21st International Conference on Pattern Recognition (ICPR 2012)
November 11-15, 2012. Tsukuba, Japan

Quantification of Age-related Brain Cortex Change using 3D Shape Analysis

A. Elnakib[1], M. Nitzken[1], M. F. Casanova[2], H.-Y. Park[1], G. Gimel'farb[3], and A. El-Baz[1] *
[1]BioImaging Laboratory, Bioengineering Department, University of Louisville, Louisville, KY, USA.
[2]Department of Psychiatry and Behavioral Sciences University of Louisville, Louisville, KY, USA.
[3]Department of Computer Science, University of Auckland, Auckland, New Zealand.

Abstract

To characterize the brain changes associated with aging, we detect brain cortex variability through a spherical harmonic analysis that represents a 3D surface supported by the unit sphere through a linear combination of special basis functions, called spherical harmonics (SHs). The proposed 3D shape analysis is carried out in four steps: (i) 3D Delaunay triangulation to construct a 3D mesh model of the brain cortex surface; (ii) mapping this model to the unit sphere; (iii) computing the SHs for the surface; and (iv) calculating the area under the error reconstruction curve for the SHs to delineate the brain cortex. We describe the brain shape complexity with a new shape index, the estimated area under the error reconstruction curve for the SHs. The initial experiments on 187 male subjects (age range, 4-22 years) and the comparison results with the cortex volumetric index suggest that our shape index is a promising supplement to current metrics that characterize age-related brain changes.

1 Introduction

Characterizing brain changes associated with aging is an important research area in modern neuroscience. It helps to recognize pathological brain development [1, 2] and to address several arising questions associated with brain development in controls [3]. Recent advances in data acquisition systems have opened the way for characterizing age associated brain changes. Magnetic resonance imaging (MRI) has revealed quantitative age-related changes through postmortem and serial *in-vivo* scanning. Courchesne et al. [3] reported changes in the whole brain volume and in the grey matter and white matter brain structures in a group of 116 volunteers,.

Analysis of cortical changes have also been investigated. Volumetric approaches reported different aging-associated changes in adults, particularly in the volume of the whole frontal cortex [4] and the lateral prefrontal cortex [5]. Salat et al. [6] estimated the cortical thickness as the distance between the gray/white boundary and the outer cortical surface, resulting in a continuous estimate across the cortical mantle. Global cortical thinning was apparent by middle age in a group of 106 non–demented participants (age range, 18–93) [6]. In addition to cortical thickness, Magnotta et al. [1] used a curvature index, measuring the curvature of the gyri and the sulci, to conclude that the aging process affects gyrification, with the brain appearing more 'atrophic' with increasing ages in a sample of 148 controls (age range, 18–82).

Instead of voxel–based approaches, which are sensitive to errors from spatial smoothing and structures segmentation, we apply our recently developed SH analysis methodology [2, 7] to characterize the whole 3D shape changes associated with aging inside an individual brain cortex. The SH analysis has been successfully applied in a host of brain applications [8, 9]. Our SH methodology has shown superior competing results in diagnosing malignant lung nodules [7] and analyzing the dyslexic brain cortex [2]. In this paper, the 3D shape of an individual brain is characterized based on a new metric that measures the area under the error reconstruction curve of the SH, which is required to approximate the individual brain cortex. Our results indicate that this newly developed metric has revealed significant differences associated with aging and can be used as a supplement to the current existing metrics.

2 3D Shape Analysis Framework

The proposed analysis begins with segmented brain cortex images from pre–segmented MRI which were provided to our research group by the National Institute of Mental Health Pediatric Brain Imaging project. A 3D mesh model of the cortex surface is mapped to a unit sphere and approximated using a linear combination of SHs. The area under the error reconstruction curve of the SHs yields a desired approximation accuracy that can be used as a new shape index to describe the complexity of the brain's shape.

2.1 Spherical harmonics shape analysis

Spectral SH analysis [10] considers 3D surface data as a linear combination of specific basis functions. In our case, the surface of the segmented brain cortex is approximated first by a triangulated 3D mesh (see Fig. 1) built with an algorithm by Fang and Boas [11]. Secondly, the brain cortex surface for each subject is mapped for the SH decomposition to a unit

*Corresponding author:- Tel:(502)-852-5092, Fax:(502)-852-6806, E-mail: aselba01@exchange.louisville.edu

sphere using our recently developed mapping approach, called "*Attraction-Repulsion,*" see Fig. 2. For more details about the Attraction-Repulsion algorithm, please see [2].

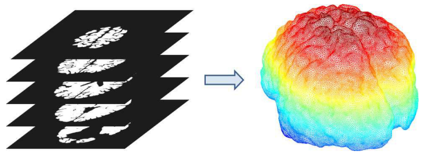
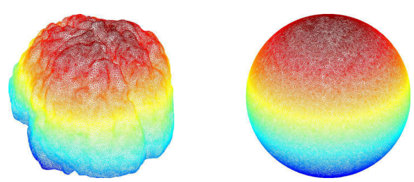


Figure 1. Generation of a 3D mesh for the brain cortex surface from a stack of successive segmented 2D T2–MR slices. Note that the colors indicate the vertical depth of the mesh points and are used for visualization purposes.



(a) (b)

Figure 2. Brain cortex mesh (a) and the Attraction–Repulsion mapping to unit sphere (b).

The original brain cortex, mapped to the unit sphere with the proposed Attraction–Repulsion algorithm, is approximated by a linear combination of SHs. The lower–order harmonics are sufficient to represent more generic information while the finer details require higher–order harmonics. The SHs are generated by solving an isotropic heat equation for the cortex surface on the unit sphere. Let $\mathcal{S} : \mathbf{M} \to \mathbf{U}$ denote the mapping of a cortical mesh $\mathbf{M}$ to the unit sphere $\mathbf{U}$. Each node $\mathbf{P} = (x, y, z) \in \mathbf{M}$ mapped to the spherical position $\mathbf{u} = S(\mathbf{P})$ is represented by the spherical coordinates $\mathbf{u} = (\sin\theta\cos\varphi, \sin\theta\sin\varphi, \cos\theta)$ where $\theta \in [0, \pi]$ and $\varphi \in [0, 2\pi)$ are the polar and azimuth angles, respectively. The SH $Y_{\alpha\beta}$ of degree α and order β is defined as [12]:

$$Y_{\alpha\beta} = \begin{cases} c_{\alpha\beta} G_\alpha^{|\beta|} \cos\theta \sin(|\beta|\varphi) & -\alpha \le \beta \le -1 \\ \frac{c_{\alpha\beta}}{\sqrt{2}} G_\alpha^{|\beta|} \cos\theta & \beta = 0 \\ c_{\alpha\beta} G_\alpha^{|\beta|} \cos\theta \cos(|\beta|\varphi) & 1 \le \beta \le \alpha \end{cases} \quad (1)$$

where $c_{\alpha\beta} = \left(\frac{2\alpha+1}{2\pi} \frac{(\alpha-|\beta|)!}{(\alpha+|\beta|)!} \right)^{\frac{1}{2}}$ and $G_\alpha^{|\beta|}$ is the associated Legendre polynomial of degree α and order β. For the fixed α, the polynomials G_α^β are orthogonal over the range $[-1, 1]$. As shown in [12], the Legendre polynomials are effective in calculating SHs, and this is the main motivation behind their use in this work.

Finally, the brain cortex is reconstructed from the SHs of Eq. (1). For SHs expansion, the standard least–square fitting does not accurately model the 3D shape of the brain cortex and can miss some of the shape details that discriminate between child and adult brains. To circumvent this problem, we used the iterative residual fitting by Shen et al. [13] that accurately approximates 3D gyrifications of the brain cortex. As demonstrated in Fig. 3, the brain cortex gyrifications increase with age and thus the model accuracy (Fig. 4) does not significantly change for the subject at 6–years old, from 30 to 60 SHs, while it continues to increase at 18 years of age.

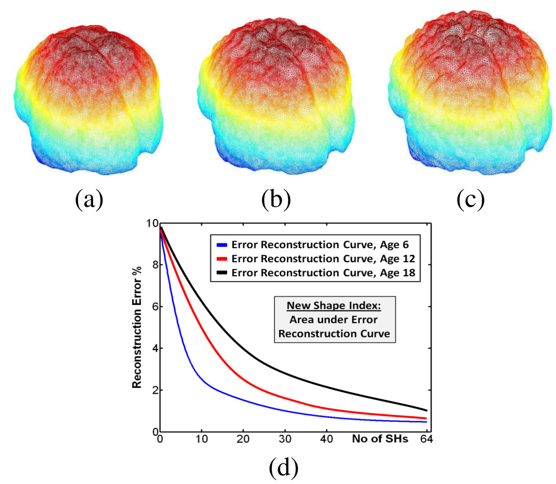


Figure 3. Original brain cortex mesh for one enrolled subject at ages 6 (a), 12 (b), and 18 (c) years, and an illustrative schematic for the proposed new shape index.

2.2 Quantitative brain cortex shape analysis

Our main hypothesis is that the brain cortex gyrifications will increase with age as demonstrated in Fig. 3(a),(b), and (c). As age increases, more SHs must be used for an accurate approximation of the brain cortex gyrifications, and thus a significant increase in the area under the SHs error reconstruction curve is obtained (see Fig. 3(d)). Note that the reconstruction error is defined as the mean Euclidian distance between the original cortex surface and its reconstructed approximation using the SHs.

3 Experimental Results

The proposed approach was tested on *in vivo* data collected from 187 healthy control male subjects, aged 4–22 years. These healthy control subjects were recruited from the community and underwent physical and neurological exams, clinical interviews, family history assessments, and extensive

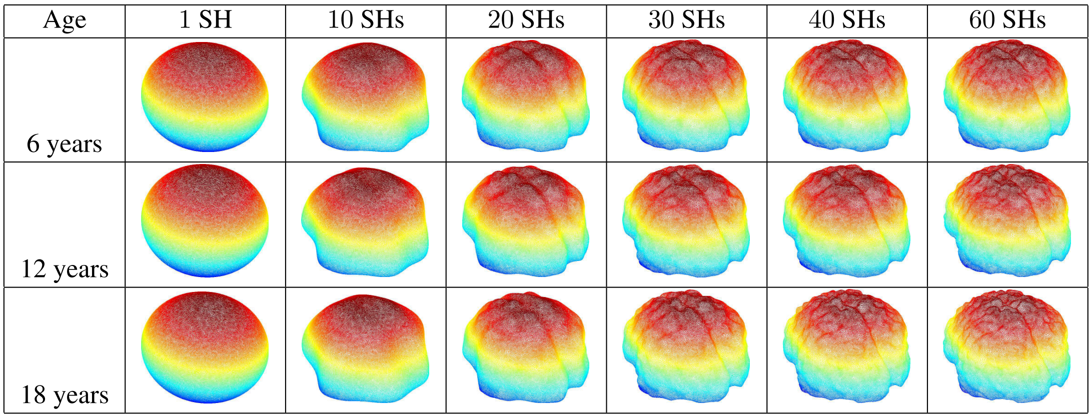


Figure 4. Approximation of the 3D brain cortex shape for the subject in Fig. 3 at ages 6, 12, and 18 years.

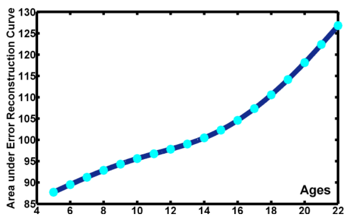
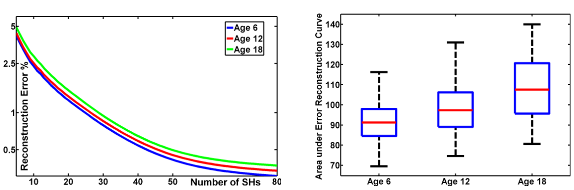


Figure 5. Mean area under the error reconstruction curve of SHs for all participants (age, 4–22); the curve is approximated using spline fitting.

neuropsychological batteries [14]. Participants were asked to return for follow–up longitudinal testing and scans at approximately 2–year intervals. All images were acquired on the same General Electric 1.5 Tesla Signa Scanner located at the NIH Clinical Center. A three–dimensional spoiled gradient recalled echo, in the steady state sequence, was used to acquire 124 contiguous 1.5–mm thick slices in the axial plane.

To characterize the changes that occur in the shape of the brain with aging, we compute the area under the reconstruction error curve of the SHs for all the scans for all participants. The mean area under the error reconstruction curve is fitted using a spline as shown in Fig. 5 (the area under the curve is calculated using the trapezoidal approximation). As demonstrated in Fig. 5, the area increases as the participant age increases. This is due to the fact that as the child grows, her brain develops more gyrifications and becomes more complex (similar findings have been reported [1]), and thus requires more SHs to approximate the shape within a given accuracy (see Fig. 4).

In order to investigate how aging affects the shape of the brain within certain age periods, we divided the data into 3 groups: group 1 (middle childhood, ages 4-9 years, mean age 6 years), group 2 (early and middle adolescent, ages 10-15 years, mean age 12 years), and group 3 (late adolescence and early adulthood, ages 16-22, mean age 18 years). Then we calculate error reconstruction curves of the SHs for each of the three groups. As expected, a more gradual convergence of the SH reconstruction curve is reported as age increases (see Fig. 6(a)). This indicates that the area under the reconstruction error curve provides a potential metric to characterize brain shape changes associated with aging. In this regard, the box plot analysis (Fig. 6(b)) shows a monotonic increment in the mean area under the reconstruction error curve between the three groups as age increases. In addition, Table 1 shows that this increment represents a significant difference, as evidenced by the P-values of the unpaired t-test performed between each pair of the three groups with respect to the area under the error reconstruction curves of the SHs (note that a P-value less than 0.05 represents a significant difference). Conversely, the cortex volumetric index, estimated as the number of segmented cortex voxels multiplied by the voxel size, failed to discriminate between the first and the second groups (Table 2). These results highlight the high efficiency of the proposed shape index to detect aging changes.



(a) (b)

Figure 6. (a) Average error reconstruction curves for three groups (mean ages 6, 12 and 18), and (b) the box plot for areas under the error reconstruction curves for the groups.

4 Conclusions

In total, these preliminary results show that the area under the SH reconstruction error curve is an efficient metric that can

Table 1. **Statistical comparative analysis for our cortex shape index for three groups, mean ages 6, 12 and 18 years.**

	Our cortex shape index		
	Group 1 (Age 6)	**Group 2** (Age 12)	**Group 3** (Age 18)
Mean	92.80	98.84	109.66
St. dev.	12.07	12.49	16.69
Group	1 and 2	2 and 3	1 and 3
P-value	$< 10^{-4}$	$< 10^{-4}$	$< 10^{-4}$

Table 2. **Statistical comparative analysis for the cortex volumetric index (mm^3) for the three groups.**

	Cortex volumetric index		
	Group 1 (Age 6)	**Group 2** (Age 12)	**Group 3** (Age 18)
Mean	1,479,601	1,474,096	1,423,523
St. dev.	41,045	44,219	1,36,421
Group	1 and 2	2 and 3	1 and 3
P-value	0.2817	$< 10^{-4}$	$< 10^{-4}$

characterize the brain changes associated with aging. Our proposal substantially differs from known techniques that exploit only volumetric descriptions of different brain structures and thus are in principle more sensitive to the selection of age and segmentation errors. In contrast, we derive a quantitative metric (the area under the SH reconstruction error curve) from the whole 3D cortex shape. Our experiments demonstrate that the differences in the proposed general geometric feature of cortex gyrifications is statistically significant for the three groups of different ages [middle childhood (4-9), early and middle adolescence (10-15), and late adolescence and early adulthood (16-22)], whereas the traditional cortex volumetric index fails to differentiate between the first and second former groups. In the future, we will use the newly developed shape index to compare between male and female subjects.

References

[1] V. A. Magnotta, N. C. Andreasen, S. K. Schultz, G. Harris, T. Cizadlo, D. Heckel, P. Nopoulos, and M. Flaum. Quantative in vivi measurement of gyrification in human brain: Changes associated with aging. *Cerebral Cortex,* 9(2):151–160, 1999.

[2] M. Nitzken, M. Casanova, G. Gimel'farb, A. Elnakib, F. Khalifa, A. Switala, and A. El-Baz. 3D shape analysis of the brain cortex with application to dyslexia. In *Proc. IEEE Int. Conf. Image Process. (ICIP'11),* Brussels, Belgium, September 11–14, 2011, pages 2713–2716.

[3] E. Courchesne, H. J. Chisum, J. Townsend, A. Cowles, J. Covington, B. Egaas, M. Harwood, S. Hinds, and G. A. Press. Normal brain development and aging: Quantitative analysis at in vivo MR imaging in Healthy Volunteer. *Radiology,* 216:672–682, 2000.

[4] D. J. Tisserand, J. C. Pruessner, E. J. S. Arigita, M. P. J. van Boxtel, A. C. Evans, J. Jolles, and H. B. M. Uylings. Regional frontal cortical volumes decrease differentially in aging: An MRI study to compare volumetric approaches and voxel-based morphometry. *NeuroImage,* 17(2):657–669, 2002.

[5] N. Raz, F. Gunning-Dixon, D. Head, K. M. Rodrigue, A. Williamson, and J. D. Acker. Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: Replicability of regional differences in volume. *Neurobiology of Aging,* 25(3):377–396, 2004.

[6] D. H. Salat, R. L. Buckner, A. Z. Snyder, D. N. Greve, R. S. R. Desikan, E. Busa, J. C. Morris, A. M. Dale, and B. Fischl. Thinning of the cerebral cortex in aging. *Cereb. Cortex,* 14(7):721–730, 2004.

[7] A. El-Baz, M. Nitzken, F. Khalifa, A. Elnakib, G. Gimel'farb, R. Falk, and M. Abo El-Ghar. 3D shape analysis for early diagnosis of malignant lung nodules. In *Proc. Inf. Process. Med. Imaging (IPMI'11),* Monastery Irsee, Germany, July 3–8, 2011, pages 772–783.

[8] M. Styner, I. Oguz, S. Xu, C. Brechbhler, D. Pantazis, J. J. Levitt, M. E Shenton, and G. Gerig. Framework for the statistical shape analysis of brainstructures using SPHARM-PDM. *J. Insight,* 242–250, 2006.

[9] R. A. Yotter, R. Dahnke, P. M. Thompson, and C. Gaser. Topological correction of brain surface meshes using spherical harmonics. *Human Brain Mapping*, 32(7):1109–1124, 2011.

[10] M. K. Chung, L. Shen, K. M. Dalton, A. C. Evans, and R. J. Davidson. Weighted Fourier series representation and its application to quantifying the amount of gray matter. *IEEE Trans. Med. Imaging,* 26(4):566–581, 2007.

[11] Q. Fang and D. Boas. Tetrahedral mesh generation from volumetric binary and gray-scale images. In *Proc. IEEE Int. Symp. Biomed. Imag. (ISBI'09),* Boston, MA, USA, June 28–July 1, 2009, pages 1142–1145.

[12] R. Courant and D. Hilbert, *Methods of mathematical physics,* Vol. II, Interscience, New York, 1953.

[13] L. Shen and M. K. Chung. Large-scale modeling of parametric surfaces using spherical harmonics. In *Proc. 3^{rd} Int. Symp. 3D Data Process. Visualiz. Transmission (3DPVT'06),* Chapel Hill, NC, USA, June 14–16, 2006, pages 294–301.

[14] J. N. Giedd, J. Blumenthal, N. O. Jeffries, F. X. Castellanos, H. Liu, A. Zijdenbos, T. Paus, A. C. Evans, and J. L. Rapoport. Brain development during childhood and adolescence: A longitudinal MRI study. *Nature Neuroscience,* 2(10):861–863, 1999.