Estimating Local Surface Complexity Maps Using Spherical Harmonic Reconstructions

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Abstract. Cortical surface complexity is a potential structural marker for certain diseases such as schizophrenia. In this study, we developed a measure of fractal dimension (FD) calculated from lowpass-filtered spherical harmonic brain surface reconstructions. A local FD measure was also computed at each vertex in a cortical surface mesh, visualizing local variations in surface complexity over the brain surface. We analyzed the surface complexity for 87 patients with DSM-IV schizophrenia (with stable psychopathology and treated with antipsychotic medication) and 108 matched healthy controls. The global FD for the right hemisphere in the schizophrenic group was significantly lower than that in controls. Local FD maps showed that the lower complexity was mainly due to differences in the prefrontal cortex.

Keywords: surface complexity, fractal dimension, spherical harmonics, schizophrenia, MRI.

1 Introduction

One aspect of brain structure that may be significantly altered in disease is the cortical folding complexity. This can be measured using a metric such as the gyrification index (GI), which is defined as the ratio of the inner surface area (or perimeter in a cross-section) to that of an outer surface convex hull. The GI can be measured in two dimensions by examining cortical slices [1], or in 3D from a reconstructed surface mesh. Differences in cortical folding complexity have been found for some regions in psychiatric disorders such as schizophrenia [2] and bipolar disorder [3]. However, the GI metric has drawbacks, as it depends on the definition of the outer hull, on the plane of section for 2D measures, and may depend on brain size.

These drawbacks can be circumvented using the fractal dimension (FD), which does not rely on the definition of an explicit outer hull (for a review, see [4]). It has been proposed that the brain is a fractal [5], at least over a certain range of scales, and this has been examined using voxel-based information on the overall geometry of the white matter [6, 7]. The FD may also be applied to measure cortical folding complexity. Prior studies found significant differences in FD in psychiatric disorders such as

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first-episode schizophrenia [8], obsessive-compulsive disorder [9], and Williams syndrome [10], as well as differences associated with sex [11], normal development [12], early-life blindness [13], and IQ [14].

Most definitions of the cortical surface FD rely on the box-counting method, where regional areas are computed at progressively lower sampling resolutions. Since the number of vertices steadily decreases, the position of these vertices can have a large impact on the FD metric and may overlook relevant cortical folding information. This concern may be addressed by aligning sulci across subjects to approximate the same cortical location for each vertex in all subjects [15]. However, alignment is a complicated endeavor that often requires manual delineation of cortical regions.

Surface complexity can also be assessed using spherical harmonic (SPH) expansions. When using SPH reconstructions, the number of vertices (sampling) is the same for all reconstructed surfaces, reducing the influence of individual vertex placement. Furthermore, structural differences in some brain disorders may be easier to detect by investigating the 3D pattern of regional changes rather than a single global metric [16, 17]. For instance, pattern classification techniques can combine signals from different parts of a map to enhance the specificity of morphometric findings [18-22]. This multi-regional information shows promise for developing a more specific brain structural signature of schizophrenia. Using SPH-derived reconstructions, a local FD can be computed at each vertex in the reconstruction, assisting with subsequent pattern-classification approaches.

In this study, we first demonstrate that the fractal dimension values obtained from SPH-derived reconstructions are a valid measure of surface complexity. This is accomplished by measuring the complexity of fractal surfaces with known FD. We then applied complexity analysis to MRI-derived cortical surfaces from schizophrenia patients and healthy controls. We hypothesized that there may be a core pattern of complexity differences that may be detectable in regions commonly implicated in schizophrenia (e.g., hippocampus and dorsolateral prefrontal cortex).

2 Methods

Our computation of the FD for a brain surface mesh has four steps: (1) Generate a surface mesh for each brain hemisphere using the standard FreeSurfer pipeline (http://surfer.nmr.mgh.harvard.edu/). (2) Extract the spherical harmonic coefficients up to a maximum bandwidth (or l-value) of $B = 1536$. (3) Reconstruct 20 brain surface meshes from a progressively increasing series of lowpass-filtered coefficients. (4) Compute global FD using the summed polygon areas of the reconstructed brain surface meshes, and compute local FD using the average area of the neighboring polygons for each vertex. Steps related to complexity measures are detailed below.

2.1 Spherical Harmonic Analysis

To analyze the harmonic content of a surface mesh, the first required step is to re-parameterize the spherical mapping so that it has regularly sampled points with respect to θ and ϕ, where θ is the co-latitude and ϕ is the azimuthal coordinate. The original spherical mapping is from the standard FreeSurfer pipeline. Then, points are generated from equally sampled values of θ and ϕ for all members in the sets, such that there are $2B$ points per set, where B is the bandwidth (or l-value). For each regularly

sampled point, the closest polygon on the spherical mapping is found. Within the closest polygon, a spatial location for the interpolated vertex is approximated using barycentric coordinates. The result is a regularly sampled spherical map in which every point is associated with a coordinate that gives its location on the original surface.

Once the surface mesh is re-parameterized, the harmonic content of a spherical mesh may be obtained using normalized spherical harmonics $Y_l^m(\theta,\phi)$:

$$Y_l^m(\theta,\phi) = P_l^m(\cos\theta)e^{im\phi}, \tag{1}$$

where l and m are integers with $|m| \le l$, and P_l^m is the associated Legendre function defined by:

$$P_l^m(x) = \frac{1}{2^l l!}\left(1-x^2\right)^{\frac{m}{2}} \frac{d^{l+m}}{dx^{l+m}}\left(x^2-1\right)^l. \tag{2}$$

A square-integrable function $f(\theta,\phi)$ on the sphere can be expanded in the spherical harmonic basis such that:

$$f(\theta,\phi) = \sum_{l=0}^{B}\sum_{m=-l}^{l} \left\|Y_l^m\right\|_2^{-2} \hat{f}(l,m)\cdot Y_l^m, \tag{3}$$

where the coefficients $\hat{f}(l,m)$ are defined by $\hat{f}(l,m) = \left\langle f, Y_l^m \right\rangle$ and the L^2-norm of Y_l^m is given by:

$$\left\|Y_l^m\right\|_2^2 = \frac{4\pi}{2l+1}\cdot\frac{(l+m)!}{(l-m)!}. \tag{4}$$

It is possible to solve this system directly by finding the bases first, but a more efficient approach is to use a divide-and-conquer scheme [23].

These coefficients can then be lowpass-filtered, such that only lower coefficients have non-zero values, and passed through an inverse Fourier transform to produce a surface reconstruction. For FD calculations, twenty reconstructions are produced using an upper l-value between 4 and 1536.

2.2 Calculation of Local and Global Complexity Values

Generally, FD is found by finding the slope of a plot regressing log(area) versus log(dimension), over a certain range of scales, where the area is the sum of polygon areas in a given reconstruction. When using spherical harmonic reconstructions, the plot is modified to use bandwidth (or upper l-value), and the slope can be found by regressing log(area) versus log(bandwidth) (Figure 1). Because the area asymptotes for higher-bandwidth reconstructions (e.g., the brain surface is accurately reconstructed if enough coefficients are included), the surface area values included in slope calculations were thresholded at 80% of the original surface area.

In the case of global FD, the area used in the regression is the total area of the reconstructions; for local FD, the area value assigned to a single vertex is the average area of the neighboring polygons. As this area value varies at a local level, the areas

were smoothed using a 25-mm Gaussian heat kernel [24]. Statistical significance was defined using a vertex-level threshold of $p < 0.05$.

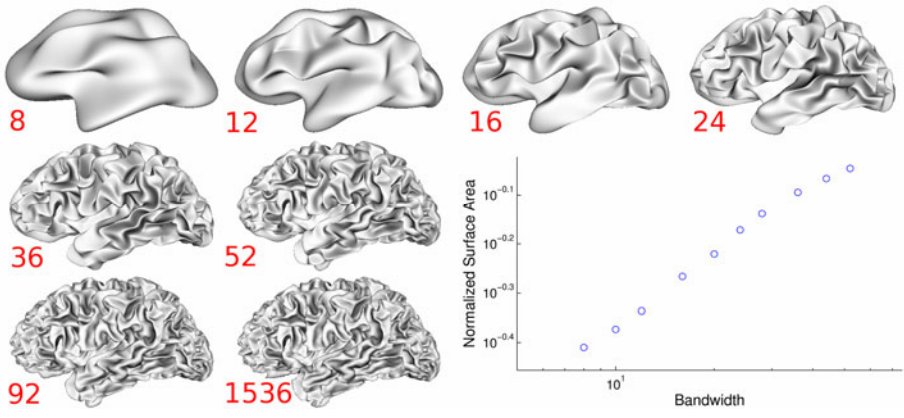

Fig. 1. Fractal dimension is found by finding the slope of a logarithmic plot of surface area versus bandwidth (or upper *l*-value), up to a maximum bandwidth. Surface areas are normalized by the original surface area. A linear approximation is reasonable over this range of scales.

2.3 Artificial Fractal Surfaces

To determine whether the FD values obtained from SPH-derived reconstructions were valid, we generated two sets of von Koch surface meshes that had either a tetrahedral or cubic structure. To avoid self-intersections, the surface meshes slightly deviated from true von Koch surfaces – a reduced length was used for projecting structures. Despite this deviation, however, the two sets of von Koch surfaces still had characteristic FD values determined by measuring the slope of a log-log plot of characteristic dimension versus surface area (Figure 2; cubic: 2.1974, tetrahedral: 2.2936). These surfaces were then processed to generate SPH-derived reconstructions, and the global FD values were extracted from the surface area of the reconstructed surfaces.

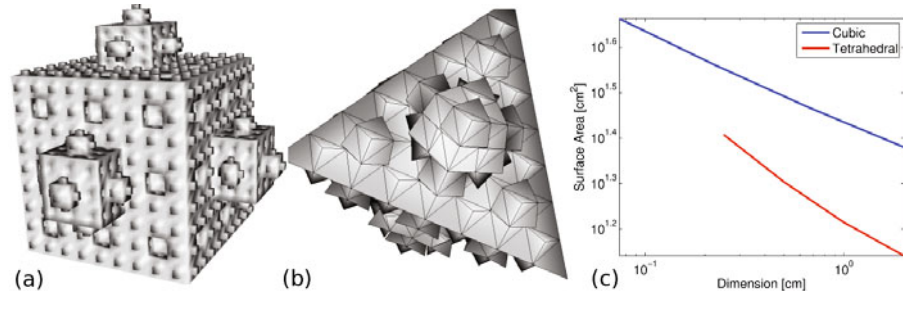

Fig. 2. Modified von Koch fractal surfaces with either a cubic (a) or tetrahedral (b) topology. Each set included surfaces with progressively more detail, obtained by inserting self-similar shapes at lower dimensions. A log-log plot of characteristic dimension versus surface area (c) resulted in a linear line whose slope was the characteristic FD.

2.4 Subject Data

MRI data was acquired from 87 patients (48 male/39 female; mean age = 35.5 years, SD = 11.0) with a DSM-IV diagnosis of schizophrenia and 108 healthy controls (68 male/40 female; mean age = 32.1 years, SD = 10.0). The patients were recruited from the Department of Psychiatry in Jena, Germany, and first screened with a semi-structured interview before being assessed by two psychiatrists establishing the DSM-IV diagnosis. Details of this patient group can be found in [25].

We obtained a high-resolution structural brain MRI from each subject on a 1.5-T Phillips Gyroscan ASCII system using a T1-weighted sequence obtaining 256 sagittal slices covering the entire brain (TR = 13 ms, TE = 5 ms, 25° flip angle, field of view [FOV] = 256 mm, voxel dimensions = 1 × 1 × 1 mm^3) for all subjects. Foam pads were used where appropriate to limit head movement. Prior to image processing, each image was checked manually for artifacts. All scans passed both the manual and automated quality checks.

3 Results

Analysis of the von Koch fractal surfaces using SPH-derived reconstructions resulted in FD values similar to the FD values calculated analytically (cubic: 2.1540 ± 0.007 SEM; tetrahedral: 2.2473 ± 0.007 SEM). Table 1 contains the mean global FD values for the schizophrenic subgroups and controls. Complexity was significantly lower for the right hemisphere in the schizophrenic group.

Table 1. Mean global FD for schizophrenic and control subjects with SEM. *: $p < 0.02$.

	left hemisphere	*right hemisphere*
Control (c)	2.5328 ± 0.0002	2.5340 ± 0.0002
Schizophrenic (s)	2.5355 ± 0.0003	2.5264 ± 0.0002 *

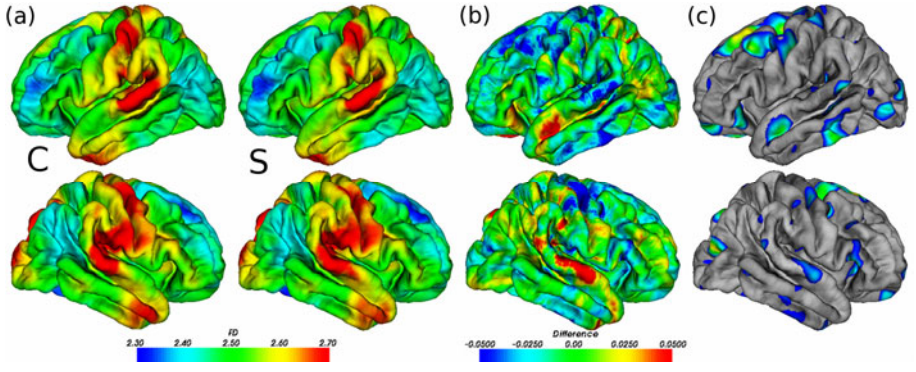

Fig. 3. Local average FD values for control (a, C) and schizophrenic (a, S) groups, for the left (*top row*) and right (*bottom row*) hemispheres. A map of mean complexity differences between groups (b) and *p*-values (c) highlight differences between the groups. In (c), vertices are highlighted if $p < 0.05$, and the values were not corrected for multiple comparisons.

The local FD mapping reveals that the lower overall complexity in the right hemisphere is due to differences in the prefrontal and temporal lobes (Figure 3). Local complexity is also lower for the prefrontal cortex in the left hemisphere.

4 Discussion

We developed a measure of cortical surface complexity that relies on spherical harmonic reconstructions to derive the fractal dimension of brain surfaces both globally and locally (up to single-vertex resolution). Analysis of fractal surfaces demonstrated that this method accurately measures the FD of surfaces. The global FD values for cortical surfaces were similar to previously published FD values [6, 9, 26], indicating that complexity measures of cortical structures based on SPH-derived reconstructions may be an accurate measure of complexity. Other groups have reported much lower FD values. This discrepancy is due to differences in measuring FD (which was usually a box-counting approach applied with relatively low-resolution resampled meshes) or in mathematical definitions of FD measures [8, 10, 11, 15]. The local mapping of complexity was a basic proof-of-concept that lends itself to improvement through inter-subject registration, region-of-interest analysis, and pattern classification methods. Such approaches would allow the extraction of complexity measures for individual lobes and potentially the recognition of schizophrenic patients through structural morphometry alone.

Applied to a large subject pool containing control and schizophrenic subjects, differences in cortical structure were significant in the prefrontal lobe, as predicted. Right hemispheric complexity was lower for the schizophrenic group. There were also significant differences near the hippocampal region, but a more detailed regional analysis needs to be conducted before reaching a conclusion. These findings corroborate earlier hypotheses on aberrant brain development. First, the global FD changes are significant in the right hemisphere, which suggest that the abnormalities are lateralized. Second, the prefrontal and medial temporal localization of FD alterations partially overlaps areas where subtle developmental cellular deficits have been shown [27, 28]. This would suggest that altered FD might be a reflection of abnormal early development of the cortical sheet.

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