Resting State fMRI of the Thalamus

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Introduction

Resting state "functional" MRI is used to access basal brain activity [1-3]. It is well accepted that the brain can be segmented into regions of synchronous blood oxygenation level dependent (BOLD) signal pattern. This pattern reflects, most probably, 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 correlation to spectral decomposition of frequency analysis. In most of these analysis schemes, the question asked is which brain areas "behave" in the time domain as a pre-specified ROI. For example, the motor related network can be visualized by choosing "seed" voxel in the M1 cortex which is correlated with SMA, thalamus and cerebellum areas [4]. This has been applied for study of the normal brain synchronized networks as well as to the study of diseased state (e.g. mild cognitive impairment and Alzheimer's disease) [5]. In this work we have applied the "resting state" fMRI framework combined with frequency analysis and clustering to study the basal activity of the thalamus. The main aim of this work was to show that sub-cortical nuclei basal activity can be obtained using "resting-state" fMRI and that there is functional-anatomical connection that can be assessed using this framework.

Methods

Seven healthy subjects (age between 22 to 42 years) were scanned in a 3T MRI scanner (GE, Milwaukee, USA). The MRI protocol included, in addition to anatomical high resolution images, a series of T2* weighted images acquired with a gradient-echo echo-planar-imaging (GE-EPI) with the following parameters: TR/TE=600/45ms, $\alpha=30^0$, matrix of 80x80 (reconstructed to 128x128), FOV of 24cm, 7-9 axial slices with slice thickness of 5 mm and no gap between them localized at the level of the thalamus (below the higher edge of the lateral ventricles). The GE-EPI protocol was repeated 800 times to produce a pixel-by-pixel time series of the T2* weighted signal (BOLD signal) of 8 minutes with time interval of 600ms (TR) in which the subject was asked to lie still with eye closed and asked 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, FIL, UCL, London, UK). Two regions were analyzed – one of the thalamus and one of the cortex following segmentation.

Image analysis included the following steps: 1) The measured time series in each voxel is normalized to fluctuate around zero; 2) The time series signal is multiplied by an line-broadening exponential decay function; 3) Subsequently the time series is Fourier transformed to the frequency domain; 4) High frequencies reflecting cardiac cycle and breathing are excluded; 4) The resulted absolute spectrums of the voxels are clustered by the K-mean algorithm (with k=3).

[4]

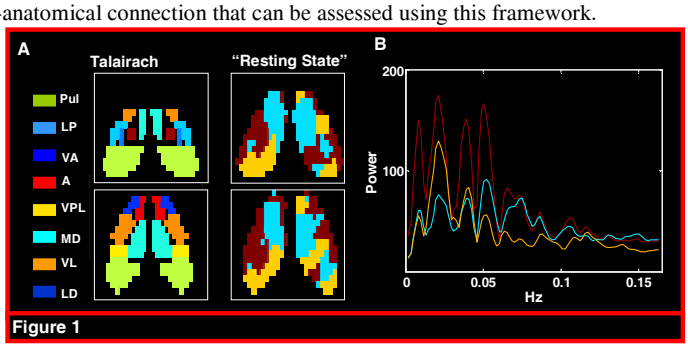

Figure 1

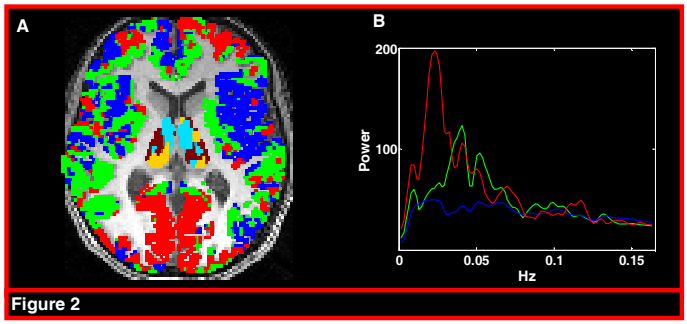

Figure 2

Results & Discussion

Fourier analysis of the time series BOLD Signal combined with the k-means clustering revealed three areas in the thalamus, separating it to distinct functional networks: the medial, posterior and ventral parts (see Figure 1A and corresponding frequency spectrum in Figure 1B). By visual comparison of the "resting state" clusters (right column in Figure 1A) to the Talairach atlas (left column in Figure 1A), a nice correlation is observed. Using this comparison we were able to assign the posterior region of the resting state clusters to the Pulvinar nucleus, the medial region to the medio-dorsal and anterior nuclei and the ventral region to the ventral and lateral group of nuclei (VL, VPL, LP, LD and VA) of the thalamus. Interestingly the localization of the three sub-thalamic clusters repeats across subjects while their specific frequencies pattern is heterogeneous.

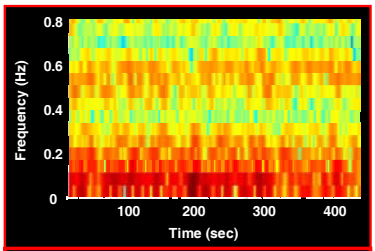

Figure 3

The thalamus frequency domain reveals scattered spectrum pattern between 0-0.1 Hz. This is in-line with previous works of cortical resting state frequency analysis that found two different resting networks in the cortex [1]. Figure 2 shows frequency analysis of the cortex for comparison with the thalamus frequencies (compare Figure 1B and 2B). Although the range of frequency spectrum is similar between the cortex and the thalamus, the spectrum pattern is different. This can results from different neuronal activity state of the cortical and sub-cortical regions. However it can also be a result of different modulations of the BOLD signal in the two regions resulting from vascular differences.

One of the pitfalls of any fMRI experiment and especially a "resting-state" one is that the subjective thoughts and actions of the subject are not controlled. To that end, we apply a fragmented frequency analysis over time (spectrogram) for selected regions (Figure 3). The frequencies description over time reveals that the measured frequencies could be constant or alternatively change over time. This kind of analysis can help to probe the subject stability during the experiment.

Conclusions

In the presented work we have showed that sub-cortical regions present unique pattern of frequency spectrum extracted from resting state fMRI experiment. This pattern can be conjugated with clustering algorithm to segment the thalamus to sub-regions that are different in their BOLD frequency pattern. Interestingly, the resting state clusters resembled known anatomical localization of the thalamus.

References

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