

Motor Cortex Hemodynamic Modulation during a Hand Grip Task: Preliminary Results from an fMRI Study

Roberta Sclocco^a, Sergio Cerutti^a, Elisa Visani^b, Isabella Gilioli^b, Ferruccio Panzica^b,
Silvana Franceschetti^b, Anna Maria Bianchi^a

^aDepartment of Bioengineering, Politecnico di Milano, Italy

^bFondazione IRCCS Istituto Neurologico "C. Besta", Milano, Italy

Correspondence: R Sclocco, Department of Bioengineering, Politecnico di Milano, Via C. Golgi 39, 20133 Milano, Italy.

E-mail: roberta.sclocco@mail.polimi.it

Abstract. A dynamical functional magnetic resonance imaging (fMRI) data analysis is performed on one healthy subject during an alternate bimanual handgrip task. Task-related regressors are obtained by dividing the whole task durations in time windows corresponding to fMRI repetition time (TR), in order to both capture dynamic variability and maintain a boxcar model. Resulting functional maps show the activation/baseline recovery dynamics with the maximum time resolution allowed by the nature of the considered protocol, as well as a difference in hemodynamic behavior between activation and recovery to basal level. In particular, the latter phenomenon shows to be faster and more synchronous among motor cortex areas than the first one, consistently with previous studies on the cerebral vasculature characteristics.

Keywords: fMRI, Motor Cortex, Dynamical Analysis, BOLD Baseline Recovery

1. Introduction

In functional magnetic resonance imaging (fMRI), a distinction is made between event-related designs, in which stimuli of different types are intermixed, and blocked designs, in which stimuli of the same type are presented in blocks [Tie et al., 2009]. Effects of interest in blocked designs are usually modeled with some form of boxcar regressor convolved with a synthetic hemodynamic response function (HRF). Implicit in this model is the assumption that steady-state synaptic activity and hemodynamics are attained within each block. In contrast, effects of interest in event-related designs are modeled by convolving each trial onset (i.e., a stick function) with a synthetic HRF. Here the hemodynamic responses to stimulus-induced neuronal transients are modeled without assuming within-block activity [Mechelli et al., 2003]. It has been shown that blocked designs can be modeled as a series of events [Huettel, 2011]: indeed, modeling the BOLD response to each stimulus within a block may capture variability that is not captured by a simple boxcar model [Price et al., 1999], [Henson, 2007]. On the other hand, for trials duration above 2 s, the response begins to plateau, meaning that a boxcar model can be a better solution [Henson, 2007]. In this work, we propose a dynamical fMRI analysis, in which the original boxcar design is maintained by modeling the BOLD response with a series of shorter blocks, having the duration of fMRI sampling time. Sequential statistical parametric maps allow therefore to follow activation and baseline recovery dynamics during the blocked design protocol. The method was applied on fMRI data acquired during an alternate bimanual handgrip and preliminary results for one healthy subjects are shown.

2. Material and Methods

2.1. Subjects and task

One healthy right handed subject (male, age 41) participated in the study which was performed at the IRCSS Istituto Neurologico “Carlo Besta”, Milan, Italy. The subject was selected within a group of acquisitions in the context of the nEUROPt project, supported by the European Community’s Seventh Framework Programme (FP7/2007-2013).

The motor task consisted of an initial rest period (20 s), followed by blocks (20 s each) of right and left handgrip alternately, and ended with another rest period (20 s), with an overall duration of 420 s (Fig. 1). The switching instructions between the different conditions were given by video signals. The subject was in a supine position with arms relaxed and head fixed with adjustable padded restrains on both sides. He was asked to move as little as possible throughout the experiment, to avoid blinking and, in general, to keep his eyes open.

2.2. fMRI acquisition

fMRI images were acquired on a 1.5 T MR scanner (Magnetom Avanto, Siemes AG, Erlangen, Germany). An axial gradient-echo echo-planar sequence was used to generate the functional images (TR = 2000 ms, TE = 50 ms, 21 slices, 2x2 mm² in-plane voxel size, 4 mm slice thickness, no gap), resulting in a total of 210 functional scans. Concurrently, electromyographic activity was recorded by a pair of Ag/AgCl electrodes positioned 2-3 cm on either side of the right index flexor muscle.

2.3. fMRI data preprocessing

The fMRI images were motion and slice timing corrected and normalized to a standard EPI template based on neuroanatomical atlas of Talairach and Tournoux [Talairach and Tournoux, 1988]. Finally, normalized images were spatially smoothed with an 8 mm x 8 mm x 8 mm full width at half maximum Gaussian kernel. All steps of fMRI data preprocessing were performed using the SPM5 software package (<http://www.fil.ion.ucl.ac.uk>).

2.4. Boxcar function-based fMRI analysis

To investigate the effect of the experimental task, a boxcar function-based fMRI analysis was first performed using regressors constructed on the basis of the motor events detectable from the EMG recording. For this purpose, the bursts of activity corresponding to the grip of the right hand were identified by a physiologist and a boxcar function synchronous with EMG bursts was created. The left hand motor events were obtained as the complement to the right one. The expected response was modeled as the convolution of this boxcar function with the SPM’s canonical HRF, including its time and dispersion derivatives. Movement parameter estimates produced by realignment procedure were also included as confounding regressors, in order to remove residual movement artifacts [Friston et al., 1996].

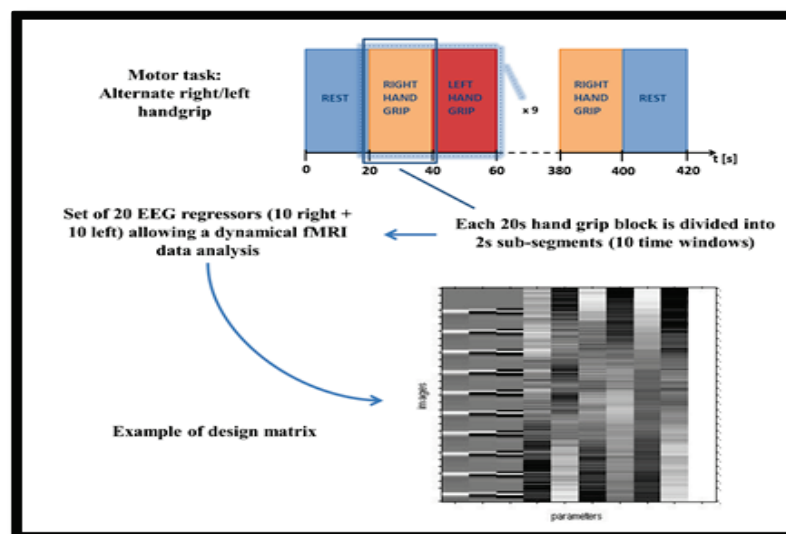


Figure 1. Dynamical fMRI analysis workflow.

The whole set of regressors was then fitted to the image data using the mass univariate approach based on General Linear Model (GLM) Theory implemented in SPM5. Inference was performed using a Student's *t* statistic ($p < 0.05$, FWE corrected for multiple comparisons) for each of the two stimulus regressors, that is, for the right and left hand grip separately.

2.5. Dynamical fMRI analysis

In order to investigate the motor cortex activation and deactivation dynamics, a second group of analyses was performed. The whole duration of each handgrip repetition (20 s) was divided into ten 2s-windows, in order to match fMRI sampling rate ($TR = 2s$).

Therefore, a set of 20 new regressors was obtained (10 for the right handgrip, 10 for the left one), each relative to a specific time segment of the handgrip block. Every regressor was then convolved with the canonical HRF and included in a design matrix for GLM estimation (Fig. 1).

Inference was performed using a Student's *t* statistic ($p < 0.05$, FWE corrected for multiple comparisons); the used *t*-contrast was positive, i.e. $[1 \ 0]$, to identify BOLD signal increases, while it was negative, i.e. $[-1 \ 0]$, to identify BOLD signal decreases. Functional maps relative to each of the 20 time windows (10 for the right handgrip, 10 for the left handgrip) were finally obtained.

3. Results

3.1. Boxcar function-based fMRI analysis

Fig. 2 shows the results of boxcar function-based fMRI analysis, while in Table 1 the resulting cluster extents and locations are tabulated. T-maps obtained from contrast analysis on right and left handgrip regressors, respectively, are superimposed to a rendered T1 template. Both left and right motor cortexes show broad activation in left and right postcentral gyri and in left and right precentral gyri; all of them correspond to functional areas involved in motor execution.

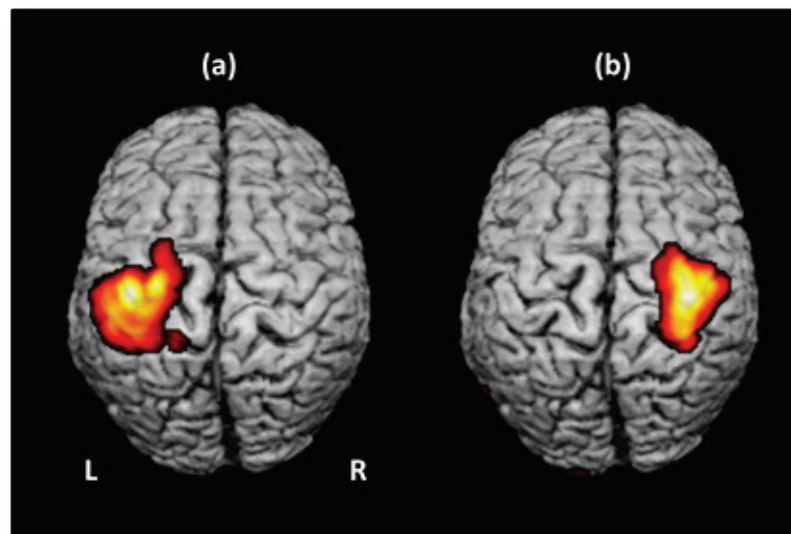


Figure 2. Inference on box car function-based fMRI analysis ($p < 0.05$, FWE): (a) right handgrip; (b) left handgrip.

Table 1. Inference on boxcar function-based fMRI analysis. First row: right handgrip; second row: left handgrip.

Cluster size [# voxels]	Talairach coordinates of maximum [mm]	Cluster location
2952	-42 -24 64	49% L Postcentral Gyrus, 28% L Precentral Gyrus
2394	38 -24 72	45% R Postcentral Gyrus, 38% R Precentral Gyrus

3.2. Dynamical fMRI analysis

Results from dynamical fMRI analysis are shown in Fig. 3. T-maps obtained from contrast analysis on right and left handgrip regressors respectively are superimposed to a rendered T1 template. In the first row contrast analysis during right handgrip is shown, while the second row is related to left handgrip. Odd time windows only (1st, 3rd, 5th, 7th and 9th) are shown for sake of simplicity. Functional maps are color-coded: yellow clusters indicate BOLD signal increase, that is, cortex activations, while blue clusters indicate BOLD signal decrease, that is, baseline recovery. As in the case of boxcar function-based fMRI analysis, also here both left and right motor cortexes show broad activation during right and left handgrip, respectively. The dynamical fMRI analysis, however, allows to visualize activation/recovery maps in different time segments, providing further information about the timing and modulation of activation and recovery phenomena. In particular, the different behaviors are emphasized in Fig. 4, which shows the extent of motor cortexes clusters resulting from contrasts analyses as a function of the considered time windows during the execution of right handgrip. As can be noticed, activation (red line) and baseline recovery (blue line) show a different behavior: while the activation curve gradually increase until a maximum value in the 7th time window (12-14 s), the baseline recovery curve shows a rapid increase, with the highest values in the 4th and 5th time windows (6-10 s). Results during left handgrip (not shown) show similar features.

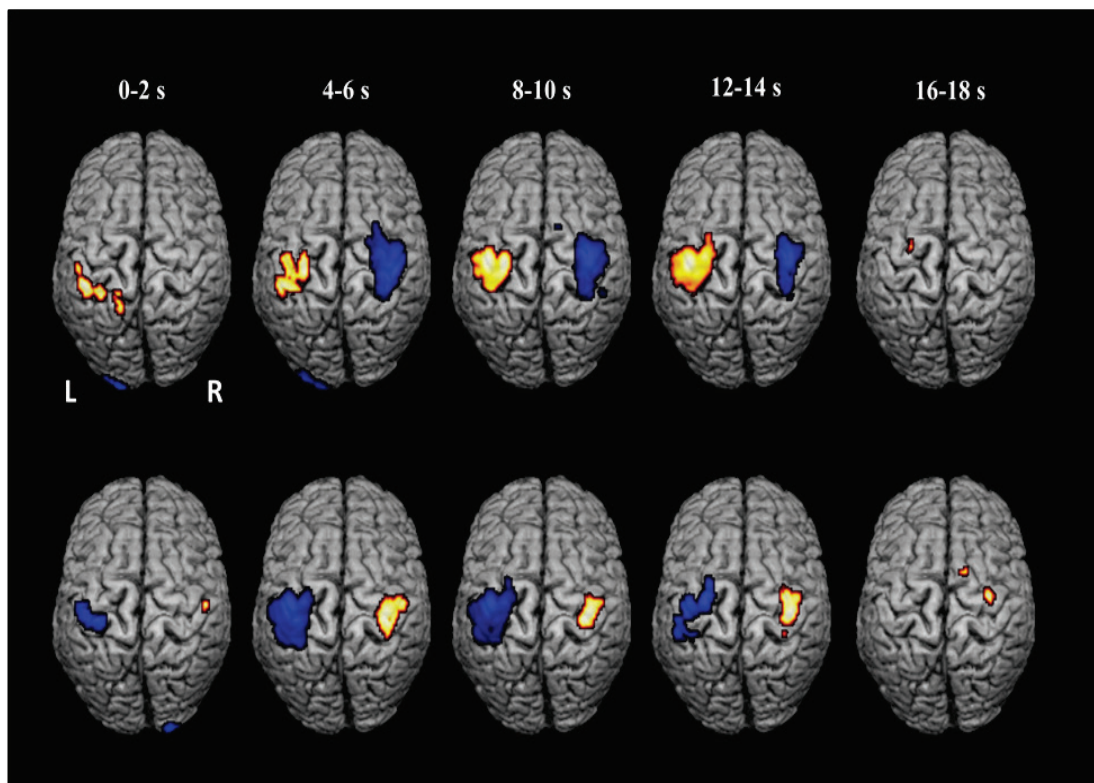


Figure 3. Inference on dynamical fMRI analysis ($p < 0.05$, FWE). Time windows-related functional maps during right (first row) and left (second row) handgrip (shades of yellow = activation, shades of blue = baseline recovery).

4. Discussion

We proposed a dynamical analysis of fMRI data acquired during a block design motor protocol, in order to explore the time windows-related activation/baseline recovery functional maps. Preliminary results during an alternate bimanual handgrip on a healthy subject show that the method is able to capture the modulating features of both BOLD signal task-related increase and return to basal level. Furthermore, the two phenomena reveal different behaviors, as shown in Fig. 4. In order to interpret this result, it should be remembered that the considered contrast analyses identify voxels with significantly increasing (activation) or decreasing (baseline recovery) BOLD signal. Therefore, the differences highlighted in Fig. 4 could be interpreted as different hemodynamic behaviors between activation and baseline recovery. In particular, while the activation process involves a growing number of voxels

during a relatively long period (up to 14 s), the baseline recovery phenomenon shows a fast and synchronous involvement of the previously activated motor areas.

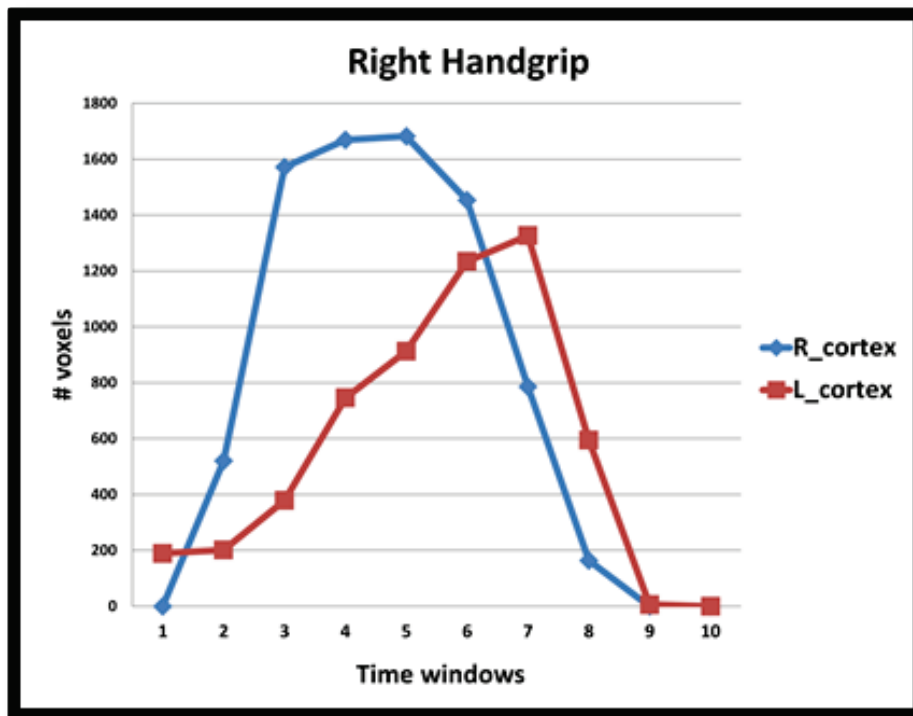


Figure 4. Extent of motor cortex clusters as a function of time windows during right handgrip.

This feature could be explained according to cerebral hemodynamic findings: the vasodilation underlying the increased blood flow has been suggested to be associated with passive dilation of venules and veins because of their balloon-like elasticity. It has been suggested, further, that this passive dilation of venules and veins may lie at the root of the post-stimulus undershoot often evident in the hemodynamic response [Buxton et al., 1999], [Mandeville et al., 1999], [Logothetis, 2003], [Buxton et al., 2004]. Therefore, the baseline recovery process could be facilitated by the intrinsic characteristics of cerebral vasculature, leading to the different dynamic behavior resulting from the analysis.

With respect to the traditional approach for block-design fMRI data analysis, represented by the boxcar function-based analysis, the main advantage of the proposed method lies in its ability to show the “evolution” of stimulus-related BOLD dynamics. Furthermore, this approach could be particularly useful for the analysis of protocols involving long stimulation periods, as in the case of sustained attention assessment, where the active time window often exceeds several minutes.

5. Conclusions

The proposed dynamical approach to fMRI block design protocols analysis seems promising for the application on a wider group of subjects in order to verify preliminary results. In addition, the ability to identify dynamical features related to activation and basal recovery could be exploited in the comparison between control and pathological groups, in order to assess possible deviations from a physiological behavior due to a pathological condition.

References

- Y. Tie, R. O. Suarez, S. Whalen, A. Radmanesh, I. H. Norton and A. J. Golby, «Comparison of blocked and event-related fMRI designs for pre-surgical language mapping,» *NeuroImage*, vol. 47, pp. 107-115, 2009.
- A. Mechelli, R. N. A. Henson, C. J. Price and K. J. Friston, «Comparing event-related and epoch analysis in blocked design fMRI,» *NeuroImage*, vol. 18, pp. 806-810, 2003.
- S. A. Huettel, «Event-related fMRI in cognition,» *NeuroImage*, doi:10.1016/j.neuroimage.2011.08.113, 2011.
- C. J. Price, D. J. Veltman, J. Ashburner, O. Josephs and K. J. Friston, «The critical relationship between the timing of stimulus presentation and data acquisition in blocked designs with fMRI,» *NeuroImage*, vol. 10, n. 1, pp. 36-44, 1999.
- R. Henson, «Efficient experimental design for fMRI,» in *Statistical Parametric Mapping: the analysis of functional brain images*, 2007, pp. 193-210.
- J. Talairach and P. Tournoux, «Co-planar stereotaxic atlas of the human brain,» Thieme Medical Publishers, 1988.
- K. J. Friston, S. Williams, R. Howard, R. S. J. Frackowiak and R. Turner, «Movement-related effects in fMRI time-series,» *Magnetic Resonance in Medicine*, vol. 35, n. 3, pp. 346-355, 1996.
- R. B. Buxton, E. C. Wong and L. R. Frank, «The post-stimulus undershoot of the functional MRI signal,» in *Functional MRI*, Mauer, Springer-Verlag, pp. 253-262, 1999.
- J. B. Mandeville, J. J. A. Marota, C. Ayata, M. A. Moskowitz, R. M. Weisskoff and B. R. Rosen, «MRI measurement of the temporal evolution of relative CMRO₂ during rat forepaw stimulation,» *Magnetic Resonance in Medicine*, vol. 42, pp. 944-951, 1999.
- N. K. Logothetis, «The underpinnings of the BOLD functional magnetic resonance imaging signal,» *The Journal of Neuroscience*, vol. 23, n. 10, pp. 3963-3971, 2003.
- R. B. Buxton, K. Uludag, D. J. Dubowitz and T. T. Liu, «Modeling the hemodynamic response to brain activation,» *NeuroImage*, vol. 23, n. 1, pp. 220-233, 2004.