Structural and functional evolution of temporal lobe epilepsy using linear regression modeling

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Target audience: Imaging scientists and neurologists interested in epilepsy, and those interested in modeling applications in imaging

Purpose: It has been well reported that temporal lobe epilepsy (TLE) results in structural and functional brain changes. We believe that the quantification of how these changes evolve as the disease progresses over years can inform decisions on surgical treatment and prediction of surgical outcome. The purpose of this work is to determine the structural and functional imaging factors that change linearly with duration of disease in TLE using a linear modeling method.

Methods: We analyzed MRI data of 16 TLE patients (8 left, 8 right) from a previous study [1]. All had surgical resection of their seizure focus (either a standard temporal lobectomy or a selective amygodalohippocampectomy) and became seizure free. Structural (three dimensional, T1weighted, 1x1x1 mm), and functional imaging (64x64, FOV = 240 mm, 30 axial slices, TE = 35 ms, TR = 2 sec, slice thickness = 4.5 mm/ 0.5 mm gap, 300 volumes, 2 series) were performed on a 3T MRI scanner using a 8 channel head coil. The structural images were processed with Freesurfer [2] to segment the brain into regions of interest (ROI) and to calculate regional gray matter volumes. Eight selected Freesurfer ROIs were applied to the functional images and functional connectivity (FC) was calculated between all pairs of ROIs using partial correlation of time series after standard preprocessing and low pass filtering at 0.1 Hz. Motion, white matter and cerebrospinal fluid time series were used as confounds. The eight ROIs included: right hippocampus, left hippocampus, right thalamus, left thalamus, precuneus, mid cingulate gyrus, right insula and left insula. The gray matter volume of these structures and of the right and left caudate, right and left putamen, right and left entorhinal cortex and the supratentoral volume, a measure of whole brain volume, were determined.

All of the volumes, the FC, age of onset and longest duration of seizure freedom of the 16 subjects (training set) were entered into an elastic net regression [3-4] in Matlab to predict duration of disease. Elastic net modeling allows for many more predictors than data samples, and so is appropriate for this application. Only linear predictors were included. Cross validation was used to optimize the regression parameters. The mean squared error of the model was evaluated using Monte Carlo sampling with 100 trials. It was further tested by applying it to nine new, similar TLE datasets.

Results: The optimum lambda 1 and lambda 2 of the model were 0.1052 and 0, respectively. The mean error of the model in the Monte Carlo sampling was 10.4 yrs. The duration vs. the estimated duration of the data determined by the model is shown in Figure 1. The table indicates the parameters of the model and their beta values. In addition, the change in duration per 10% decrease in parameter value is indicated. In the table, vol indicates gray matter volume in mm3, conn indicates connectivity, L and R indicate left and right.

Table 1. Imaging parameters linearly related to disease duration

predictor	beta	change in yrs per 10% decrease in predictor value
L Thalamus vol	-0.0059	4.04
R Putamen vol	-0.0035	1.67
L Entorhinal vol	-0.0089	1.46
onset of disease (yrs)	-0.4252	0.65
R Hippocampus vol	-0.0017	0.59
L Hippocampus to R Insula conn	31.9817	-0.57
L Insula to R Insula conn	-8.0742	0.44
L Putamen vol	-0.0005	0.24
R Hippocampus to L Thalamus conn	16.3082	-0.14
L Precuneus vol	-0.0001	0.08
L Midcingulate vol	-0.0002	0.03
R Hippocampus to Midcingulate conn	2.5698	0.03
Precuneus to Midcingulate conn	-3.675	-0.02
Precuneus to L Insula conn	0.9803	0.02

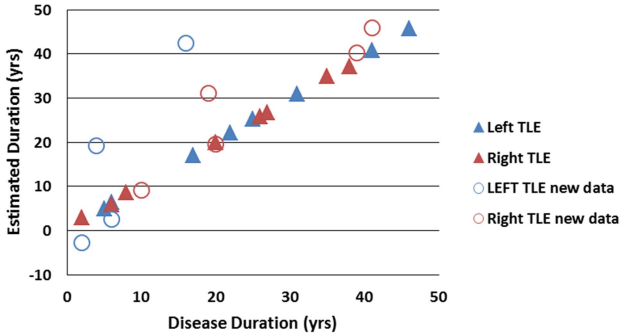

Figure 1. Elastic net regression model fit of training data (closed triangles) and new data (open circles). The blue and the red indicate left and right TLE, respectively.

Discussion and Conclusion: The model determined by the elastic net regression fit the training data well and also well characterized six of the nine new patients. This suggests that the identified parameters are highly influenced by duration of disease in these TLE patients. Decreases in brain volumes had the largest effect in determining the duration of disease, but several FC values also played a role. Interestingly, some connectivity measures increased with duration of disease (pos beta), while others decreased (neg beta).

References: [1] Morgan VL, et al. Epilepsia 2012;53(9):1628-35. [2] http://surfer.nmr.mgh.harvard.edu/ [3] Carroll MK, et al. NeuroImage 2009:112-122 [4] Zhou H and Hastie T. J Royal Stats Society, Series B 2005;67(2):301-320.
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