The Use of Neurofeedback with Real-Time Functional MRI to Suppress Physiological Noise.

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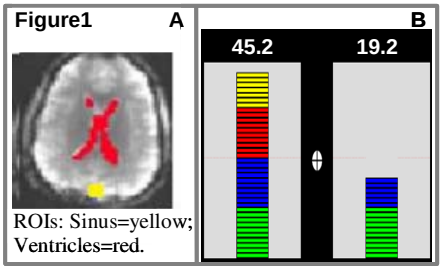
INTRODUCTION: Neurofeedback refers to experiments and therapeutic techniques that present subjects with real-time information about their own measured signal, such as brain activity measured with functional magnetic resonance imaging (fMRI). The most extended form of neurofeedback is ECG-Neurofeedback, which has been reported to be successful for clinical applications [1,2]. However, one important limitation of ECG-Neurofeedback is low spatial resolution. Real-time fMRI (rtfMRI) was introduced more than a decade ago [3] but, recent rapid advances in MRI signal reception and detection hardware (multi-channel detectors, better RF coils, faster imaging) as well as computer technologies (increases in image reconstruction speed) resulted in wider implementation of the real-time fMRI [4]. The neurofeedback techniques based on rtfMRI offer excellent spatial resolution and the ability to feedback activity from specific brain structures. Using rtfMRI-Neurofeedback, experimenters have already proven that subjects can self-regulate: pain perception [5], activation on areas such as the hand motor area [6], or the amygdala [7].

In the present study, we employed rtfMRI neurofeedback to investigate whether healthy subjects can learn to self-regulate the variability of the fMRI response in areas affected by high levels of physiological noise [8]. In particular, subjects were asked to attempt to reduce the standard deviation (SDEV) of the fMRI signal in the ventricles and in the posterior sinus. We hypothesized that learning to self-control the variability of the fMRI signal in these extra-cortical areas would be accompanied by increased fMRI time series temporal signal to noise ratio (TSNR=mean voxel time course signal/time course standard deviation [8]) in both white (WM) and gray (GM) matter compartments.



MATERIAL and METHODS: ***MRI Imaging:*** Six subjects (3 males/3 females) were scanned in a 3T General Electric HDx MRI Scanner equipped with home made rtfMRI system. Sixteen-element receive-only brain array (Nova Medical Inc) and Gradient Echo single shot EPI were used. Physiological noise localizer parameters (EPI, TR/TE=400/27ms, FA=35°, FOV/slice=240/4mm, matrix=64x64, #Slices=7, #Volumes=400). All other functional runs (EPI, TR/TE=2000/30ms, FA=90°, FOV/slice=240/4mm, matrix=64x64, #Slices=20, #Volumes=140, first 4 volumes were not used in data analysis to ensure fMRI signal steady state).

Neurofeedback Display: Figure 1A shows ROIs used. Two dynamic bars (Figure 1B) left bar sinus ROI, right ventricles) associated with the SDEV of the subject fMRI signal in the selected two ROIs were presented back to the subject. Bar height was updated with each acquired volume. SDEV was calculated using a running window that expanded back six volumes from the last acquired volume.

Experimental Paradigm: No specific instruction how to control their brain signals were given to all subjects except requests to stay calm, avoid movements and breath regular. Scans: 3-Plane Localizer; Physiological Noise Localizer to determine 2 ROIs (sagittal sinus, ventricle); Resting Runs: eyes closed (BEFORE training: REST1,REST2); Training: subjects learned to regulate neurofeedback signal (3 runs); Reduce SDEV + Finger Tapping: keep SDEV as low as possible and perform finger tapping on a block design (2 runs). Reduce SDEV: keep SDEV as low as possible with no additional task (AFTER training, REST1,REST2).

Data Analysis: Performed with AFNI. We focus solely on the comparison of before- and after-training resting runs (no finger tapping). Processing steps: (1) motion correction to 4th volume, (2) tissue segmentation over EPI volumes using method described in [8], (3) calculate TSNR values for white and gray matter compartments.

Training Evaluation: (1) Qualitative evaluation: the mean value of the SDEV time series was computed for each subject and each ROI. These mean SDEV values were subsequently used to calculate percent change associated with training; and were also used as input to a paired t-test devoted to evaluate the significance of the observed changes

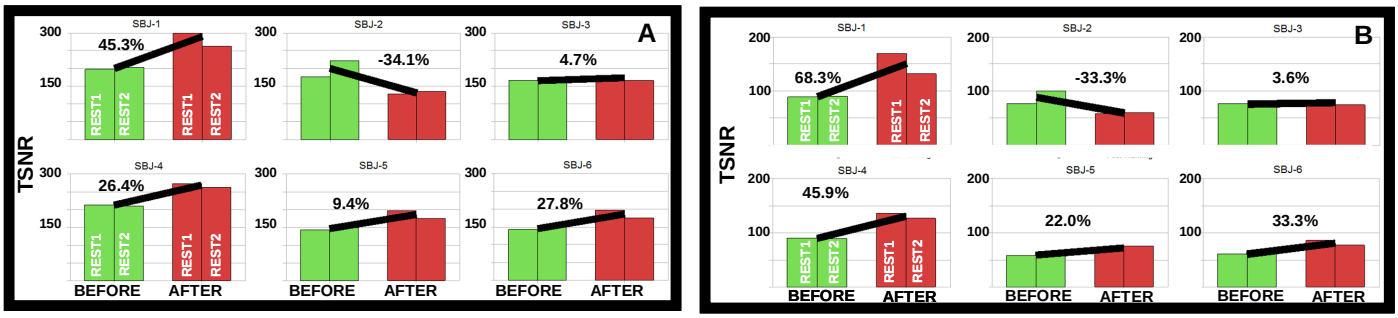


Figure 2. Examples of TSNR change before and after training in the white matter (A) and the gray matter (B) compartments for all subjects. TSNR improved significantly for five of six subjects due to neurofeedback training. Black % values indicate the percentage increase in TSNR for each subject .

RESULTS and CONCLUSIONS: All except one (subject SBJ2) subjects were able to self-regulate the variability of the fMRI signal in the selected ROIs. We have observed a substantial variability across subjects in the amount of control achieved. Five subjects showed significant reduction (p=0.013) of SDEV in the ventricles, and four subjects (p=0.002) in the posterior sinus (mean+/-sdev=(-30.8+/-12.5)% and (-37.0+/-16.7)%, respectively). For the five subjects who were able to decrease variability in any of the ROIs, the TSNR associated with after-training runs is significantly higher than for pre-training runs in both white (p=0.028) and gray matter (p=0.029) compartments (Figure 2A and 2B, respectively). Mean TSNR percentage increases from five subjects (mean+/sdev) for GM and WM were: (35+/-24)%, (23+/-16)%, respectively. These results show: (1) that subjects can actively reduce SDEV of the fMRI signal in the ventricles and the posterior sinus using fMRI neurofeedback; and (2) such SDEV decrease is accompanied by a significant increase of fMRI TSNR in both white and gray matter compartments.

References:[1]Fox et al. (2005): Appl Psych. Biofeed 4:365-373;**[2]**Kotchoubey et al. (2001): Epilepsia 42:406-416;**[3]**Cox et al. (1995) Magn Reson Med 33:230-236 **[4]**deCharms (2008): Nat Rev Neurosci 9:720-729;**[5]**deCharms et al. (2005) PNAS 102:18626-18631;**[6]**Yoo et al. (2006) Neuroreport 13:1377-1381; **[7]**Posse et al. (2003): Neuroimage 18:760-768;**[8]**Bodurka et al. (2007): Neuroimage 34:542-549.