Thalamic Functional Connectivity in Healthy Volunteers with and without Task Engaged

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Introduction:

Research interests on the study of functional MRI during resting state (RS-fMRI) have demonstrated a consistent pattern of slow fluctuations in the blood oxygenation level dependent (BOLD) signal referred to as the "default mode" of brain function [1]. Such spontaneous neuronal activity plays a role in maintaining baseline human cognition and metabolic equilibrium in the resting brain. The thalamus, as the centrally located relay station for transmitting information throughout the brain, participates in communication with many associative brain regions and involves global multi-functional pathways. The purpose of this study was to investigate whether this low frequency resting state network (RSN) associated with thalamic function is reliably showing the some transmitting pathways throughout the brain in some circumstances.

Method:

Seventeen right handed healthy subjects (ranging in age from 23 to 49, with a median age at 36 years, mean age at 35 years old, including 11 males and 6 females) were studied. All subjects were recruited after meeting the following inclusion criteria: no history of alcohol or drug abuse; no history of neuropsychological diseases before injury; and no history of other neurologic diseases including stroke, epilepsy, and somatic disorders.

MR images were acquired on a 3T whole body scanner (Siemens Medical System, Erlangen, Germany). In addition to conventional T2-weighted imaging, twenty T1-weighted anatomic images were collected parallel to AC-PC line with 5mm slice thickness and 1mm gap and positioned to cover the whole cerebrum. The functional images were collected in the same planes, using a gradient echo EPI sequence (TR/TE=2s/30ms, flip angle=70^o, FOV=$22x22cm^2$ and acquisition matrix size=128x128), then a whole brain 3D T1-weighted MPRAGE sequence were also acquired. During the two RS-fMRI sessions, all subjects were instructed to close eyes but keep awake. Each scan lasted 5 minutes and 6 seconds. The repeated RS-fMRI was also performed in 2 volunteers from different days. And ten of the healthy volunteers also performed two simple block-design finger tapping task sessions of 30 seconds tapping the left or right index finger with the rhythm of 1Hz cued by the blinking cross showed to them on the back projector and 30 resting. Each session also lasted 5minutes and 6 seconds.

All MRI data were analyzed using SPM2 (Statistical Parametric Mapping, http://www.fil.ion.ucl.ac.uk) and MRIcro (http://www.mricro.com) and additional in house programs running under MATLAB (Mathworks, Natick, MA). fMRI data were preprocessed for the analysis by first motion corrected, realigned, co-registered, then registered to standard Talaraich coordinates and spatial smoothed in SPM2. We used the signal from the seed regions – bilateral thalamus to define the reference time course, then calculated the correlation coefficient to all voxel's time series within the whole brain to generate a functional connectivity map. Fisher's z' transformation was used to compute Fisher's z' maps for each subject, and then one sample T-test was performed to quantitatively get group contrast maps which show all areas that are significantly correlated to the seed ROIs (r>0.6 so z'>0.55). Same ROI studies were also perform to get the group contrast maps showing areas that are significantly correlated to both left and right thalamus during tapping tasks for those 10 healthy volunteers who performed tapping tasks as well.

Results:

In healthy volunteers, a consistent pattern of thalamic functional activation map was found in different sessions including data acquired in the same day or different days. The thalamic functional network shown on RS-fMRI *only* includes both sides of the thalamus (Figure 1). This pattern was consistent when the seed regions were placed in either the right or left side of thalamus. The functional connectivity with thalamus for all healthy volunteers showed a very clean, focused functional network, none of the normal controls showed diffuse functional connectivity at this level of the significance (r>0.6).

During task-related sessions, conventional motor activation maps showed that the thalamic areas are not involved in these task-related activation networks as expected. However the thalamic connectivity network, which were obtained by placed the seed region at both sides of thalamus and performed whole brain correlation calculations, scattered to some cingulated gyrus and superior temporal gyrus and even some secondary motor areas (Figure 2), it is not longer as focus as they are in resting-state (Figure 1). From general view of brain function that refers to Brodmann map, we found Brodmann area (BA) 24, 40, 8 and 6 were involved. These areas are involved in secondary motor and somatosensory perception. Though they do not directly participate in the activation in react to the tasks, they surround and supplement the conventional motor activation.

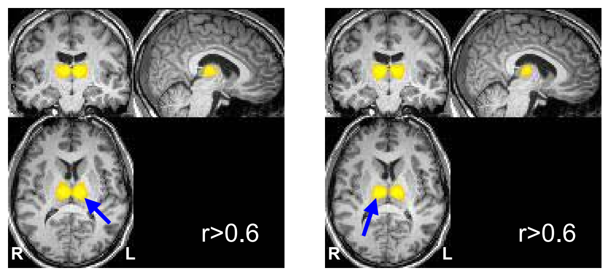

Figure 1.In resting state, group thalamic RSN in 3D views, (r>0.6). The blue arrows show where the seeds are placed.

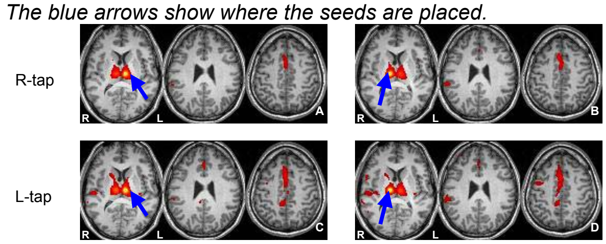

Figure 2. Group thalamic functional correlation network (r>0.6, z'>0.55) during motor task sessions in 2D views. The blue arrows show where the seeds are placed, the patterns of left (L) and right (R) thalamic functional network were shown in different columns.

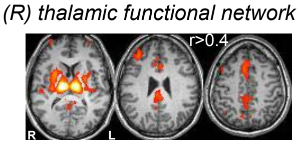

Figure 3. In resting state, group thalamic RSN in 2D views, r>0.4.

Conclusion & Discussion:

The thalamus is important to communication among many associative brain regions including sensory, motor, cognitive, and behavior and it is one of the key elements of neuronal organization in the global function of the brain related to the rich thalamocortical interconnectivity[2]. This study demonstrates for the first time the thalamic functional network during both resting state and task related sessions in healthy volunteer. The well-defined homogeneous thalamic functional connectivity maps (Figure 1) were shown in healthy volunteers in resting state, meanwhile such functional activities have been shown to be increased in task-related sessions as compared to resting state sessions. Thalamic areas in normal controls are inhibited in resting-state, they might be in a ready status that seems showing no significant or loose connectivity with other brain areas since when we lower the significance level to r>0.4, more brain regions are showing (Figure 3). Once in the task related state, they showed an active link with some functional areas that supplement the activation in response to the task (Figure 2). These supplemental areas were enhanced and shown at the higher level of significance (r>0.6) in the task state while they can only be shown correlations at the lower significance level (r>0.4) in resting state. This suggests that though thalamus in resting-state shows less significant correlation with other brain areas, it actually is ready to work, and well prepared to be connected to many functional areas once needed.

Reference: [1] Fox MD, Raichle ME. Nat Rev Neurosci 2007; 8(9): 700-11. [2] Guillery, R.W., J Anat, 1995. 187 (Pt 3): 583-92.

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