FRACTAL COMPLEXITY OF THE HUMAN CORTEX IS INCREASED IN WILLIAMS SYNDROME

[1]Paul M. Thompson, [1]Agatha D. Lee, [1]Rebecca A. Dutton, [1]Jennifer A. Geaga, [1]Kiralee M. Hayashi, [1]John D. Bacheller, [2]Mark A. Eckert, [1]Arthur W. Toga, [2]Allan L. Reiss

[1]Laboratory of Neuro Imaging, Brain Mapping Division, Dept. Neurology, UCLA School of Medicine, Los Angeles, CA 90095
[2]Stanford Psychiatry Neuroimaging Laboratory, Stanford University School of Medicine, Stanford, CA 94305

We developed a new algorithm to measure the fractal dimension, or complexity, of the human cerebral cortex. Cortical complexity was found to be significantly increased in Williams syndrome, a genetic condition associated with deletion of ~20 contiguous genes on chromosome 7 [cf. 1,2]. Most prior complexity measures such as the gyrification index [2,3] typically measure the cortical contour in a specific image slice. By contrast, the proposed fractal dimension takes into account the full 3D cortical surface geometry, and is independent of brain scale, orientation and the direction of image acquisition.

Methods. 75 T1-weighted MRI scans (256x192x124 SPGR volumes; FOV=24 mm, slice thickness 1.2 mm) were acquired on a GE-Signa 1.5 Tesla scanner from 36 subjects with genetically-confirmed Williams syndrome (mean age: 29.3±1.6SE years, 14M/22F) and 39 age-matched healthy controls (age: 29.3±1.6 years; 16M/23F). All 43 MRI scans were aligned to ICBM space, and 72 sulci per brain were traced on parametric surface models of each subject's cortex. A cortical pattern matching technique [4] then used these sulcal landmarks as anchors to reparameterize the cortex so that corresponding sulci occurred at the same parameter space locations [4]. The resulting deformed spherical parameterization was discretized in parameter space using a hierarchy of quadtree meshes of size NxN, for N=2 to 256. The cortex was remeshed at each spatial frequency and its surface area measured. The rate of increase of surface area with increasing spatial frequency was estimated by least squares fitting of a linear model to the area versus frequency, on a log-log plot [5]. If A{M(N)} represents the surface area of the cortical surface mesh M(N), the fractal dimension or complexity was computed as DimF=2+{d(A{M(N)})/d ln N}. The gradient of the multifractal plot is obtained by regressing ln A{M(N)} against ln N. For a flat surface, this slope is zero, and the dimension is 2; representing the surface at a higher spatial frequency adds no detail. Values above 2 indicate increasing surface detail and greater gyral complexity.

Findings. Left hemisphere complexity in the Williams group (2.2509±0.0018SE) was greater than that in controls (2.2450±0.0017SE; $p<0.019$). Right hemisphere complexity was also increased (2.2482±0.0018SE in the Williams group versus 2.2413±0.0015 in controls; $p<0.0019$). Differences were significant with or without adjusting for effects of age and gender.

Interpretation. These results support prior anatomic findings of regional gyral patterning anomalies and polymicrogyria in Williams syndrome [2]. Increased cortical complexity may result from disturbed developmental processes during cortical pattern formation *in utero*. The fractal dimension measure detects subtle cortical abnormalities that conventional volumetrics and structural brain mapping approaches may miss. We are now analyzing cortical subregions to determine whether these differences are regionally specific.

References.

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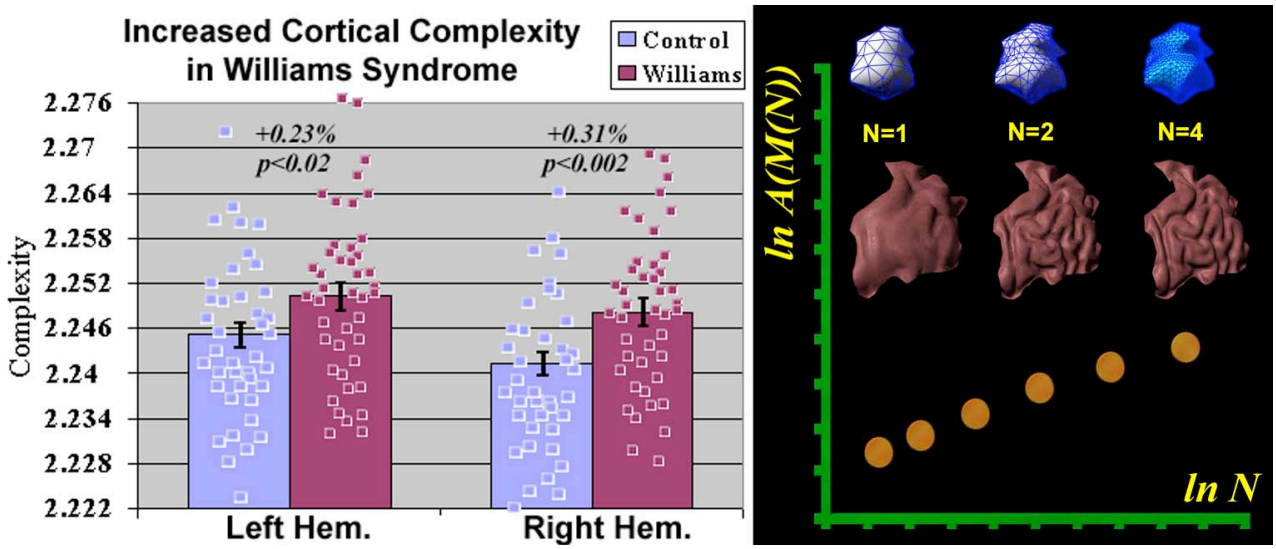

Figure 1. Cortical Complexity in Williams Syndrome (left); Multifractal Plot (right)