Mapping reduced cortical thickness and complexity in mesial temporal lobe epilepsy with hippocampal sclerosis

Jack J Lin[1,4], Noriko Salamon[2], Agatha D Lee[3], Rebecca A Dutton[3], Jennifer A Geaga[3], Kiralee M Hayashi[3], Eileen Luders[3], Arthur W Toga[3], Jerome Engel, Jr.[4,5], Paul M Thompson[3]

[1]*Dept. of Neurology, University of California, Irvine School of Medicine*
[2]*Dept. of Radiology, David Geffen School of Medicine at UCLA*
[3]*Laboratory of Neuro Imaging, Brain Mapping Division, Dept. of Neurology, David Geffen School of Medicine at UCLA*
[4]*Seizure Disorder Center, Dept. of Neurology, David Geffen School of Medicine at UCLA*
[5]*Dept. of Neurobiology, David Geffen School of Medicine at UCLA*

Objective: We detected and mapped patterns of decreased cortical thickness in patients with mesial temporal lobe epilepsy (MTLE) and pathologically verified hippocampal sclerosis (HS). We also measured the fractal dimension (complexity) of the human cerebral cortex in 3D and found that MTLE patients had significantly reduced cortical complexity in multiple lobar regions.

Methods: 30 pre-operative T1-weighted 1.5 Tesla SPGR volume MRI scans were acquired from 15 right (age: 31.9±9.7SD years, range: 19-48) and 15 left (mean age: 30.8±8.4SD years, range: 18-40) MTLE patients who were seizure-free for two years after anteriomesial temporal resection for drug resistant epilepsy. 19 healthy controls were also scanned (mean age: 24.8±3.9SD years, range: 18-26). Scans were aligned to the ICBM space and maps of gray matter, white matter and CSF were created. To better align anatomy across subjects, a cortical pattern matching technique used 72 sulcal landmarks traced on each subject's cortex to constrain the nonlinear mapping of one cortex onto another in 3D space. Cortical thickness was mapped at 65,536 homologous points in each subject, based on the 3D distance from the cortical gray-white matter interface to the external gray-CSF boundary. Thickness maps were compared and averaged across subjects at each cortical surface location to produce spatially detailed maps of local thickness differences within and between groups. To measure cortical complexity, each hemisphere was divided into four surface meshes (frontal, temporal, parietal, and occipital). Cortical pattern matching was used to anchor sulcal landmarks to the reparameterized cortex so that corresponding sulci and cortical regions occurred in the same parameter space locations across subjects. The resulting deformed spherical parameterization was discretized using a hierarchy of quadtree meshes of size NxN, for $N=2$ to 256. The rate of increase of surface area with increasing spatial frequency was estimated by least-squares fitting of a linear model to the estimated surface area versus frequency, on a log-log plot. If $A\{M(N)\}$ represents the surface area of the cortical surface mesh $M(N)$, the fractal dimension is $DimF=2+\{d(A\{M(N)\})/d \ln N\}$. Here the gradient of the multifractal plot was obtained by regressing $\ln A\{M(N)\}$ against $\ln N$.

Results & Discussion: Compared to healthy controls, both MTLE groups showed 30% bilateral deficits in cortical thickness, in the frontal poles, frontal operculum, orbitofrontal, lateral temporal and occipital regions. In both MTLE groups, cortical thickness was asymmetrically reduced in the right angular gyrus and primary sensorimotor cortex surrounding the central sulcus. Cortical complexity was decreased in left temporal, parietal and occipital regions, and

right temporal and occipital regions. In left MTLE, cortical complexity was also reduced in left frontal and right parietal regions.

Conclusions: These cortical maps offer detailed characterization of the deficit pattern in MTLE. MTLE patients exhibited reduced cortical thickness and complexity in multiple cortical regions, suggesting that the epileptogenesis involves a distributed neuronal network extending beyond the hippocampus. The extrahippocampal gray matter damage may result from chronic seizure propagation from the diseased hippocampus to the neocortex via established reciprocal pathways.