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Unique developmental trajectories of cortical thickness and surface area

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ABSTRACT

There is evidence that the timing of developmental changes in cortical volume and thickness varies across the brain, although the processes behind these differences are not well understood. In contrast to volume and thickness, the regional developmental trajectories of cortical surface area have not yet been described. The present study used a combined cross-sectional and longitudinal design with 201 MRI-scans (acquired at 1.5-T) from 135 typically developing children and adolescents. Scans were processed using FreeSurfer software and the Desikan–Killiany atlas. Developmental trajectories were estimated using mixed model regression analysis. Within most regions, cortical thickness showed linear decreases with age, whereas both cortical volume and surface area showed curvilinear trajectories. On average, maximum surface area occurred later in development than maximum volume. Global gender differences were more pronounced in cortical volume and surface area than in average thickness. Our findings suggest that developmental trajectories of surface area and thickness differ across the brain, both in their pattern and their timing, and that they also differ from the developmental trajectory of global cortical volume. Taken together, these findings indicate that the development of surface area and thickness is driven by different processes, at least in part.

Introduction

The human brain undergoes dynamic structural changes during development that continue into early adulthood and beyond. Interestingly, factors such as gender, cognitive ability, or psychiatric disorders are often more related to changes in the developmental trajectories of brain areas than to differences in brain structure at any time point in development (Lenroot et al., 2007; Shaw et al., 2006; 2012; Tamnes et al., 2011). Furthermore, different tissue types, brain structures, and neural circuits follow distinct developmental trajectories: whereas white matter increases monotonously until early adulthood, gray matter volume follows an inverted U-shaped trajectory, peaking in late childhood (Giedd and Rapoport, 2010; Lenroot et al., 2007; Reiss et al., 1996; Sowell et al., 1999; 2002; Wilke et al., 2007). The volume of cortical gray matter is likely to reflect numerous characteristics of the underlying neural architecture, such as the number of columns and cells (Panizzon et al., 2009; Rakic, 1995). In turn, these microstructural characteristics may be reflected differentially in its two composite dimensions: cortical thickness and cortical surface area.

The global pattern of early increases in cortical volume and thickness followed by decreases in adolescence is seen throughout the cortex. However, there are regional differences in the timing of this pattern (Giedd et al., 1999; Gogtay et al., 2004; Sowell et al., 2001). Studies have suggested that primary sensory areas show peak volume and thickness first. This is then followed by peaks in higher order association areas in parietal and prefrontal regions (Shaw et al., 2008; Sowell et al., 2004). Although cortical volume is defined as the product of cortical thickness and surface area, very few studies have actively investigated surface area. One recent study by Raznahan et al. (2011) showed curvilinear development of total surface area, with the peak occurring later in males than in females. Most studies have investigated only one of these three measures (cortical volume, thickness or surface area). However, it is not necessarily the case that developmental changes observed in only one dimension give the best assessment of maturation, as other biological factors may contribute to the changes in cortical thickness and surface area (cortical volume is the product of the two). Furthermore, it is unclear to what degree the developmental trajectories of cortical thickness and surface area vary locally, both in terms of their patterns and their timing. Therefore we set out to investigate regional developmental changes in cortical volume, thickness and surface area in typically developing children. We used a surface based method to compare these developmental trajectories in a combined cross-sectional and longitudinal study design. More than 200 MRI scans from 135 typically developing children and adolescents were included. We hypothesized that the developmental trajectories of cortical thickness and surface area would not be parallel, but would differ both in their onset and timing. Second, we hypothesized that the developmental patterns of cortical thickness and surface area would differ between cortical regions.

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Materials and methods

Participants

The present study included a total of 201 MRI-scans from 135 typically developing individuals (92 males; 43 females); 49 participants were scanned twice or more, with an average interval of two years, and an interval range from 1.5 to 5.5 years. Participants were aged between 7.0 and 23.3 years, with above average intellectual levels (see Table 1 for participant characteristics). Participants were recruited through schools and educational centers in the area. For all participants under 18 years of age, a parent participated in a semi-structured interview session with a trained rater to confirm the absence of any psychiatric diagnosis (Diagnostic Interview Schedule for Children [DISC-P])(Costello et al., 1985). In older subjects, the Mini-International Neuropsychiatric Interview (MINI) was conducted to confirm the absence of psychopathology (Sheehan et al., 1998). Individuals with a psychiatric diagnosis (current or prior), major physical illness of the cardiovascular, the endocrine, the pulmonary or the gastrointestinal system, neurological illness, a history of head trauma with unconsciousness, organic brain damage or disease, alcohol or other drug dependence, or full-scale IQ below 75 were excluded from participation. In addition, individuals with a first-degree relative suffering from a psychiatric illness were excluded.

Written informed consent was obtained from all participants. For children under 18 years of age, a parent signed for consent. All individuals participated in at least one or more MRI scanning session and a neuropsychological assessment (Wechsler Adult Intelligence Scale/Wechsler Adult Intelligence Scale-Third Edition [WAIS/WAIS-III] (Wechsler and Wechsler, 2000); Wechsler Intelligence Scale for Children-Revised/Wechsler Intelligence Scale for Children-Third Edition [WISC-R/WISC-III] (Van Haasen et al., 1986). Furthermore, participants and their parents filled out a questionnaire on hand preference (van Strien, 2003) and a questionnaire related to major physical or neurological illness. Children under 13 years of age were acclimated to the scanning procedure in a dummy-scan session prior to the actual MRI session (Durston et al., 2009). An independent clinical neuroradiologist evaluated all MRI-scans. No gross abnormalities were reported for any of the participants. The procedure was approved by the Institutional Review Board of the University Medical Center Utrecht, The Netherlands.

Image acquisition

Magnetic resonance imaging (MRI) scans were acquired on two identical Philips Achieva 1.5 Tesla scanners, using identical 6 element SENSE receiver head coils (Philips, Best, The Netherlands). For definition of all brain measures, a whole brain T1-weighted three-dimensional fast field echo scan with 160–180; 1 mm × 1 mm × 1.2 mm contiguous coronal slices was acquired (256 × 256 matrix, FoV = 256 mm, echo time (TE) = 4.6 ms, repetition time (TR) = 30 ms, flip angle = 30°). There were no significant differences between scanners on any measures.

Table 1
Demographic details.

	Group	
Characteristics	Male	Female
Number of individuals, *n*	92	43
Hand preference, *n*		
Righthanded	73	39
Other	19	4
Height, mean (SD)	163.6 (20.9)	155.2 (17.2)
Weight, mean (SD)	53.66 (19.3)	49.09 (16.2)
IQ, mean (SD)	113.2 (16.2)	123.5 (14.2)
Sibling, *n*	30	6
Total number of scans, *n*	145	56
Number of scans, *n*		
1	52	34
2	28	5
>3	12	4
Age at scan, years		
Mean (SD)	12.6 (4.0)	12.5 (4.2)
Range	7.0–23.3	7.0–23.0

SD, standard deviation; and IQ, intelligence quotient.

Image processing

Cortical reconstruction and volumetric segmentation

All MRI scans were coded to ensure rater blindness to subject identity. Scans were processed and analyzed using the neuroimaging computer network of the department of Psychiatry, University Medical Center Utrecht. Cortical thickness and surface area were estimated using FreeSurfer v5.1.0 software. This is a well-validated and well-documented software program that is freely available for download online (http://surfer.nmr.mgh.harvard.edu/). Technical details of the automated reconstruction scheme are described elsewhere (e.g. Dale et al., 1999; Fischl et al., 1999).

In short, the automated reconstruction involves motion correction, removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Clarkson et al., 2011; Segonne et al., 2004), Talairach transformation (affine registration), segmentation of subcortical white matter, deep gray matter structures and cerebellar structures (Fischl et al., 2004a,b; Hutton et al., 2009; Salat, 2004), intensity normalization (Sled et al., 1998); tessellation of gray white matter boundary automated topology correction (Fischl et al., 2001; Segonne et al., 2007), and surface deformation.

Thickness measurements for each vertex on the tessellated surface were obtained by calculating the closest distance between representations of the cortical surface and the gray/white matter border (Fischl and Dale, 2000). Because the maps are not restricted to the voxel-resolution of the original data, this vertex wise surface reconstruction is a powerful method to detect sub-millimeter change. The morphometric procedures have been demonstrated to show good test–retest reliability across scanner manufacturers and across field strengths (Han et al., 2006; Reuter et al., 2012).

For each individual scan, surface-based maps were constructed for analysis. Thirty-four cortical structures were labeled per hemisphere using the Desikan–Killiany atlas (Desikan et al., 2006). This labeling process involved surface inflation (Fischl et al., 1999) and registration to a spherical atlas based on subject specific cortical folding patterns (Fischl et al., 2004a,b). As information from multiple morphological properties was used to define anatomical landmarks, the accuracy was larger than for volume-based registration approaches in children (Ghosh et al., 2010). For each labeled cortical structure, average thickness (in mm) surface area (in mm^2) and volume (in mm^3) was calculated (as is illustrated in Fig. 1.).

Before quantitative analyses could be performed, output required qualitative inspection (Dewey et al., 2010). Surface reconstruction, cortical parcellation and white matter segmentation were therefore evaluated for accuracy by three experienced raters. Manual edits were performed where needed. Edits included removal of non-brain tissue and perfecting the white matter mask. For these manual interventions standard procedures, documented on the FreeSurfer website, were used.

Longitudinal processing

In order to reduce within subject scan session variability, a longitudinal stream was developed for FreeSurfer by Reuter and Fischl (2011). This method increases repeatability and statistical power (Reuter et al., 2010). All scans in the longitudinal series (n = 49) were processed using this procedure. An unbiased within-subject template and an average image were created, using inverse consistent registration. This reduced the potential over-regularization of longitudinal image processing (Reuter et al., 2012).