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Regionally constrained voxel-based network of left hippocampus in left medial temporal lobe epilepsy

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Introduction:

Network representation can reveal the topological dysfunctions of brain function [1]. Recently brain network construction of whole brain voxels has been introduced using the epsilon neighbor method [2, 3]. However, this method has a difficulty in regional network interpretation. Thus we propose the voxel-based network construction on gray matter of FDG-PET image via the epsilon neighbor method with regional constraint using anatomical information. It was applied to left medial temporal lobe epilepsy (LMTLE) patients, showing abnormal metabolic connectivity compared to healthy controls.

Methods:

Data:
Twenty-four patients with pharmacologically intractable LMTLE (LMTLE - 11 males, 19-47 years old, mean: 28.7 ± 7.1) underwent PET scans during presurgical interictal state to obtain resting FDG-PET images. The LMTLE patient was included who only had hippocampal sclerosis on preoperative MRI without any other deficits. Age-matched thirty healthy normal controls (15 males, 19 -43 years old, mean: 29.8) also participated for comparison with the patients.

Connectivity map:
The proposed pipeline for network construction is given in Fig. 1. Following spatial normalization of all images to the Korean Statistical Probabilistic Anatomical Map (K-SPAM) template [4], the voxels was defined by K-SPAM template which consists of 75 regions of gray matter. This resulted in regional information for each voxels, which was used as regional constraint in controlling the epsilon neighbor during the network construction. The

voxels were subsampled at 18mm within each anatomical region in order to reduce computational burden. The network was obtained from Pearson's correlation coefficient between FDG uptake of all voxels after partialling out age in general linear models. In this study, the left hippocampus was used as the seed region. The connectivity between a seed region and whole voxels were controlled by false discovery rate (FDR) (q = 0.01). The significant connections were used to construct network via the epsilon neighbor method [2, 3] with regional constraints.

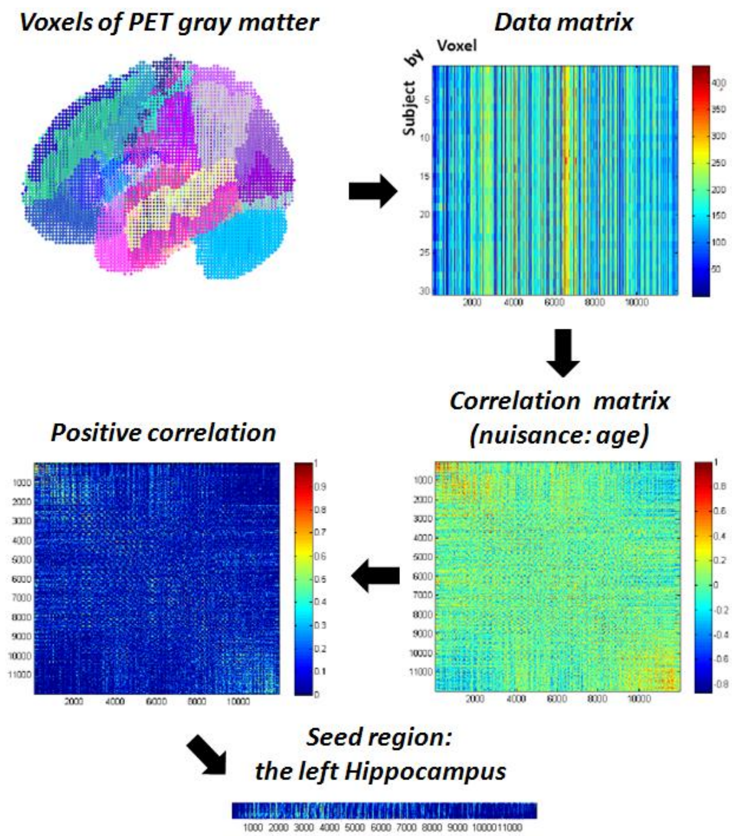

Figure 1. The preparation steps for epsilon neighbor network construction.

ε-neighbor network construction:

The schematic presentation of the ε-neighbor network construction with regional constraint was displayed in Fig. 2. Network was constructed in an iterative fashion by adding a connection to an existing network. At the k-th iteration, a new connection can be added. Any one end point of connection, p, can be the ε-neighbor of predefined graph Gk-1 if it satisfies both two criteria: Firstly the shortest distance between p and all node of Gk-1 is less than given ε in mm unit. Secondly, the regional information of p is identical with that of the node which located less than ε mm from the point p. The point p cannot be the ε-neighbor if it satisfies only one criterion. The ε-neighbor network can be constructed as a function of ε resolution 20, 30 and 40mm [Fig. 3]. Additionally the number of edges merged into one node can be thresholded to find the region which had more possibility of connecting with a seed region.

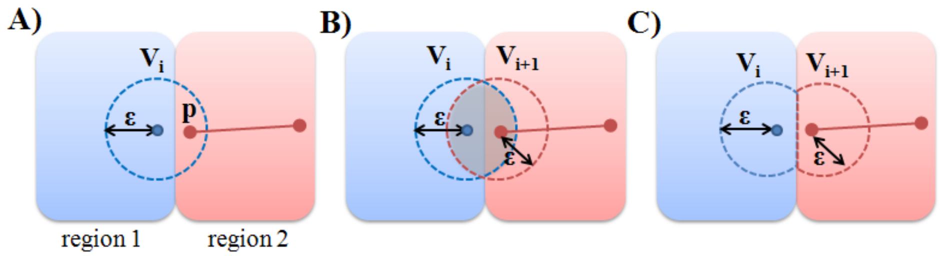

Figure 2. Schematic representation on ε-neighbor network construction with regional constraint. Suppose the i-th node V_i is given in a graph in region 1(blue). At the k-th iteration, a connection (red line) is added to the preexisting graph and possible to be a ε-neighbor of V_i since distance between V_i and one end point of connection (p) is less than ε-radius. However, the regional information of p is region 2, so that its regional inforamtion is not identical with that of V_i. Thus p is not merged, but create a new node, V_{i+1}, of graph. In gray colored area (B), it is valid only for the connection of which point belongs to corresponding area. Finally the actual range of epsilon resolution can be illustrated like (C). In this way, anatomically distinct region cannot be merged into one region.

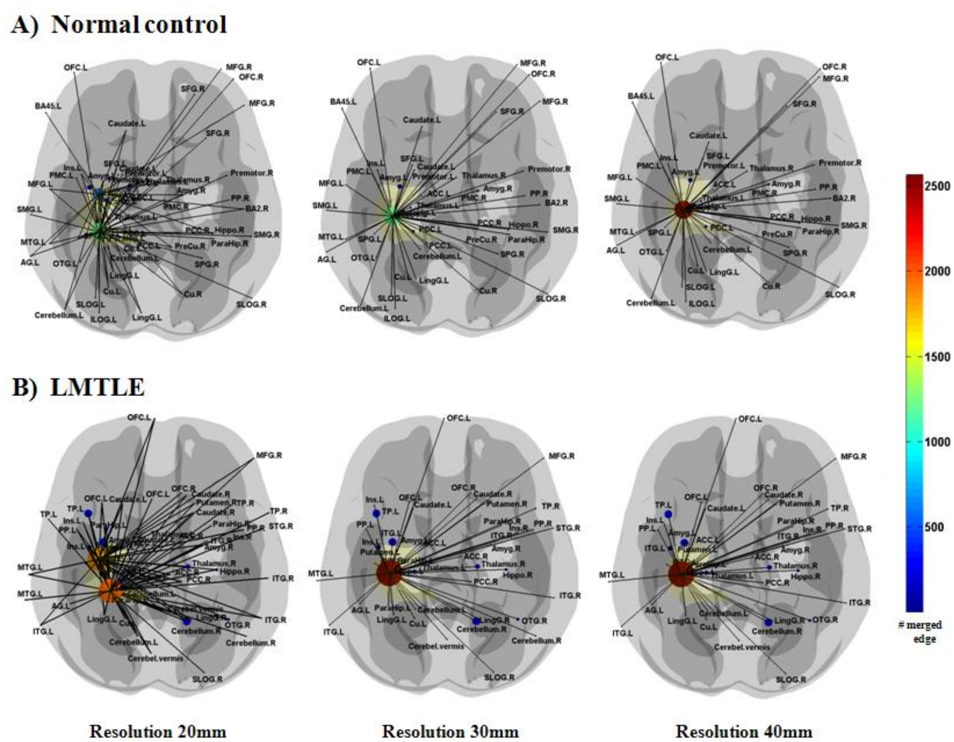

Figure 3. The epsilon neighbor network as a function of epsilon resolution (20, 30 and 40 mm). At the resolution 30mm, seed region (light yellow) had two epsilon-neighbors, but at 30 mm they merged into one node. The network showed showed metabolic connectivity of normal control in the upper row and of LMTLE patients in lower row. The color and size of circle showed the number of merged edges corresponding epsilon neighbor.

Results:

We found different connectivity patterns between control and LMTLE patients and displayed the node which merges over 10 edges at resolution 30mm [Fig. 4]. In normal controls, the left hippocampus had 1278 edges and which were connected with the left parahippocampus and bilateral amygdale as well as the left posterior cingulate, angular gyrus, the right premotor and cuneus. In LMTLE patients, it had 2566 edges and they had connectivity with ipsilateral and contralateral temporal area and cerebellum.

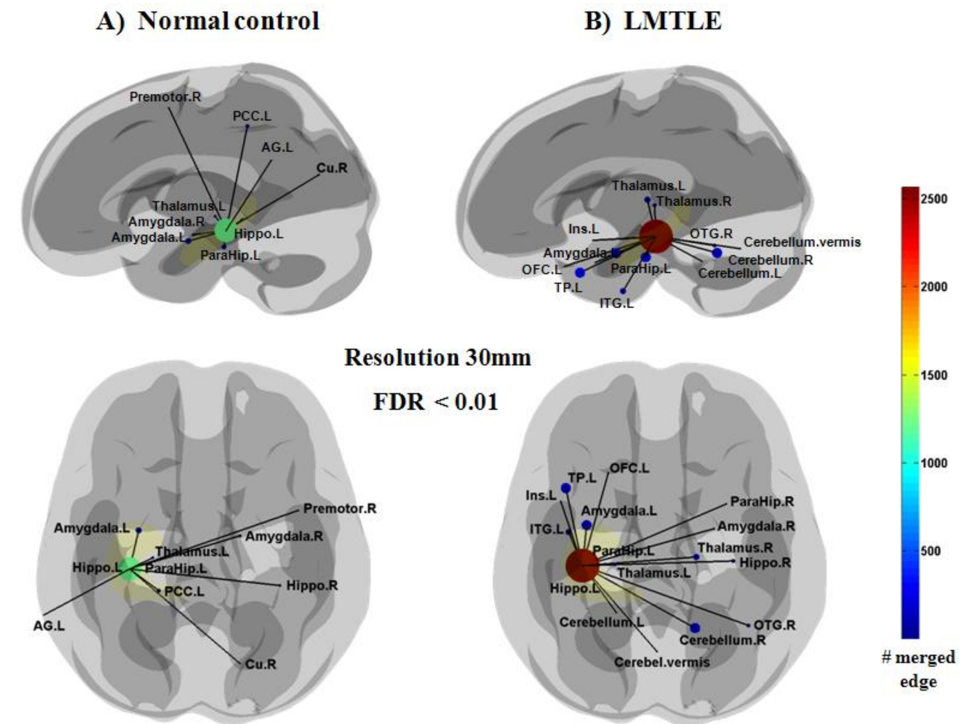

Figure 4. Within-group connectivity. Network showed connectivity of each group focusing on the left hippocampus (light yellow) as a seed region after FDR correction (q=0.01). The color and size of circle indicated the number of merged edges corresponding epsilon neighbor. The figure showed the node which merged more than 10 edges at resolution 30mm (upper: sagittal, lower: axial view).

Conclusions:

This regionally constrained network construction approach could simplify voxel-based network and locally identify network component in lesion brain. In LMTLE patients, the left hippocampus, as epileptogenic focus, showed extensive metabolic coupling with ipsilateral and contralateral temporal regions, which might reflect the influence of seizure propagation.

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