

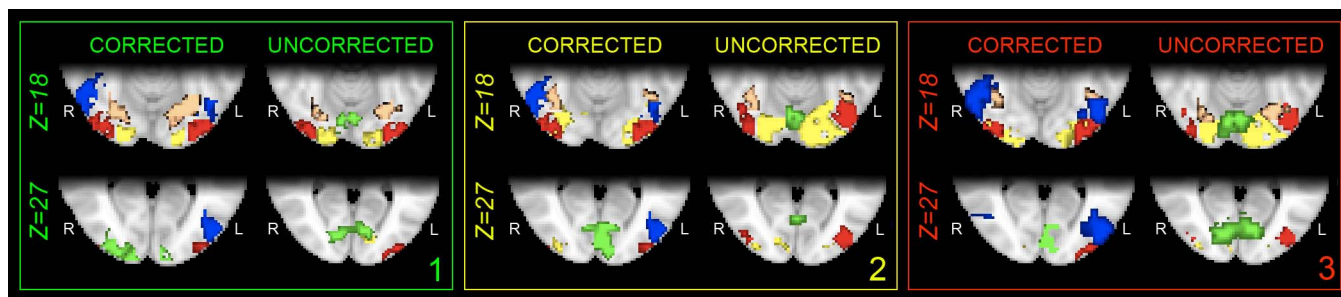
A random-walk driven segmentation of resting state fMRI data: evaluation of visual cortex sub-communities is enhanced by physiological noise correction

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Introduction Resting-state functional connectivity MRI (fc-fMRI) uses task-free blood oxygenation level dependent (BOLD) time courses [1] to measure the temporal correlation between different regions of the brain. Parcellation of the cortex into individual subunits based on correlations in resting-state data opens up the possibility of developing a subunit atlas analogous to the Brodmann areas but based on cortical function rather than cytoarchitecture. A number of clustering techniques have been suggested for segmenting the brain using resting-state fMRI, including independent component analysis (ICA) [2] and hierarchical clustering [3]. Graph theory is a common methodology for studying complex networks [4,5]. Graph-based clustering approaches have also been applied to the analysis of brain networks using resting-state fMRI [6,7]. Here we used a random-walk-based algorithm [8] to parcellate visual cortex in healthy subjects in a resting-state condition. Moreover we demonstrate the need for physiological noise removal to obtain consistent results across subjects from this functional segmentation method.

Methods Twelve healthy right-handed subjects participated in this study after giving informed consent. All the participants underwent one resting state fMRI scan: no task, eyes open. Functional data were collected by using a gradient-echo echo-planar imaging at 3T (GE HDx) using a BOLD weighted imaging sequence (TR=3 s, TE=35 ms, matrix=64x64, FOV/slice=20.5 cm/3.2 mm, flip=90°, 53 slices). A T1 weighted whole-brain structural scan was also acquired (1x1x1 mm voxels). **PREPROCESSING:** After the regression of the physiological signals (breathing and cardiac cycles) [9], each data set was motion corrected using rigid-body volume registration and slice-timing corrections applied. Anatomical scans were registered to the functional data and segmented to extract grey matter (GM) probability maps using the SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>). Afterwards, the six realignment parameters (3 translations and 3 rotations) from rigid body transformation were modelled and regressed from the data. In addition, the data were temporally band-pass filtered (0.01–0.15 Hz). Scanner drift was corrected by linear detrending, the time series means and possible spikes were removed by a demeaning-despiking algorithm. A common grey matter mask (CGM) was created considering the intersection in the standard (MNI) space of the grey matter probability maps (obtained by the segmentation procedure) thresholded at 0.9. These steps were carried out using custom software written in Matlab (the Mathworks, Inc.). Before clustering, data were normalised to standard (Montreal Neurological Institute, MNI) space (preserving the functional images resolution 3.2x3.2x3.2) and smoothed (8x8x8 fwhm). **CLUSTERING:** A functional link between two time series $x_i(t)$ and $x_j(t)$ was defined by means of the linear cross-correlation coefficient r_{ij} . During construction of the networks, a functional connection between two brain sites was assumed as an undirected and weighted edge (being the weight $w_{ij}=r_{ij}$). For each subject a correlation matrix was calculated representing connections among the voxels in the CGM back-projected to the subject space. A threshold was applied to the correlation matrix, above which individual voxels were said to be connected. This threshold was defined such that the relationship $S \sim \log(N)/\log(D)$ was the same across subjects, where N was the number of nodes and D the average of the number of connections between nodes (the average degree of the network). To partition the functional networks in communities, we used a random-walk-based algorithm [8], whose clustering ability stems from the fact that a random walker on a connected graph tends to remain in densely connected subsets corresponding to independent modules.



Figures 1-3 Three axial projection of the segmented visual cortices are reported both for data corrected and uncorrected for physiological noise. The color code of the sub-communities is V1=green, V2=yellow, V3=red, V4=brown, V5=blue. The upper row in each figure refers to the MNI coordinate $z=18$, while the lower one refers to $z=27$.

Results The clustering algorithm was applied twice: first on the entire brain network and then on the community of voxels related to the visual cortex. Each initial thresholded network was composed of ~30,000 voxels, while the number of voxels within the visual cortex community was ~1,000. Figures 1 to 3 show three examples of sub-community segmentation of the visual cortex. It can be seen that, according to MNI atlas, in data corrected for physiological noise the separation of the visual cortex in V1, V2, V3, V4, V5 (bilaterally) is tidy and consistent across subjects, while the uncorrected data shows the absence of V5 areas and a displacement of V1 towards the cerebellum. We noticed that for all subjects both V1 and V5 in the uncorrected data show a tendency to be highly functionally connected with the cerebellum.

Discussion and Conclusions We reported the ability of a graph-theory based method to reliably segment resting state networks across subjects. Moreover we showed that it is possible to find sub-communities within a specific module, eliciting the similarity of groups of voxels, whose cortical location is typically associated to a specific function. We also highlighted the role of robust pre-processing in order to obtain consistency and specificity of the separate sub-communities. Specifically our results show that it is possible to obtain a fine segmentation of the visual cortex in to V1, V2, V3, V4 and V5 regions bilaterally. The random walk based clustering could have a significant impact in producing an atlas of minimal functional subunits (minimal in the sense that they are as small as possible while maintaining across subject consistency). This would have application in reporting fMRI task-based results, for providing starting regions of interest for further connectivity analyses of diseased or healthy populations, and for further analysis of network properties in the brain.

References [1] Ogawa S, *et al*, Proc. Natl. Acad. Sci. USA 87, 9868, 1990; [2] Damoiseaux, JS, *et al*, Proc. Natl. Acad. Sci. USA 103, 13848, 2006; [3] Achard S *et al*, Neuroscience 26, 63, 2006; [4] Watts DJ, Strogatz SH, Nature 393, 440 1998; [5] Sporns O, , PLoS One 2, e1049, 2007; [6] Schwartz A, *et al*, Magn. Reson. Imag. 26, 914, 2008; [7] Shen X, *et al*, NeuroImage 50, 1027, 2010; [8] Valencia M, *et al*, Chaos 19, 023119, 2009; [9] Chang C, Glover GH, Neuroimage 47 1448, 2009.