Identification of state changes from spontaneous fluctuations in fMRI data

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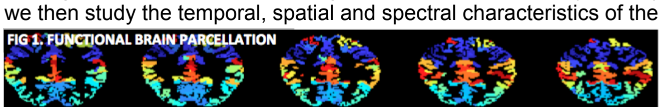
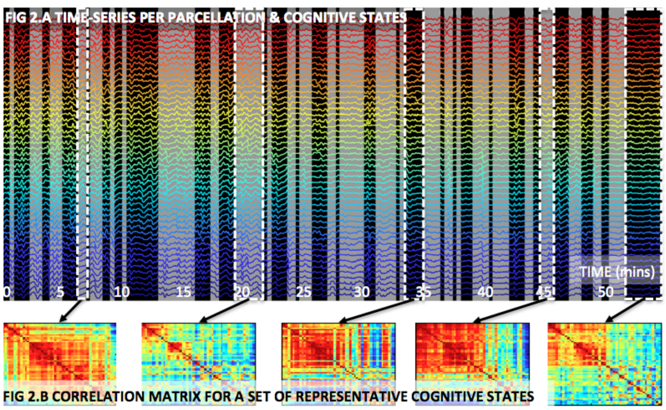
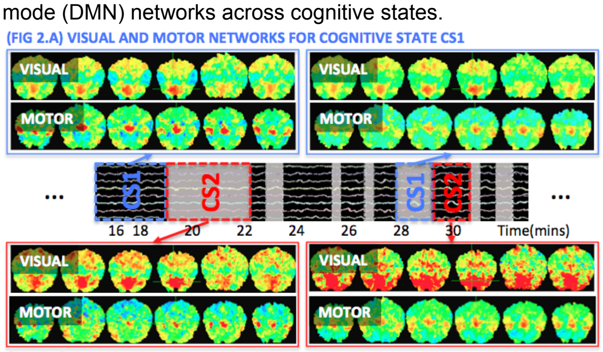
INTRODUCTION: The brain is continuously adapting to respond to the environment; and therefore, continuously changing its functional configuration to better serve such endeavors. In the course of an hour of resting state scanning, our subjects can be expected to engage in several different cognitive states/tasks for variable periods of time (i.e., relaxing, planning dinner, relaxing again, deciding on how to drive home, focusing on the scanner noise, napping, etc.). Each of these states/tasks, which have different cognitive characteristics, are expected to be accompanied by changes in connectivity patterns across the whole brain [1]. Still, some level of stability in the connectivity profile can be expected for the periods of time during which subjects remain within a given cognitive state/task [2]. Here, we automatically identify these stable cognitive states in one-hour long fMRI resting scans looking at how different cortical regions pass in and out of synchrony with each other as time progresses. For each cognitive state, we then study the temporal, spatial and spectral characteristics of the connectivity patterns that uniquely define the state.



METHODS: 5 healthy volunteers underwent anatomical, functional and resting state scans on a 7T scanner (Siemens, VB17). Resting scans consisted of 11 slices positioned to best intersect visual, motor and default mode network (GRE-EPI, Duration= 54 mins, TR=400ms, 2mm x 2mm x 2mm, FOV=20cm). To aid with slice positioning 2 localizer scans (flickering checkerboard, finger tapping task) were acquired per subject. Resting state data analysis consisted of 3 phases: pre- processing; functional parcellation of the brain; and detection of cognitive states and their transitions. *Pre-processing*: (1) slice time correction; (2) head motion correction; (3) spatial smoothing (FWHM = 4mm); and (4) low pass filtering (cutoff freq = 0.1Hz). *Functional Brain Parcellation*: pre-processed scans were input to a 25 ICA analysis (FSL MELODIC) resulting in an N (number of voxels) x 25 (number of ICA components) matrix of Z-scores per subject. Fifty cortical regions with similar stable functional connectivity patterns— meaning their level of participation within each of the 25 ICA components is similar—were defined using hierarchical clustering (MATLAB, linkage=ward, distance=Euclidean) on the 25 feature space matrix created via the ICA analysis. Average time-series for each of these 50 functionally coherent regions were generated. *Cognitive states detection:* averaged time-series were broken up into 1- minute blocks; and, for each 1-minute block the pair-wise correlations between all 50 regional time-courses were computed. In this way, a description of the functional organization of the brain at each minute in time is constructed in terms of all possible pair-wise correlations between all 50 considered regions. A k-means algorithm was subsequently used to assign each minute of data into one of 16 possible cognitive states according to the similarity in these pairwise correlation patterns. For each 1 hour scan, we now have (at a resolution of 1 minute), in which of the 16 possible cognitive states our subject was. We can now combine blocks that belong to a given cognitive state and study its characteristics under the assumption of stability in functional connectivity. As a first approach, we looked at spatial correlation maps for visual and default mode (DMN) networks across cognitive states.





RESULTS: Figure 1 shows resulting functional parcellations for a representative subject. Figure 2.A shows averaged time-series for the parcellations in Fig. 1 (the color of a time-series corresponds to the color of the region the time-series belongs to in Fig. 1). It can be observed how some regions fall in and out of synchrony as time progresses. Figure 2.B shows the correlation matrix of 5 representative cognitive states, as well as to which periods in time they correspond. It can be observed that while at some states most of the brain is correlated with each other (left most matrix), at other states high correlations exist only for a subset of the regions, and other regions show low or negative correlation. Figure 3 shows the configuration of DMN and visual network for two different cognitive states (CS1 and CS2) at two different moments within the 54 minutes scan. It can be observed how these 2 networks look more similar across distant blocks in time that were classified as being part of the same cognitive state (e.g., the networks in blue boxes look very similar to each other), than across contiguous blocks of time classified as part of two different cognitive states (the networks in blue and red boxes look more different).

DISCUSSION & CONCLUSSIONS: The dynamic nature of the brain poses a significant challenge when trying to identify functional networks, and/or trying to study their spatial and spectral characteristics. As time progresses, connectivity patters and power spectra change; making difficult the use of any analytical tools (i.e., Pearson correlation, frequency analysis) that rely at some level on the assumption of stationarity for the processes or signals under study. The possibility of automatically and accurately identifying periods with stable whole brain functional connectivity will help us, not only better understand the temporal scale of this dynamic behavior, but also to obtain snapshots of functionally stable configurations that we can further analyze under the assumption of stationarity. Our results show how functional connectivity for DMN and visual networks is more similar across distant time periods classified as part of the same cognitive state, than for contiguous periods of time classified as part of different states. This suggests that our method is good at capturing when the brain stays at a given configuration and when it changes. The work presented here is a work in progress, and next steps include investigating potential similarities in cognitive states (connectivity matrices) across subjects, as well as studying the spectral characteristics of individual resting state networks within each identified cognitive state.

REFERENCES: [1] Buchel C and Friston KJ. Modulation of Connectivity in Visual Pathways by Attention: Cortical Interactions Evaluated with Structural Equation Modelling and fMRI. *Cerebral Cortex* (1997) 7(8):768-778. [2] Anderson, JS et al, Reproducibility of Single-Subject Functional Connectivity Measurements. *Am J of Neuroradiology* (2011) 32(3):548-555.