The anatomical basis of rest functional MRI

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Interdiction:
Resting state "functional" MRI is used to access basal brain activity[1-3]. According to this theory the brain can be segmented into regions of synchronous blood oxygenation level dependent (BOLD) signal pattern. This pattern may reflect a brain network of neurons working in conjugate (functional connectivity). During recent years, few signal processing schemes have been suggested to analyze the "resting state" BOLD signal from simple correlations to spectral decomposition. In most of these analysis schemes, the question asked is which brain areas "behave" in the time domain similarly to a pre-specified ROI. In this work we applied the "resting state" fMRI framework combined with short time frequency analysis and clustering to study the basal activity of the brain. The main aim of this work was to characterize and quantify the rest signal.

Methods:
Nine healthy subjects age 22-42, were scanned in a 3T MRI scanner (GE, Milwaukee, USA). The MRI protocol included a series of gradient-echo echo-planar-imaging (GE-EPI) images with the following parameters: TR/TE=600/45ms, $\alpha=30^0$, matrix of 80x80, FOV of 24cm, 7 axial slices with slice thickness of 5 mm and no gap localized at the level of the thalamus. The GE-EPI protocol was repeated 800 times to produce a pixel-by-pixel time series of the BOLD signal for 8 minutes in which the subject was asked to lie still with eye closed and not to perform any special task. Pre-processing of the images included re-alignment to account for head movement and normalization to the Talairach coordinate space (using SPM2, UCL, London, UK). Three regions were analyzed: thalamus, cortex and white matter following segmentation. Image analysis included the following steps: 1) The normalized time series; 2) The Fourier transformed (FT) time series or the windowed term FT (spectrogram); 3) Low pass filtering; 4) Clustering with the k-mean algorithm (with k=3-9). The clusters were assigned to atlas based region based on similarity index.

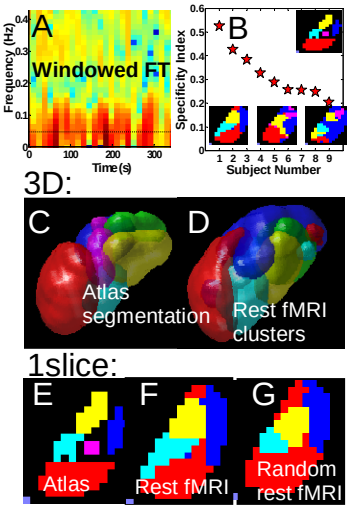

Figure 1

Results:
Windowed FT analysis of the time series BOLD Signal (Fig 1A) combined with the k-means clustering revealed six distinct clusters in the thalamus (Fig 1D,F). The comparison between the "resting state" clusters to the Talairach atlas (Figure 1C,E) using similarity index (Fig 1B) yielded segmentations that is very similar to the anatomical one. Interestingly the localization sub-thalamic clusters repeats across subjects (Fig. 1B) while their specific frequencies pattern is heterogeneous. In addition, the spectrogram power is also heterogeneous in time (Fig. 1A).Anatomical pattern of the resting state clusters was also obtained for the cortex (Figs. 2A, B) and white matter (Figs. 2C, D). Similar to thalamus, the cortical and the white matter resting state fMRI frequency's power fluctuates in time and substantially variable between subjects. Interestingly, when a rest fMRI signal is randomly shuffled in time the FT spectrum appears as white noise. However, the clustering of this "noise" spectrogram also results with clusters that resemble the atlas anatomical appearance of the tissue (Figure 1G).

Conclusions & Discussion:
We have showed that brain regions (gray matter, white matter and sub-cortical nuclei) present unique pattern of frequency spectrum extracted from resting state fMRI experiment. This pattern can be conjugated with clustering algorithm to segment those regions based on their different BOLD fMRI pattern. These findings may results from different basal neuronal activity state of these regions. Nevertheless, the fact that the white matter and the random fMRI rest signal also provides similar results implies that the rest signal might also be affected by morphological factors (i.e. vascular morphology and cyto-architecture)

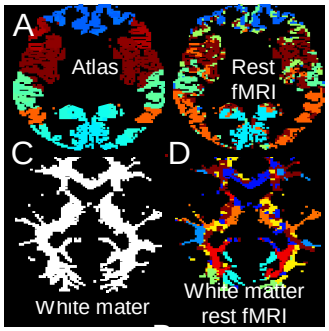

Figure 2

References:
1)Fox MD, Snyder AZ, Vincent JL et-al., PNAS, 2005, 102:9673-8; 2) Grecius MD, Krasnow B, Reiss AL, Menon V. PNAS, 2003, 100: 253-8; 3)Cordes D, Haughton VM, Arfanakis K, et-al. AJNR, 2001, 22:1326-33; 4) Lowe MJ, Mock BJ, Sorenson JA. Neuroimage, 1998, 7: 119-132; 5) Greicius MD, Srivastava G, Reiss AL, and Menon V. PNAS 01: 4637-42