Graph Theory Based Functional Connectivity in Lateralized Temporal Lobe Epilepsy

Sharon Chiang, B.A.1, John M. Stern, M.D.2, Jerome Engel Jr., M.D., Ph.D.2,3,4,5, Harvey S. Levin, Ph.D.6, Zulfi Haneef, M.D., F.R.C.P7,8

1Department of Statistics, Rice University, Houston, Texas; 2Department of Neurology, University of California, Los Angeles, California; 3Department of Neurobiology, University of California, Los Angeles, California; 4Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, California; 5The Brain Research Institute, University of California, Los Angeles, California; 6Department of Physical Medicine, Baylor College of Medicine, Houston, Texas; 7Department of Neurology, Baylor College of Medicine, Houston, Texas; 8Neurology Care Line, VA Medical Center, Houston, Texas

**Background**
- Temporal lobe epilepsy (TLE) is associated with atrophy and reorganization of the limbic system.
- We examine lateralized differences in how limbic system functional connectivity is affected by left versus right TLE, using graph theory analysis of resting state fMRI.

**Results**
- **Edgewise connectivity**
  - Limbic edgewise functional connectivity was predominantly reduced in both left and right TLE.
  - More reductions were present in right TLE. The most prominent change was reduced interhemispheric connectivity between bilateral insula and bilateral hippocampi.
  - Left TLE patients had a larger number of increased connections. Most of these increases were interhemispheric.
- **Functional topology**
  - Right TLE exhibited decreased average betweenness centrality and increased contralateral hippocampal betweenness centrality.
  - Left TLE exhibited a much weaker increase in contralateral hippocampal betweenness centrality.

**Conclusions**
- Graph theory analysis of the limbic network in TLE reveals several lateralized differences in its functional connectivity and reorganization.
- Both left and right TLE show pronounced reductions in connectivity, more so with right TLE. Left TLE exhibits changes that suggest tendency toward reorganization.
- Ipsilateral hippocampal as well as other limbic system hubs appear re-routed to the contralateral hippocampus in right TLE.
- Our results are consistent with structural fiber loss detected in the TLE limbic network previously (Bonilha et al. 2012), as well as previous findings or more pronounced connectivity reductions in right TLE, and evidence of reorganization in left TLE (Haneef et al., 2012; Vlooswijk et al., 2010).

**Methods**
- Graph theory analysis of 10 bilateral limbic regions of interest was performed.
- Estimates of functional connectivity for healthy controls (n=12) were computed and compared to left TLE (n=14) and right TLE (n=11).
- Groups were compared with respect to:
  1. Edgewise functional connectivity
  2. Global functional topology (average betweenness centrality, clustering coefficient, global efficiency)
  3. Regional functional topology (betweenness centrality, nodal clustering coefficient, local efficiency)

**References**