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# A multi-target motor imagery training using EEG-fMRI Neurofeedback: an exploratory study on stroke

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## Authors:

Simon Butet<sup>1</sup>, Giulia Lioi<sup>2</sup>, Mathis Fleury<sup>2</sup>, Anatole Lécuyer<sup>3</sup>, Christian Barillot<sup>2</sup>, Isabelle Bonan<sup>1</sup>

## Institutions:

<sup>1</sup>CHU Rennes, Médecine physique et de réadaptation, Rennes, France, <sup>2</sup>Univ Rennes, Inria, CNRS, Inserm, IRISA, EMPENN ERL U1228, Rennes, France, <sup>3</sup>Univ Rennes, Inria, CNRS, IRISA, Hybrid Project Team, Rennes, France

## Introduction:

Upper limb recovery after stroke is a complex process involving a variety of structures and mechanisms, and current rehabilitation techniques have limitations (Langhorne, Bernhardt and Kwakkel, 2011). Recent studies have revealed the potential of neurofeedback training (NF) (Cervera et al., 2018) as an alternative or in aid to traditional therapies. Studies on cerebral plasticity and recovery after stroke indicate that premotor areas (supplementary motor area -SMA, premotor cortex PMC) should be a preferred target for NF in the most severe patients (Plow et al., 2015) while M1 stimulation may be more efficient for patients with better recovery potential (Favre et al., 2014). Moreover, fMRI-NF studies (also on stroke patients) have shown that SMA is a robust correlate of motor imagery, while the activation of M1 is more difficult to achieve, especially for short training sessions (Mehler et al., 2019). Based on these results, in this exploratory work we tested a dynamic NF training more strongly rewarding SMA activation in the first NF training session and then increasing the M1 activation contribution in the final NF session. We tested this novel approach on four stroke patients in a multisession bimodal EEG-fMRI NF training. To this end, we defined an adaptive cortical region of interest (ROI) equal to a weighted combination of ipsilesional SMA and M1 activities and then varied the weights in order guide the patient training towards an improved activation of M1.

## Methods:

Four chronic stroke patients with left hemiparesis participated to the study. The experimental protocol included an alternation of bimodal EEG-fMRI NF (N=2) and unimodal EEG-only NF (N=3) sessions. For each bimodal NF session, the protocol included a calibration step (motor imagery of hemiplegic hand) and 3 NF training blocks (5 minutes each). Each NF block consisted of epochs of rest (20 s) alternated to period of closed-loop MI training (20 s). MRI imaging was performed using a Siemens 3T Prisma scanner and 64 channels EEG was recorded using an MRI compatible Brain Product solution. The experiment was run using a NF platform (Mano et al., 2017) performing real-time EEG-fMRI processing and NF presentation. The NF metaphor consisted of a ball moving on a gauge proportionally to the average BOLD and EEG activity in regions of interest (ROI) identified over the ipsilesional motor cortex during calibration. The fMRI NF score was calculated as a weighted combination of the activity in the SMA and M1 cortical areas. For the first session, an equal weight of 0.5 was attributed to SMA and M1, while in the second session the activity in the primary motor area was much heavily weighted (0.75) than the SMA (0.25) (Figure 1).

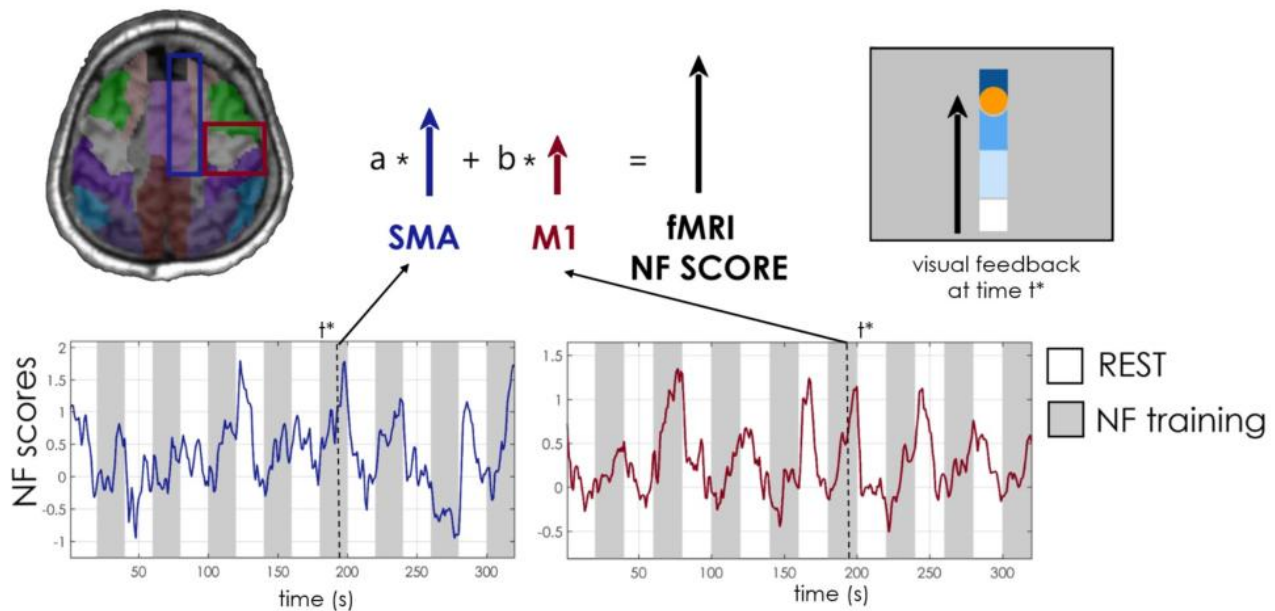


Figure 1. fMRI NF scores calculation schematic. The fMRI visual feedback is updated each second with the weighted sum of contrast (NF TASK>REST) activation in the SMA and M1 areas. The weights assigned to the two contributions vary from the first training session ( $a=0.5$ ,  $b=0.5$ ) to the second ( $a=0.25$ ,  $b=0.75$ ). For ease of visualization only the composite fMRI score is represented here, however during bimodal NF training the visual feedback is equal to the average of the fMRI and EEG scores.

## Results:

All the patients were able to upregulate the brain activity in the target cortical areas during the NF training (as compared to rest). The increase in brain activation during the NF task was particularly significant for the BOLD signal, but varied depending on the ROI targeted (SMA, M1) and the subject. The EEG activity was harder to modulate than the BOLD activity. Two patients, that had a less severe upper limb deficit, showed significant increased activation of the ipsilesional M1 at the end of the training ( $p < 0.001$ , Wilcoxon test across training blocks) and exhibited a larger involvement of the ipsilesional motor and premotor areas (with respect to controlesional ones) in the second NF training session (Figure 2). These preliminary results, on a short training duration, indicate the potential of a dynamic, multi-target/multimodal NF training approach on chronic stroke patients.

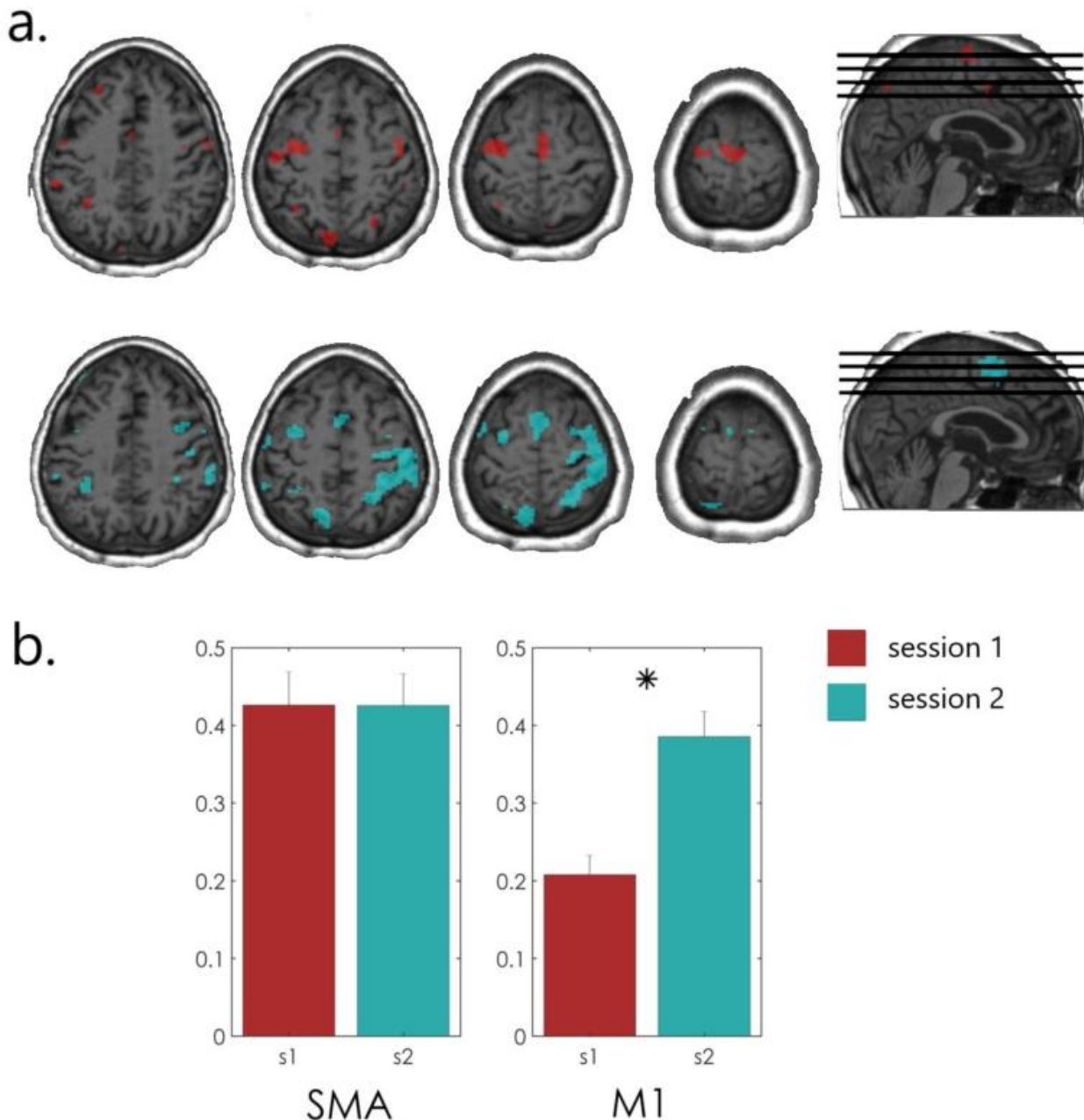


Figure 2. Example of fMRI activation during NF training in one patient. A. Individual contrast activation maps (NF TASK>REST;  $p > 0.05$  FWE corrected, voxel-based analysis) during NF training in session 1 (red) and 2 (cyan). B. Contrast activation mean amplitude in SMA (left bar plot) and M1 (right bar plot) with relative standard error and statistics ( \* indicates statistical significant difference as assessed with a Wilcoxon test across blocks of the same training session,  $p=10^{-9}$ )

### Conclusions:

We tested a novel adaptive NF training strategy on four chronic stroke patients using bimodal EEG-fMRI NF. This approach consisted in rewarding adaptively across training sessions two cortical motor target: SMA and M1. Preliminary results confirmed the feasibility of this approach and showed its potential in relation to the severity of the stroke deficit.

### Disorders of the Nervous System:

Stroke<sup>2</sup>

### Imaging Methods:

BOLD fMRI <sup>1</sup>

EEG

Multi-Modal Imaging

### Learning and Memory:

Neural Plasticity and Recovery of Function

### Keywords:

Electroencephaology (EEG)

FUNCTIONAL MRI

Motor

Plasticity

Other - Neurofeedback

<sup>1|2</sup>Indicates the priority used for review