# Resting state functional connectivity correlated with neuropsychological tests in temporal lobe epilepsy patients

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## Purpose

Patients with temporal lobe epilepsy (TLE) typically have memory deficits as a result of structural damage to the left hippocampus (LH) [1]. Neuropsychological tests are commonly used to help localize and quantify the depth of memory loss in these patients. The objective of our analysis is to identify regions whose resting connectivity to the LH is correlated to a neuropsychological test focused on verbal memory storage and retention in TLE patients. Further, we compared the connectivity of these regions of interest to the LH in healthy controls.

## Methods

60 patients diagnosed with TLE underwent functional MRI imaging using a 3T MRI scanner (Philips Healthcare, Inc., Best, Netherlands) using T2* weighted gradient-echo, echo planar blood oxygen-level dependent (BOLD) fMRI scan (64 x 64, 3.75 mm x 3.75 mm, FOV = 240mm, 4.5 mm thick/0.5 mm gap, TE = 35 ms, TR = 2 sec, 300 volumes per series, 2 series per subject). Participants were asked to lie still with their eyes closed. Of the 60 patients, 19 were classified as left TLE by electroencephalography without other lesions. From those 19, 9 (mean age = 33.8, range 19 – 48, 7 female) had undergone neuropsychological testing and were appropriate for analysis.

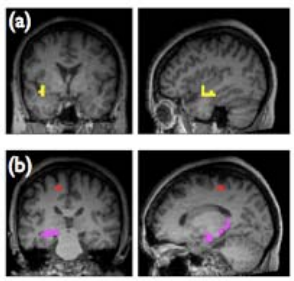


Fig. 1. (a) *Activated cluster in the left temporal lobe from second-level analysis positive correlation map.* (b) *Activated cluster in the left limbic region from second-level analysis negative correlation map (in red). Left hippocampus seed shown in magenta.*

Data preprocessing and data analysis was performed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm). Preprocessing included correction for slice timing effects, motion correction, spatial normalization to the Montreal Neurological Institute (MNI) template and smoothing using an 8mm FWHM kernel. The preprocessed data was then low-pass filtered at 0.1 Hz. For the connectivity analysis we chose our region of interest (ROI) to be the LH, as defined by WFUpickatlas (http://fmri.wfubmc.edu/software/PickAtlas) and shown in Figure 1 (b). For each patient, we calculated the averaged time course across all voxels in the LH as the seed time course for the connectivity analysis. Using the low-pass filtered fMRI images for each patient, the seed time course, the cerebrospinal fluid (CSF) time course and the six motion time courses were used as regressors in the general linear model analysis. This resulted in resting state functional connectivity maps to the LH for each patient. The analysis was replicated in 12 healthy controls using the same seed region.

A multiple regression second-level analysis was performed using the beta images created in the first-level functional connectivity analysis of the patients; a ratio of the California Verbal Learning Test (CVLT) [2] retention scores, which correspond to a measure of verbal memory storage from learning, were used as covariates. This resulted in maps showing regions whose connectivity to the LH were correlated with the CVLT ratio across the group of patients. This correlation map was thresholded at $P < 0.01$ (uncorrected) and cluster size > 10 voxels. Regions of connectivity both positively and negatively correlated with the scores were determined. From the positive correlation we chose a cluster of 12 voxels in the left temporal lobe that included Brodmann Area 21, the insula and the claustrum; this region is shown in Figure 1 (a). From the negative correlation we selected a 13 voxel cluster in the left limbic lobe including Brodmann Area 31 and the left middle cingulum, shown in Figure 1 (b).

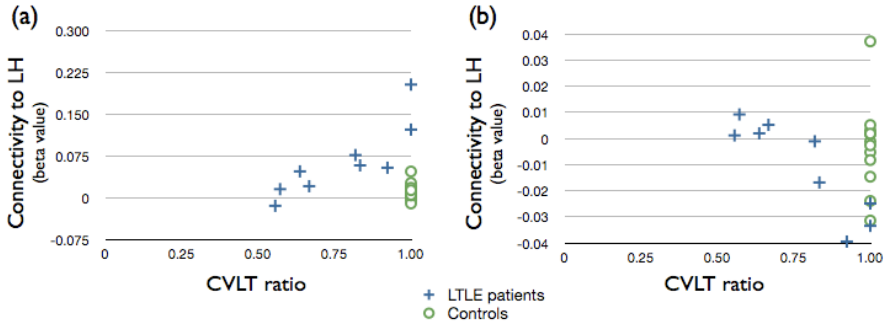


Fig. 2. (a) *Positive correlation between connectivity to the left hippocampus and a ratio of CVLT retention scores in the left temporal lobe region in Fig. 1(a).* (b) *Negative correlation between connectivity to the left hippocampus and a ratio of CVLT retention scores in the left limbic lobe shown in Fig. 1(b). Controls are shown at a score of 1, which is assumed to be a normal score.*

## Results and Discussion

We calculated the connectivity (in the form of beta values) for both regions found in our second-level analysis. The connectivity to the LH (beta values) vs. a ratio of CVLT retention scores is plotted in Figure 2. There were no significant differences in connectivity to the LH between patients and controls in these regions. These results suggest that in order for patients to overcome their memory deficits (and perform well), they must increase connectivity between the LH to the left temporal region and decrease their connectivity to the left limbic lobe region. In fact, this increase (or decrease) in connectivity may need to be greater (or less) than that of healthy controls to compensate for the LH damage in the patients.

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