Dynamic thalamus parcellation based on resting-state fMRI data

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Purpose Resting-state fMRI (RS-fMRI) is a non-invasive method which is used to examine the functional connectivity (FC) and other properties of blood–oxygen-level-dependent (BOLD) signals of the brain without the performance of specific tasks. Until recently, most fMRI studies have implicitly assumed that the statistical interdependence of signals of functional networks is constant throughout recording periods of task-free experiments. However, more explicit investigations of resting-state FC dynamics have unequivocally demonstrated the time-varying nature of both connectivity strength and directionality[1], which may contain additional information regarding FC. The thalamus is generally believed to act as a relay center between a variety of sub-cortical areas and the cerebral cortex, so delineation of the thalamus nuclei is important for many applications. The purpose of this study was to exploit the dynamic nature of FC in the parcellation of thalamus, based its connectivities with the cortex. By explicitly taking into account of the dynamic variation of the FC, we were able to identify two dominant states and derive two similar but distint parcellations depending on the states. These parcellations, examined separately or combined, provide better correspondence with anatomic landmarks.

Methods In this study, the resting-state fMRI data, obtained from the 1000 Functional Connectomes Project website were used. Forty two (21.23 ± 2.13 years old, 21 females) out of one hundred and ninety-eight right-handed healthy subjects from this dataset with whole brain coverage were chosen. Standard rs-fMRI preprocessing steps were performed using AFNI. In the dynamic analysis approach, a time window of fixed length was selected, and the window was then shifted in time by increments of 1 TR. Within each time window, correlations between each thalamic voxel and 14 cortical ROIs[2] (see Fig. 1) were calculated and used as the metric for clustering. The affinity propagation (AP) algorithm was applied to define centroids for the initial centers of k-means, and the k-means algorithm was then used iteratively to cluster the data of each subject at each time point. A second level clustering was applied to the clustering results of individual subjects and time points to derive dominant connectivity patterns (and states). For each dominant state, its patterns were subsequently input to spectral clustering with spatial constraints to parcellate thalamus. For comparison, a static parcellation based on the entire time window without considering nonstationarity was also obtained.

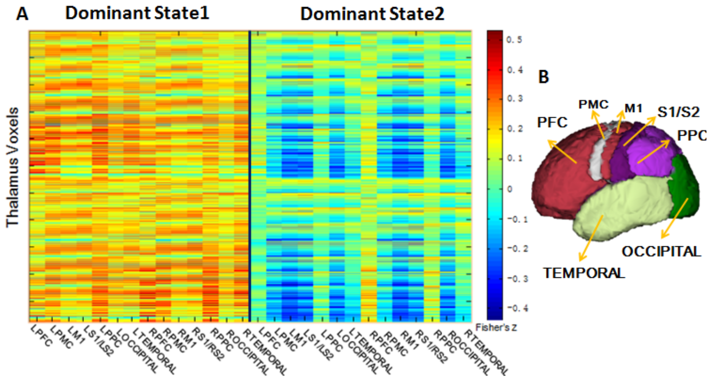

Figure 1. Functional connectivity between cerebral cortex and thalamus. (A) FC strengths were displayed based on two dominant states. (B) Cortical subdivisions.

Results and Discussions In Figure 1A, functional connectivity patterns of two dominant states between thalamus and cortical ROI are presented. These two dominant states occur widely in the healthy subjects (88% in 42 healthy subjects). As seen from two dominant states, FC between thalamus and cortex is nonstationary and evolves with time substantially. Thalamus parcellations corresponding to the two dominant states shown in Figure 2 (iii and iv). The difference between them could reflect the dynamic nature of the thalamus as a relay station, particularly the evolution of the resting state brain activity mediated by it. The divisions in both parcellations have correspondence in the known anatomic structures (Figure 2i). Compared with static parcellation (Figure 2ii), the dynamic results exhibit finer details (Figure 2i). Furthermore, when the parcellations are collated (Figure 2v), three additional components,central lateral nucleus, ventral posteromedial nucleus and medial geniculate nucleus, emerge.

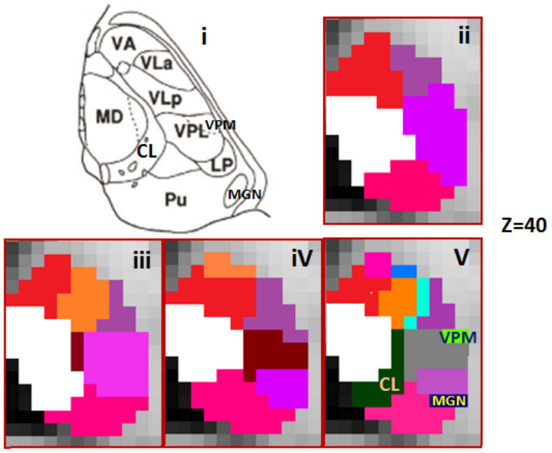

Figure 2. Variation of connectivity-based thalamic subdivision. (*i*) Human histology. (*ii*) Subdivision of the thalamus in a single subject for an axial slice based on the static state. (*iii*)&(iV) Parcellation results of the thalamus based on dominant states. (*V*) Segmenataion of the thalamus based on overlaid dominant states.

Conclusions The dynamic nature of functional connectivity between thalamus and cortex was exploited to derive state dependent segmentations of the thalamus. The results, which are consistent with known anatomy, may reflect dynamic roles the thalamus plays at resting state, and also provide finer parcellations of the thalamus based on resting state data.

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