Relationship between gray matter concentration and resting functional connectivity to the thalamus: Evidence of the temporal lobe epilepsy seizure network

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Purpose

Temporal lobe epilepsy (TLE) is associated with gray matter loss and changes in functional connectivity. The goal of this research is to examine the voxel-wise relationship between gray matter concentration (GMC) and resting state functional connectivity to the thalamus in TLE. Voxel based analysis revealed a significant decrease in GMC in the thalamus in the patient population as compared to controls. The thalamus has been implicated as an important part of the epileptogenic network; it is synchronized with remote cortical structures during TLE seizures [3]. Therefore, we hypothesize that decreases in GMC may be associated with changes in functional connectivity from the thalamus to affected cortical regions in the epileptic network.

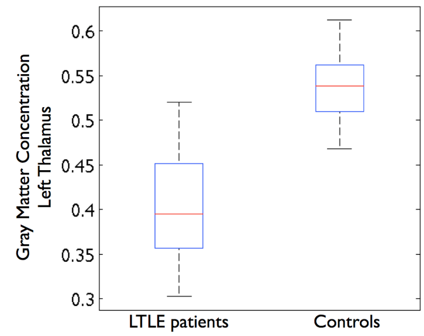

Fig. 1. *Box plot of gray matter concentration in left temporal lobe patients and controls in the left thalamus. Unpaired t-test: $p = 1.2434 \times 10^{-07}$.*

Methods

We studied 15 patients with left TLE (LTLE) as determined by presurgical evaluation. All study participants underwent an MRI scan using a 3T MRI scanner (Phillips Healthcare, Inc., Best, Netherlands). Conventional MRI included 3D anatomic T_1-weighted images (voxel dimensions 1 x 1 x 1 mm) and 2D T_1-weighted images. Functional images of the whole brain were acquired axially using a gradient-echo, echo planar imaging (EPI) fMRI scan (TR = 2000 ms, TE = 35 ms, scan resolution = 64 x 64, FOV = 240 mm, 30 slices and 300 dynamics).

Preprocessing of fMRI data was performed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm), which included correction for slice timing effects, motion correction, spatial normalization to the Montreal Neurological Institute (MNI) template and smoothing with an 8mm FWHM kernel. The preprocessed data was low-pass filtered at 0.1 Hz. (1) Resting state functional connectivity analysis – Functional connectivity measures the level of co-activation of fMRI time series between a seed region and other brain regions. Our seed region was the left thalamus, defined by WFUpickatlas (http://fmri.wfubmc.edu/software/PickAtlas). General linear model analysis was used to create whole brain functional connectivity maps to the thalamus. (2) Voxel-based morphometry (VBM) – VBM analysis was performed using SPM2 and segmented gray matter images were created following the standard optimized VBM protocol. (3) Biological Parametric Mapping (BPM) - Multiple regression analysis was performed in BPM [1] and robust BPM (rBPM) [2] using segmented gray matter images as the dependent modality and resting state connectivity maps as the independent imaging covariate. The rBPM results were thresholded at $P < 0.05$ (uncorrected) and cluster size > 10 voxels. Regions of GMC both positively and negatively correlated with the connectivity to the thalamus were determined.

Results

The following regions demonstrated a decrease in GMC with increased connectivity to the thalamus. *Positive Correlation* – A region in the left precuneus/posterior cingulate showed an increase in negative connectivity to the left thalamus as GMC decreased. *Negative Correlation* – A region in the left putamen/insula displayed an increase in connectivity as GMC decreased in the thalamus. Among LTLE patients and controls, there is no statistically significant difference between the connectivity values or the GMC values.

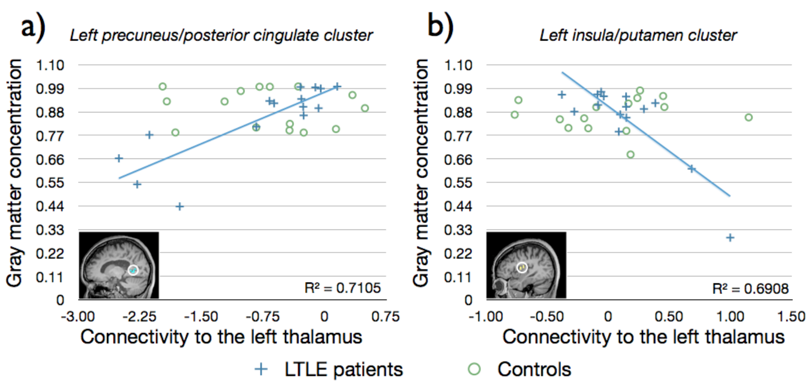

Fig. 2. a) *Positive correlation between gray matter concentration and connectivity to the left thalamus in the left precuneus/posterior cingulate cluster (MNI coordinate: -38,-2,2).* b) *Negative correlation between gray matter concentration and connectivity to the left thalamus in the left insula/putamen (MNI coordinate: -18,-60,4).*

Discussion

The thalamus is involved in the transmission of information to the cortex; as a result most areas of the cortex project to the thalamus, including the precuneus and posterior cingulate [3,4]. In addition, it is a part of the epileptogenic network in TLE [5]. The posterior cingulate, the precuneus and the insula are associated with consciousness and seizures [5,6]. Therefore, the decrease in GMC in these regions along with increased (positive/negative) functional connectivity to the left thalamus suggests the negative influence of seizure propagation on GMC in these structures as well as the functional connectivity between each structure and the left thalamus. These changes also provide further evidence for their involvement in seizure propagation network in TLE.

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References: [1] Casanova, R. et al. *Neuroimage.* 34. 137 (2007). [2] Yang, X. et al. *Neuroimage.* 57. 423 (2011). [3] Taber, K. et al. *The Journal of Neuropsychiatry & Clinical Neurosciences.* 16. 127 (2004). [4] Zhang D. et al. *Cerebral Cortex.* 20. 1187 (2010). [5] Guye, M. et al. *Brain.* 129. 1917 (2006). [6] Isnard, J. et al. *Annals of Neurology.* 48. 614 (2000).