NeuroImage 76 (2013) 216–224

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Development of cortical anatomical properties from early childhood to early adulthood

Jingxin Nie [a,b], Gang Li [b], Dinggang Shen [b,*]

[a] School of Psychology, South China Normal University, China
[b] Department of Radiology and BRIC, University of North Carolina at Chapel Hill, NC, USA

ARTICLE INFO

Article history:
Accepted 6 March 2013
Available online 21 March 2013

Keywords:
Cortex development
Cortical thickness
Cortical folding
Anatomical network

ABSTRACT

Human brain matures in temporal and regional heterogeneity, with some areas matured at early adulthood. In this study, the relationship of cortical structural developments between different cortical sheet regions is systematically analyzed using interregional correlation coefficient and network methods. Specifically, 951 longitudinal T1 brain MR images from 445 healthy subjects with ages from 3 to 20 years old are used. The result shows that the development of cortex reaches a turning point at around 7 years of age: a) the cortical thickness reaches its highest value and also the cortical folding becomes stable at this age; b) both global and local efficiencies of anatomical correlation networks reach the lowest and highest values at this age, respectively; and c) the change of anatomical correlation networks reach the highest level at this age, and the convergence of different anatomical correlation networks starts to decrease from this age. These results might inspire more studies on why there exists a turning point at this age from different viewpoints. For example, is there any change of synaptic pruning, or is it related to the starting of school life? And how can we benefit from this in the real life?

Introduction

Human brain matures at different rates across time and different regions, with some areas matured at early adulthood. Specifically, the total size of the brain reaches approximately 90% of its adult size at 6 years of age (Giedd, 2004; Reiss et al., 1996). Cortical thickness and volume have been shown to follow an inverted U-shaped developmental course, with a period of initial childhood increase and a subsequent adolescent decline (Courchesne et al., 2000; Giedd, 2004; Gogtay et al., 2004; Kennedy et al., 2002; Pfefferbaum et al., 1994; Reiss et al., 1996; Shaw et al., 2008). The early cortical thinning may reflect pruning in the form of use-dependent selective synapse elimination (Bourgeois and Rakic, 1993; Huttenlocher and Dabholkar, 1997; Shaw et al., 2008), which could play a key role in shaping neural circuits and could be a biological basis for ongoing development of cognitive abilities and behavior (Hensch, 2004; Knudsen, 2004). Thus, quantitative characterization of brain maturation might be essential to reveal the relationship between cortical structural connection and high-level functional development, and also for understanding neurodevelopmental disorders (Schlaggar et al., 2002; Stiles, 2000).

Longitudinal structural neuroimaging provides a powerful tool for developmental neuroscience to measure anatomical changes over time (Raznahan et al., 2011). In recent years, neuroimaging methods have provided fundamental insights into characterizing the features of human brain maturation, and revealing the difference related to sex, cognitive ability, genetic profile, and disease status during neurodevelopment (Giedd and Rapoport, 2010). Though the development of cortical structures shows regional heterogeneity in humans in recent studies (Gogtay et al., 2004; Shaw et al., 2008; Sowell et al., 2004), the underlying relationship between structural developments between different cortical sheet regions still needs to be quantified (Raznahan et al., 2011).

Human brain could also be characterized as a complex anatomical and functional network developing over the whole life (Achard et al., 2006; Eguiluz et al., 2005; Salvador et al., 2005; Sporns et al., 2004; Stam, 2004; Stam et al., 2007). The functional network in human brain has been explored extensively using electroencephalogram (EEG) (Micheloyannis et al., 2006; Stam et al., 2007), magnetoencephalography (MEG) (Stam, 2004), and functional magnetic resonance imaging (fMRI) (Achard et al., 2006; Eguiluz et al., 2005; Gao et al., 2011; Salvador et al., 2005). The small-world property (Watts and Strogatz, 1998), which indicates that most nodes in the network are not neighbors of one another, but can be reached from every other by a small number of hops or steps, has been found in the functional network of the adult brain (Achard et al., 2006; Eguiluz et al., 2005; Salvador et al., 2005). Meanwhile, the network of anatomical connections in the human brain has also been studied recently (Gong et al., 2009a, 2012; He et al., 2007; Sporns et al., 2004). The correlations of cortical thickness between different regions across subjects have been measured and

* Corresponding author at: Radiology and BRIC, UNC-CH School of Medicine, MRI Building, CB #7513, 106 Mason Farm Road, Chapel Hill, NC 27599, USA.
E-mail address: dgshen@med.unc.edu (D. Shen).

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2013.03.021

formed as structural connections (He et al., 2007; Sporns et al., 2005). The anatomical connection could also be estimated by regional diffusion-based anatomical connectivity using probabilistic tractography (Gong et al., 2009a, 2012).

In this study, the relationship between cortical structural developments in different cortical sheet regions is systematically analyzed using interregional correlation coefficient and network methods. Specifically, 951 longitudinal T1 brain MR images from 445 healthy subjects with ages from 3 to 20 years old are used, and for each subject at each time point its cortical thickness and cortical folding are first calculated on its inner cortical surface (the interface between white matter and gray matter) that has been parcellated into 78 regions of interest (ROIs). Then, the correlation matrices for cortical thickness and cortical folding at each time point and also at all time points are constructed, respectively, by computing the interregional Pearson's correlation coefficient of any pair of ROIs across subjects.

To analyze the development of the interregional correlation coefficient, the development of left/right hemispheric symmetry is particularly measured by the correlation value between corresponding left and right regions at different longitudinal times. Then, by using the interregional correlation coefficient as the regional similarity, the whole cortex is clustered into several large regions with distinct structural developmental patterns by a clustering method (Frey and Dueck, 2007).

Finally, the presence/absence pattern (i.e., binary pattern) of the connection network is constructed from each interregional correlation matrix, and its statistical and anatomical properties, especially the small-world property and connectivity distribution using graph theoretical analysis, are adopted to analyze the longitudinal development of anatomical networks.

Methods

Subjects and image acquisition protocol

Data were obtained from the Pediatric MRI Data Repository (Release 4.0) created for the NIH MRI Study of Normal Brain Development (Evans, 2006), a multi-site longitudinal project aimed at providing a normative database to characterize healthy brain maturation in relation to behavior. This database includes subjects from neonates to 21 years of age who underwent extensive cognitive, neuropsychological and behavioral testing along with multiple MRI brain imaging sessions. 951 sessions from 445 subjects with ages from 3 to 20 years old were used here. As this study aimed to study healthy subjects, exclusion criteria included (but were not limited to) prior history of medical illnesses with CNS implications, IQb70, and intra-uterine exposure to substances known or highly suspected to alter brain structure or functions (Evans, 2006; Waber et al., 2007).

A three-dimensional T1-weighted (T1W) Spoiled Gradient Recalled (SPGR) echo sequence from 1.5 T scanners was obtained on each participant, with 1 mm isotropic data acquired sagittally from the entire head. Slice thickness of ~1.5 mm was allowed for GE scanners due to their limit of 124 slices. In addition, T2-weighted (T2W) and proton density-weighted (PDW) images were acquired using a two-dimensional (2D) multi-slice (2 mm) dual echo fast spin echo (FSE) sequence. Total acquisition time was about 25 min and was often repeated when indicated by the scanner-side quality control process.

Image processing

In order to measure cortical attributes for each session, T1-weighted images were adopted. For each T1-weighted image, the skull stripping was first performed to remove non-cerebral tissues, and also the cerebellum and brain stem were further removed (Smith, 2002). Then the brain image was segmented into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) regions (Zhang et al., 2001). After topology correction of the WM volume, the inner and outer cortical surfaces were reconstructed and represented by the triangular meshes, composed of a set of vertices and triangles (Liu et al., 2008). Based on the automated anatomical labeling template (Tzourio-Mazoyer et al., 2002), each cortical surface was parcellated into 78 regions of interest (ROIs) by a high-dimensional nonlinear hybrid volumetric/surface registration method (Liu et al., 2004; Shen and Davatzikos, 2002). The 78 cortical surface regions of interest defined by the template are provided in Table S1.

Cortical thickness can be measured by various distance metrics between inner and outer cortical surfaces, such as the linked distance (Kim et al., 2005), curved streamline distance (Jones et al., 2000) and shortest distance (Fischl and Dale, 2000; Li et al., 2012). For our ROI-based study, cortical thickness was measured in the native space using the shortest distance between inner and outer cortical surfaces at each vertex. For each session, regional cortical thickness was defined as the average thickness of all vertices belonging to the same ROI. The curvedness (Koenderink and Vandoorn, 1992) of the inner cortical surface was adopted to characterize the local cortical folding as did in Nie et al. (2012). Recent comparison on the curvature-based measurement and the gyrification index (Rodriguez-Carranza et al., 2007) shows that these two types of measurements perform similarly on the inner cortical surfaces. For each session, regional cortical folding was defined as the average curvedness of all vertices belonging to the same ROI.

Measurement of correlations between ROIs

The statistical similarity between two cortical regions can be measured by computing the interregional Pearson's correlation coefficient of cortical properties across subjects after removing the effects of multiple confounding variables. Since the anatomical features of brain might not develop uniformly during this age range (3 to 20 years of age), statistical similarity between two cortical regions might change with ages. Thus, the interregional correlations across all ages and at each age are calculated as below.

Correlations across all ages

A linear regression analysis was performed at each cortical region across all sessions (with one session defined as a scan of a subject, thus each subject probably having several sessions at different ages) in order to remove the effects of multiple confounding variables: gender, and overall mean cortical thickness and curvedness (He et al., 2007). The residual of the regression was treated as the raw value of each ROI. Then, the statistical similarity between two cortical regions was measured by computing the interregional Pearson's correlation coefficient of cortical thickness or cortical folding across all sessions. Since the variable age is not removed in the linear regression, the calculated correlation could represent the similarity between regions across all ages.

Correlations at each year

Another potential analysis method is to calculate the correlation coefficient at each year, and then measure the change of correlations with the age. However, since the number of sessions at certain ages (such as 4 and 5 years of age) is small as shown in Fig. 1, the correlation value might not be estimated accurately at these ages. Thus, a weighted correlation coefficient (Bland and Altman, 1995) is adopted herein to include more sessions at each year (t) by assigning small weights to sessions at other years:

$$r(t)=\frac{\sum_{i=1}^{n} w_i^t x_i y_i-\sum_{i=1}^{n} w_i^t x_i \sum_{i=1}^{n} w_i^t y_i / \sum_{i=1}^{n} w_i^t}{\sqrt{\left(\sum_{i=1}^{n} w_i^t x_i^2-\left(\sum_{i=1}^{n} w_i^t x_i\right)^2 / \sum_{i=1}^{n} w_i^t\right)\left(\sum_{i=1}^{n} w_i^t y_i^2-\left(\sum_{i=1}^{n} w_i^t y_i\right)^2 / \sum_{i=1}^{n} w_i^t\right)}} \quad (1)$$