

Characterizing functional brain networks of relatively homogeneous subjects under resting state

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We investigated the activity of specific brain areas by highly resolved fMRI data [1] looking at dynamic synchronous events in a *Resting State* condition (Fig. 1). More specifically, the activity of 90 ROI, identified in the brain BOLD functional images of 180 healthy individuals, has been followed for 8 minutes at a resolution of 2 seconds. A preliminary assumption is that each single ROI may have three functional states: activated [+1], non-activated [0] and deactivated [-1] as a result of filtering and then binarizing the intensity of time-dependent signals by appropriate thresholds (Fig. 2). Liu and Duyn [2] using a discrete events method show how the use of few critical peaks (when signal intensities overcome an arbitrary threshold) allows to characterize stable spatial patterns in functional brain signals. Such an approach stems from the idea that filtering peaks of large amplitude by arbitrary thresholds in the BOLD signals, can occur without substantial reduction of information [3]. In addition, the filtering corresponds to a noise-cleaning method in which increasing threshold values remove more and more random events from the subsequent analysis of the $3^2 = 9$ possible combinations, estimated by Pointwise Mutual Information (PMI) [4], of the above mentioned states in coupled regions.

The PC1 and PC2 extracted from the multivariate analysis of such 9 combinations seem to indicate 2 phenomena: the first including co-activation [1;1] and co-deactivation [-1;-1] states; the other related to mutual deactivation [1;-1] and [-1;1]. Both phenomena are reflected by an in-phase (or positively related) and anti-phase (or negatively related) signals, respectively, from the corresponding brain regions [5] (Fig. 3). The first and second loadings of the PC1 corresponding to co-(de)activations and the third and fourth loadings of the PC2 corresponding to mutual deactivations were extracted and a series of 1-way ANOVA were performed. Three groups were characterized using the gender (Female, F and Male, M) and the aging (median 21; max and min values 17 and 26) of subjects: 1= $F \leq 21$ (63 subjects); 2= $M > 21$ (31); 3= $M \leq 21$ (70). The fourth group ($F > 21$) is removed since no subjects appear with these features. The results show a significant effect only for the third ($p < 0.01$, $F: 35.7$, $df: 2$) and fourth ($p < 0.01$, $F: 13.5$, $df: 2$) loadings of the PC2. In Fig. 4 a post-hoc analysis points out a significant increase and decrease values of third and fourth loadings (PC2) of the group 3, respectively, as a function of the age subjects but not for the gender. In the same figure non-significant results of the first and second loadings (PC1) are shown.

As a general remark our results indicate a possible dependence of aging and mutual deactivations. As a matter of fact, anti-phase signal relations in fMRI data considered as anti-correlation were already related to aging [6], as well as cognitive performance, at least in particular anti-correlated brain networks: Default Mode Network (DMN) and Task Positive Network (TPN). Our results, considering to a general feature of mutual deactivations over the whole brain system, point to a pervasive dependence between this functional brain interaction and the aging process. Moreover, this relation is not replicated for the co-(de)activation brain system suggesting again a possible independent mechanism underlying these two kinds of brain interactions.

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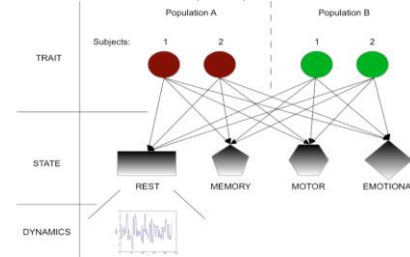


Figure 1. **Modeling the dynamics of brain functional states.** Top: different static activity patterns reflecting “Structural”, phenotypic differences between subjects (1,2) even within different groups (red, green). Middle: different dynamical patterns associated to specific experimental conditions (functional state). Bottom: Variability of connectivity patterns between brain areas in a well-defined functional state.

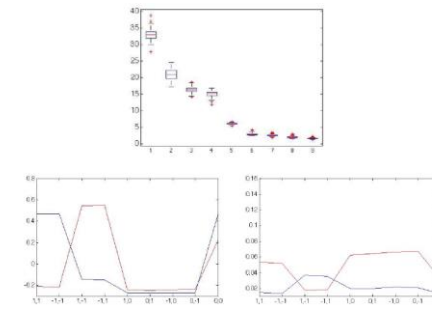


Figure 3. **Principal component and loadings values in the PCA analysis.** Top: Principal Components extracted from the nine variables (see the text). Bottom left: Average values over the subjects included in the study of the loadings in the PC1 (blue line) and PC2 (red line). Bottom right: Corresponding St. Dev. All plots refer to the highest threshold used (z-score: 1 / -1).

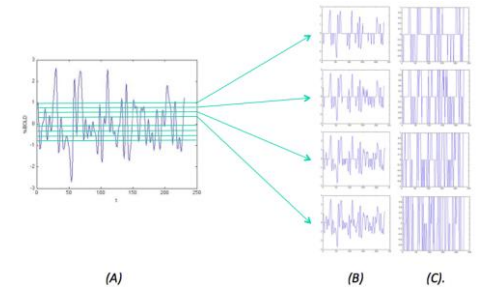


Figure 2. **Thresholding and binarizing the BOLD signal.** (A): the normalized BOLD signal (z-score values) is thresholded at 4 levels defined in terms of Standard Deviation (0.25-0.50-0.75-1). (B): Only values above the positive threshold and below the negative one are considered. (C): coding of active (+1), deactive (-1) and null events.

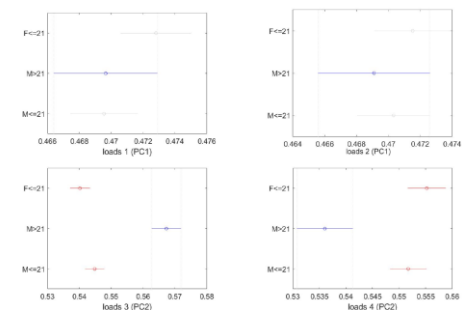


Figure 4. **Anova analysis of loadings.** Top panels and bottom panels: mean differences in the first and second loadings of PC1 and third and fourth loadings of PC2, respectively. y-axis refers to the three phenotype (gender and aging) combinations used as groups. Notice a significant difference only in the bottom panels between subjects as a function of aging.

