## fMRI informed EEG Neurofeedback from the IFG

I. Klovatch-Podlipsky<sup>1\*</sup>, A. Or-Borichev<sup>1</sup>, R. Sar-el<sup>1</sup>, T. Hendler<sup>1,2,3,4</sup>

<sup>1</sup>Functional Brain Center, Wohl Institute for Advanced Imaging, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel. <sup>2</sup>The School of Psychological Sciences, Tel-Aviv University, Tel-Aviv, Israel. <sup>3</sup>Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel. <sup>4</sup>Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

\*6 Weizman st. Tel-Avv, Israel. E-mail: ilanap@gmail.com

*Introduction:* The Right Inferior Frontal gyrus (rIFG); has a pivotal role in attention deficit disorders [1], hence gaining control over its activity could facilitate better treatment and recovery. Learning to volitionally regulate IFG activity was thus far possible only via real-time fMRI. In the present study a novel fMRI enriched EEG model (herby, "EEG-Finger-Print") of the rIFG, was developed to enable the prediction of its fMRI-BOLD activity using only EEG. Simultaneous EEG/fMRI neurofeedback (NF) was conducted in the current study to test whether the rIFG-EFG reliably predicts IFG fMRI-BOLD activity and can be used by subjects to regulate IFG activity.

*Methods*: A model of the rIFG activity was constructed using simultaneous EEG/fMRI data from 10 subjects from a different study [2, 3] based on a previously described method [4] using EEG data extracted from electrode F8. The resulting estimated model correlates well with the rIFG BOLD activity (r=0.6, p<0.5). 14 healthy subjects performed rIFG EEG-NF training simultaneously with fMRI acquisition in the scanner. The training included two test runs and one sham run. The EFP-NF training was implemented as a game where a skateboard rider and speedometer above the riders head were displayed on the screen. The game included 5 blocks of three conditions: 1.'Rest' condition (60 seconds), subjects instructed to passively view the skateboard rider which was moving at a constant speed; 2. 'Play' condition (60 seconds), the speed represented the corresponding level of EEG-EFP activity. Subjects were instructed to increase the speed of the skateboard as much as possible by practicing mental strategies of their choosing; 3. At the end of each NF block a bar indicating the average speed during the current block was presented. In the EFP-Sham runs subjects had the same instructions but received visual feedback driven by their rIFG-EFP signal from a previous EFP-NF run that was randomly assigned.

*Results*: Success rate index, which represents the percentage of the time in which the mean EFP value was significantly higher than mean baseline value, during all runs was defined. As expected this index was significantly positive (one sample T-test, t(26)=18.92, p<0.001; Mean=66.59±18.29). The whole-brain random-effects (RFX-GLM) analysis using rIFP-EEG signal as a regressor, revealed correlation with the right IFG-BOLD activity with full respect to the region originally used to develop the model (p<0.017, FDR p<0.1, n=11). Block design whole brain (RFX-GLM) group analysis overall NF runs vs baseline (n=14 subject; 27 NF runs) revealed significant BOLD activations in the rIFG that was originally used to develop the model within a network of functionally relevant areas. Analysis of weighted beta values extracted from rIFG-EFP during NF relative to baseline indicated that, as hypothesized, the EFP-NF runs responded differently from the EFP-Sham runs. Paired samples T-test revealed a significant difference between EFP-NF (NF=0.73±0.45, n=10) and EFP-Sham (Sham=0.43±0.37, n=10); (t(9)=2.46, p<0.03). In order to evaluate the neural impact of successful rIFG-EFP modulation, different patterns of brain activations between successful and unsuccessful runs will be explored.

*Discussion*: The results obtained by the simultaneous recording of EEG and fMRI show that the rIFG-EFP model reliably predicts fMRI-BOLD activity in the rIFG ROI, for which it was originally developed. Remarkably the rIFG-EFP NF training elicited distributed activation in the rIFG ROI that was used to develop the model. Additionally, as evidenced by the results, subjects managed to up-regulate the activation in the rIFG during neurofeedback relative to baseline significantly higher during rIFG-EFP-NF runs compared to rIFG-EFP-Sham runs.

*Significance*: The current work demonstrated the potential of the EFP imaging approach to enhance the spatial resolution of EEG alone and to be used as a monitor for specific regional activation. Furthermore, our results suggest that implementing the EFP approach in NF training could be used by subjects to facilitate up-regulation of rIFG activity without the use of fMRI.

## References

[1] Rubia, Katya et al. Effects of Stimulants on Brain Function in Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis. Biological Psychiatry , Volume 76 , Issue 8 , 616 - 628

[2] Kinreich, S., Podlipsky, I., Intrator, N. & Hendler, T. Categorized EEG neurofeedback performance unveils simultaneous fMRI deep brain activation, in: *Machine Learning and Interpretation in Neuroimaging*, (Springer Berlin Heidelberg, 2012), pp. 108-115.

[3] Kinreich, S., Podlipsky, I., Jamshy, S., Intrator, N., & Hendler, T. Neural dynamics necessary and sufficient for transition into pre-sleep induced by EEG NeuroFeedback. *NeuroImage*, **97**, 19-28 (2014).

[4] Meir-Hasson, Y., Kinreich, S., Podlipsky, I., Hendler, T. & Intrator, T. An EEG Finger-Print of fMRI deep regional activation. *NeuroImage***102**, 128-141 (2014).