Normalized edge weight connectivity measure derived from diffusion weighted images: Application to the limbic system.

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Introduction: The structural basis of limbic epilepsy, one the most common forms of focal epilepsy [1], is not well defined. Structural connectivity in the limbic system can be estimated using diffusion weighted imaging (DWI) to create white matter (WM) fiber maps between regions of interest and estimate the strength of connections between limbic structures. In WM, water diffuses mainly along the direction of fiber bundles. With high angular resolution measurements, the direction and rate of water translational diffusion in each image voxel can be calculated and the estimated fiber tracks can be used to infer connectivity between regions of interest [2]. Our objective is this work was to develop network connectivity measures that are independent of the method used to calculate connectivity (i.e. seed density and voxel resolution) once the diffusion displacement has been adequately determined. We introduce a new normalized edge weight (see below), which is a modification of the edge weight parameter proposed by Hagmann [3]; normalized by the voxel seed density (number of seed points per voxel, N_{voxel}, divided by the voxel volume, V_{voxel}). This normalized edge weight provides a measure of connectivity that can be applied across data sets acquired with different parameters of resolution and fibers calculated with different number of seed points and distributions. To test these measures, we defined a low-resolution network of the limbic system in excised rat brains, using regions of interest (ROI's) in the amygdala(AM), thalamus (TH), hippocampus (HC) and entorhinal cortex (EC), can estimated connectivity.

Methods: DWI data was measured from an excised rat brain using a diffusion-weighted multiple-slice, spin echo sequence on a 17.6T magnet system with an isotropic measurement resolution 0.190 mm. Data processing was performed with in-house software and the diffusion displacement within each voxel was modeling using the method of Wishart (MOW) distributions [4]. DWI data was measured with uniform diffusion weightings of 100 s/mm² in 6 directions with 8 averages/direction, and 2225 s/mm² in 30 directions with 2 averages/direction [5]. We calculated the fiber tracks from seed points equally spacing in all voxels throughout the brain, with variable seed points per voxel, using a tracking step size of 0.5 voxel width, restricting track angular deviations to no more than 50° from step-to-step, and a very low diffusion anisotropy [2] stopping criteria (fractional anisotropy (FA) = 0.05). The ROI's in the limbic system were defined using FA images. Then these ROI's were used to filter the fiber tracking results. Finally we created a brain network graph and calculated the network parameters, normalized edge weight, w(e), and connection strength of a node, s(n), defined below. The ROI's become the nodes, n, and fibers connecting ROI's define an edge, e, between nodes in the network.

$$w(e_{ij}) = \frac{V_{voxel}}{N_{voxel}} \frac{2}{(S_i + S_j)} \sum_{f \in n_i n_j} \frac{1}{l(f)} \qquad s(n_i) = \sum_{j=1}^{k} w(e_{ij})$$

Where S is the surface area of the connected nodes (n_i and n_j) and l(f) is the length of the fibers, f, connecting the nodes.

Results: We defined ROI's as nodes in a low resolution network (HC, AM, TH and EC) in the limbic system (see Figure below). With fiber tracks estimated from the DWI measurements, we calculated the normalized edge weight and node connection strength in this network at seed densities of 8, 27, 64 and 90 seed points per voxel. We observe only small variation (maximum 1.03%) in edge weights, and node strengths (maximum 1.00%) with changes in the number of seed points per voxel (i.e. seed density).

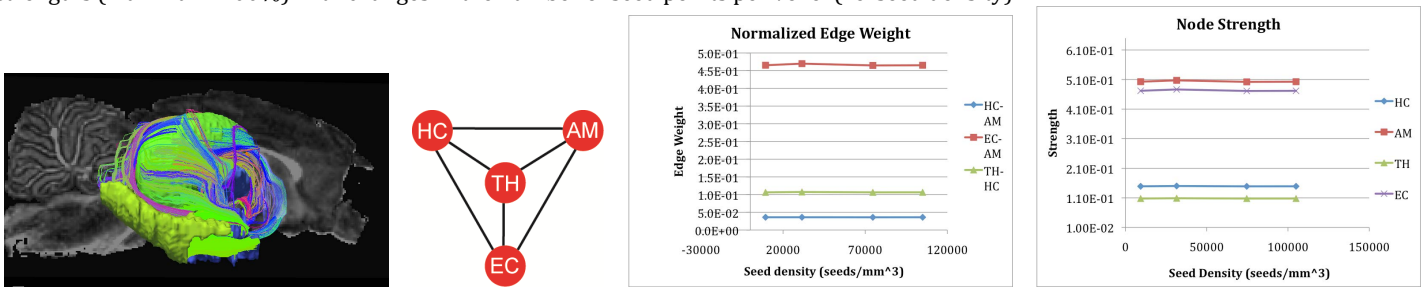

Figure: Top left image shows fibers connecting the ROI's in the limbic structures (see text). The next image on the right is the low resolution network graph between limbic nodes. Node strength and Normalized Edge Weight results respectively using acquisition parameters, b= 2225 s/mm², isotropic resolution of 190μm. We varied seed density with 8, 27, 64 and 90 seeds per voxel in each plot

Conclusion: Using this form of a normalized edge weight and associated node connectivity strength, we successfully created a connectivity map of the low resolution network in the limbic system, which show only small variations with changes in the seed density. Therefore, this normalized edge weight may provide a parameter that is suitable for the evaluation of modifications to procedures for measurement and processing of brain networks. This initial work may be extended to higher resolution network, e.g. dividing the hippocampus in its sub-regions. Ultimately these connectivity maps may prove useful in diagnosing and tracking the progression of limbic epilepsy.

References

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