features
- One modality can be regulated at the expense of the other

Summary

- We conducted a study that compared for the first time EEG-fMRI-nf to EEG-nf and fMRI-nf
- Main results
  - Participants are able to regulate hemodynamic and electrophysiological activity simultaneously during unimodal and bimodal MI-based NF
  - BOLD activity higher during EEG-fMRI-nf than during EEG-nf

Published in : **L Perronnet**, A Lécuyer, M Mano, F Lotte, M Clerc, C Barillot (2017). Unimodal versus bimodal EEG-fMRI neurofeedback of a motor imagery task. *Frontiers in Human Neuroscience*.



Outline

- Related works
  - Contribution 1 (methodo) : Taxonomy of EEG/fMRI NF studies
- Contribution 2 (techno) : EEG/fMRI NF platform
- Contribution 3 (study): Unimodal vs bimodal NF
- **Contribution 4 (methodo + study): Towards integrated feedback**
- Conclusion
- Perspectives

Feedback design for EEG-fMRI-nf

- In EEG-fMRI-nf, greater amount of information with non trivial relationship

  => How to represent the EEG and fMRI features simultaneously?

- Problem of separate feedbacks
  - 2 feedbacks, 2 targets ~ 2 concurrent regulation tasks
  - High cognitive load
  - Does not allow to define a NF target characterized by the pair of features

[Zotev et al., 2013]

- **Concept**: we propose to *integrate the EEG and fMRI features in a single feedback*

To appear

Under review

Outline

- Related works
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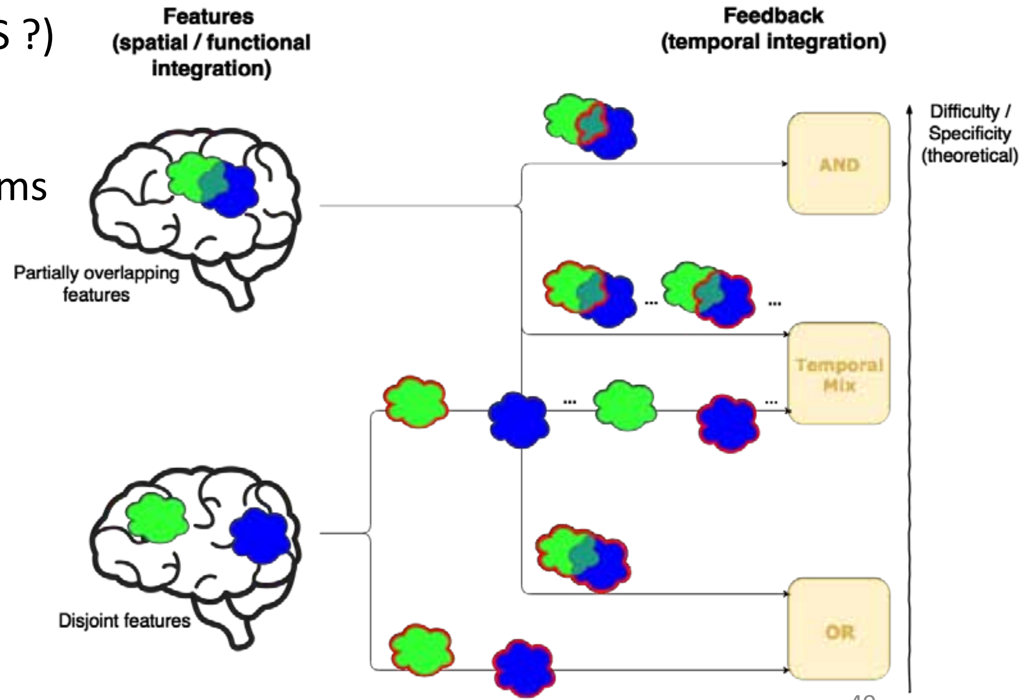
Conclusion

- Goal : design novel NF approaches combining EEG and fMRI

- Contribution 1 (*methodo.*) : Taxonomy of EEG/fMRI NF studies
  - The taxonomy shows there are many ways of combining EEG and fMRI for NF purpose
  - We have focused on EEG-fMRI-nf: simultaneous online use of EEG and fMRI as NF signal
  - There is still room left for improvements and for the development of new approaches
- Contribution 2 (*techno.*) : EEG/fMRI NF platform
  - We have developed an efficient platform that allowed us to test and evaluate methods for bimodal NF
  - It will continue to be improved and used for experiments
- Contribution 3 (*study*): Unimodal vs bimodal NF
  - We have demonstrated that during an MI task bimodal EEG-fMRI-nf triggers stronger BOLD activations than unimodal EEG-nf
- Contribution 4 (*methodo. + study*): Towards integrated feedback
  - We have introduced the concept of integrated feedback for EEG-fMRI-nf (one feedback / one target)
  - We have proposed two integrated feedback strategies, a 2D and a 1D
  - The 1D feedback is easier to control on a single session
  - The 2D feedback triggers more activation in the right SPL and encourages subjects to explore mental strategies

Perspectives

- Experimental design
  - Mixed protocols
  - Investigate other modality couples (EEG+fNIRS ?)
- Feedback
  - Investigate other integrated feedback paradigms
  - Multi-sensory bimodal feedback
- Applications
  - Upcoming clinical tests (depression, stroke)



Publications

- Journal
  - **L Perronnet**, A Lécuyer, M Mano, F Lotte, M Clerc, C Barillot (2017). Learning 2-in-1: towards integrated EEG-fMRI-NF. *[Review in progress].*
  - **L Perronnet**, A Lécuyer, M Mano, F Lotte, M Clerc, C Barillot (2017). Unimodal versus bimodal EEG-fMRI neurofeedback of a motor imagery task. *Frontiers in Human Neuroscience.*
  - **L Perronnet**, A Lécuyer, F Lotte, M Clerc, C Barillot (2016). Entraîner son cerveau avec le neurofeedback / Brain training with neurofeedback. *Les interfaces cerveau-ordinateur 1 : Fondements et méthods / Brain-Computer Interfaces 1: Foundations and Methods.* pp. 277-292, (Wiley-ISTE).
  - M Mano, A Lécuyer, E Bannier, **L Perronnet**, S Noorzadeh, C Barillot (2017). How to build a hybrid neurofeedback platform combining EEG and fMRI. *Frontiers in Neuroscience, 11,* 140.
- Conferences
  - **L Perronnet**, A Lécuyer, F Lotte, M Clerc, C Barillot. Neurofeedback unimodal ou bimodal ? Intérêt de l'EEG et de l'IRMf. *2ème journée nationale sur le neurofeedback*, ESPCI Paris, France, January 2017. [Invited talk]
  - **L Perronnet**, A Lécuyer, M Mano, E Bannier, F Lotte, M Clerc, C Barillot. EEG-fMRI neurofeedback of a motor imagery task. *22nd Annual Meeting of the Organization for Human Brain Mapping (OHBM 2016)*, Palexpo, Geneva, Switzerland, June 2016. [Poster]
  - M Mano, E Bannier, **L Perronnet**, A Lécuyer, C Barillot. Design of an Experimental Platform for Hybrid EEG-fMRI Neurofeedback Studies. *22nd Annual Meeting of the Organization for Human Brain Mapping (OHBM 2016)*, Geneva Palexpo, Switzerland, June 2016. [Poster]
  - **L Perronnet**, Anatole Lécuyer, Marsel Mano, Elise Bannier, Fabien Lotte, Maureen Clerc, & Christian Barillot. HEMISFER: Hybrid EegMrI and Simultaneous neuro-FEedback for brain Rehabilitation. *1ère journée nationale sur le neurofeedback*, ICM, Paris, France, January 2016. [Poster]
  - E Bannier, M Mano, S Robert, I Corouge, **L Perronnet**, J Lindgren, A Lécuyer, C Barillot (2015). On the feasibility and specificity of simultaneous EEG and ASL MRI at 3T. *Proceedings of ISMRM.* [Abstract]

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- All the members of the jury
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- Angélique, Armelle, Nathalie
- Visages and Hybrid members
- The MR technicians
- Doctors
- Family
- Friends
- Shiatsu teacher
- The person present by his absence
- And all of you !

https://lowpe.github.io/lorraineperronnet/

Le neurofeedback-EEG-IRMf: quand ça marche