Retinal and Optic Disc Findings in Adolescence: A Population-Based OCT Study

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Purpose. To examine the distribution of macular and peripapillary nerve fiber layer (NFL) thickness and optic disc parameters in early-adolescence Australian children and to compare these with previously reported findings in younger children.

Methods. The Sydney Childhood Eye Study is a population-based cross-sectional survey of children's eye health. During 2004 and 2005, 2367 (75.3%) of 3144 eligible year 7 students from a random cluster sample of 21 secondary schools in Sydney, Australia, were examined. The comprehensive eye examination included measurement of macular and NFL thickness and optic disc parameters by optical coherence tomography (StratusOCT; Carl Zeiss Meditec, Dublin, CA).

Results. Macular, NFL thickness, and optic disc parameters were normally distributed in early-adolescence children. Mean (±SD) thicknesses of the central 1 mm, and inner and outer macular rings were 197.4 ± 18.7, 271.9 ± 15.0, and 239.5 ± 13.5 μm, respectively. The foveal minimum thickness was 161.6 ± 19.9 μm. The mean (±SD) of average NFL thickness was 103.6 ± 10.6 μm. Mean (±SD) vertical and horizontal disc diameters were 1.88 ± 0.25 and 1.61 ± 0.20 mm; corresponding cup-to-disc ratios were 0.39 ± 0.14 and 0.44 ± 0.16. There were minimal sex differences in these parameters after adjustment for multiple ocular and demographic variables. Compared with parameters in the childhood group, the macula was generally slightly thicker and the optic disc slightly larger in the early-adolescence group, although differences between these two age groups were small. The foveal minimum and NFL thickness were similar between the two age groups.

Conclusions. This study describes the normative distribution of macular, NFL, and optic disc parameters in early-adolescence children and also demonstrates minimal differences between the sexes. These parameters were also largely unchanged between early childhood and early adolescence, although the comparisons were made in two cross-sectional samples, rather than from longitudinal measures. (*Invest Ophthalmol Vis Sci.* 2008;49:4328–4335) DOI:10.1167/iovs.07-0699

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Qualitative assessment of the macula, peripapillary nerve fiber layer (NFL), and optic disc are important in the diagnosis and management of many retinal and optic nerve conditions. Quantitative assessment can be a useful adjunct, particularly when accurate determination of temporal change is required or when clinical assessment is suboptimal because of patient- or clinician-related factors. Morphometric changes may also be detected before the onset of clinical disease. Meaningful quantitative assessment of these parameters, however, requires precise data on their normative distributions and physiological relationships.

We have reported data on macular,[1] NFL,[2] and optic disc[3] parameters, obtained using optical coherence tomography (OCT), in a large group of predominantly 6-year-old Australian children. Many different studies have reported these data in adults,[4–8] but data on adolescent children are scarce.[9–11] Previous work has also been based on small samples or has been performed with an earlier model or prototype OCT that had lower resolution and scanning speed than the model used in the present study.[9,12]

The transition from childhood to adolescence is also associated with further ocular development, which includes changes in axial length[13] and astigmatism.[14,15] It has been shown in several studies that retinal parameters are associated with ocular biometric variables such as axial length and refraction.[1–4] Several studies have reported changes in retinal parameters with age, although the samples were small.[16–18] Thus, data on age-related changes in retinal biometry, particularly from large datasets, are still scarce.

The purposes of the present study were to examine the normative distribution of macular, NFL, and optic disc parameters in a population-based sample of early-adolescence children and to compare these data with those previously reported in younger children.[1–3]

Methods

The Sydney Myopia Study is a population-based survey of eye health in school children. It was approved by the Human Research Ethics Committee, University of Sydney, the Catholic Education Office, and the Department of Education and Training, New South Wales, Australia. Study procedures adhered to the tenets of the Declaration of Helsinki. We obtained informed written consent from at least one parent and verbal assent from each child before the examinations began.

Detailed study methods,[19] including OCT scanning protocols in the early-childhood group,[1–3] have been described previously. The same procedures and instruments were used in this group of older children and will be described briefly. The city of Sydney was stratified by socioeconomic status, according to data from the Australian Bureau of Statistics (2001 national census), and a random cluster sample of 21 high schools were selected that included a proportional mix of public and private or religious schools. All students in year 7 of the selected schools were eligible to participate. Examinations were conducted during 2004 and 2005. There was no overlap between the early-childhood and -adolescence groups of children examined.

OCT was performed with a StratusOCT (OCT3, software v.4.0.1; Carl Zeiss Meditec, Dublin, CA). The instrument uses partially coherent

Table 1. Characteristics of Children with (Included) and without (Excluded) Scans of the Macula, Peripapillary NFL, and Optic Disc

	Macular Scans		Nerve Fiber Layer Scans		Optic Disc Scans	
	Included *n* = 2068	Excluded *n* = 269	Included *n* = 2132	Excluded *n* = 205	Included *n* = 2098	Excluded *n* = 239
Age (y), *n* (%)						
<12	88 (4.3)	12 (4.5)	92 (4.3)	8 (3.9)	92 (4.4)	8 (3.4)
12–13	1444 (69.8)	189 (70.3)	1490 (69.9)	143 (69.8)	1468 (70.0)	165 (69.0)
13+	536 (25.9)	68 (25.3)	550 (25.8)	54 (26.3)	538 (25.6)	66 (27.6)
Boys, *n* (%)	1071 (51.8)	113 (42.0)*	1106 (51.9)	78 (38.1)*	1089 (51.9)	95 (39.8)*
Ethnicity						
Caucasian	1252 (60.5)	147 (54.7)	1291 (60.6)	108 (52.7)	1277 (60.9)	122 (51.1)†
East Asian	296 (14.3)	54 (20.1)	308 (14.5)	42 (20.5)	296 (14.1)	54 (22.6)
Middle Eastern	147 (7.1)	17 (6.3)	150 (7.0)	14 (6.8)	148 (7.1)	16 (6.7)
Other‡	373 (18.0)	51 (19.0)	383 (18.0)	41 (20.0)	377 (18.0)	47 (19.7)
SEq (D)§	0.53 ± 1.27	0.15 ± 1.73*	0.52 ± 1.29	0.19 ± 1.71*	0.52 ± 0.03	0.23 ± 0.11*
AL (mm)§	23.38 ± 0.84	23.45 ± 0.93	23.39 ± 0.84	23.38 ± 0.93	23.39 ± 0.02	23.38 ± 0.06
VA (letters)§	56.4 ± 5.7	55.1 ± 7.3*	56.4 ± 5.7	55.3 ± 7.7	56.4 ± 0.1	55.5 ± 0.5
Height (cm)§	156.1 ± 8.0	156.3 ± 7.7	156.1 ± 7.9	156.5 ± 7.8	156.1 ± 0.2	156.4 ± 0.5

SEq, spherical equivalent; AL, axial length; VA, logMAR VA.

* $P < 0.05$, included vs. excluded children.

† $P = 0.003$ (χ^2).

‡ Children of South Asian (Indian/Pakistani/Sri Lankan), South American, African, Indigenous Australian, and Melanesian/Polynesian backgrounds.

§ Mean ± SD.

laser light (wavelength 820 nm) in an interferometer to perform multiple axial (A) scans along straight or circular paths. A thresholding algorithm based on the reflectivity of various components of the retina was used to determine key retinal boundaries. Measurements made by this instrument have recently been shown to be reliable.[20,21]

Scans were performed through dilated pupils by using fast scan protocols and were monitored with an infrared-sensitive video camera. Scan quality was assessed during scanning to maximize the quality of the scans and minimize such problems as centration and focus. Poor scans were repeated until the best scans were obtained. Macular scans consisted of six bisecting 6-mm long line scans, each of which comprised 128 A-scans. The 6-mm diameter macular region was subdivided into quadrants and concentric regions: central macula (radius 0.5 mm), inner macula (annulus with outer radius 1.5 mm), and outer macula (annulus with outer radius 3 mm). The peripapillary nerve fiber layer scan comprised 256 A-scans in a circular scan path 3.4 mm in diameter. Optic disc scans were similar to macular scans, except that individual scan lines were 4 mm long. The optic disc margin was defined as the termination of the retinal pigment epithelium, whereas the optic cup margin was at the intersection of the vitreoretinal interface and a plane 150 μm anterior to the plane of the optic disc margin. Optic nerve head parameters were corrected after the scan for magnification secondary to refractive error and axial length.[3]

The detailed examination protocol also included assessment of best corrected visual acuity, ocular motility, cycloplegic autorefraction (Canon RK-F1; Canon, Tokyo, Japan), measurement of axial length, corneal power, and anterior chamber depth (IOLMaster; Carl Zeiss Meditec, Inc.), aberrometry, slit-lamp biomicroscopy, and mydriatic digital fundus photography. Cycloplegia was achieved by instilling cyclopentolate 1%, 2 minutes after administration of amethocaine. Phenylephrine 2.5% (1 drop) was also instilled in a small number of children to obtain adequate mydriasis (at least 6 mm).

A 173-item questionnaire was used to obtain data on a wide range of topics, such as ocular and general medical history, birth parameters, visual habits, and demographics. Ethnicity was determined on the basis of self-identification by the parents, combined with information on the child's place of birth. Each child was categorized into a particular ethnic group if both parents shared that ethnic origin; otherwise, the child was identified as having mixed ethnicity.

Statistical Analysis

Analyses were performed with commercial software (SAS, ver. 9.1.3; SAS Institute, Cary, NC). Only complete scans with signal strengths greater than 5 were used, and an average of three macular, NFL, and optic disc scans were used in the analyses. The distribution of each retinal or optic disc parameter was analyzed using Proc Univariate. Comparisons of means between sex categories were made with mixed models (Proc Mixed) adjusting for covariates (ANCOVA) with school indicator as the random effect. The distributions of retinal and optic disc parameters in year 1 and 7 students were compared by using the Kolmogorov-Smirnov two-sample test. Levene's test for homogeneity was used to compare the variance of measurements. Results are presented for right eyes only, as there were no significant differences in measures between the right and left eyes.

Results

General Characteristics

Of 3144 eligible year 7 students, 777 did not agree to participate, leaving 2367 (75.3%) participants. Fourteen participating children were not examined, because they were absent from school, leaving 2353 participants who were examined. Sex and ethnic background were similarly distributed between participants and nonparticipants (girls 48.4%; European Caucasian 67.8%). Children with ophthalmic disease ($n = 7$) were excluded from the present study. These included congenital glaucoma, optic nerve hypoplasia, microphthalmos, congenital nystagmus, and cortical blindness due to cerebral palsy. Among the remaining children, the number who had macular, NFL, and optic disc scans of adequate quality were 2068 (88%), 2132 (91%), and 2098 (90%), respectively. The characteristics of the included and excluded children are shown in Table 1. Among the children included in this analysis, 95% were aged 12 or 13 years (range, 11.1–14.4 years). Boys constituted just under 52% of the sample. Mean spherical equivalent, axial length, visual acuity and height were approximately +0.50 D, 23.4 mm, 56 logMAR letters, and 156 cm, respectively. There were no significant differences in age, axial length, and height between the included and excluded children for any of the scan proto-

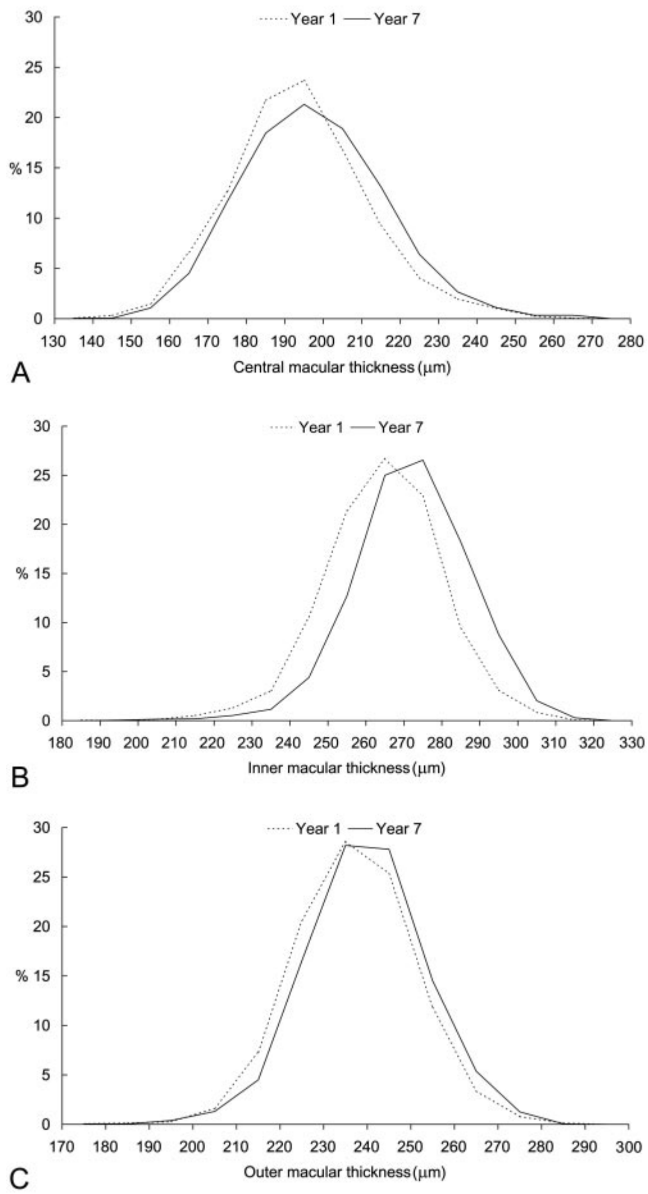

FIGURE 1. Comparative distribution in right eyes of (**A**) central, (**B**) inner, and (**C**) outer macular thickness between year 1 (n = 1543) and year 7 (n = 2068) students.

cols. Visual acuity was around 1 letter worse in the children excluded from the analysis. but this was statistically significant only for the macular scans. The children excluded were also slightly less likely to have a hyperopic refraction, were more likely to be female or to have East Asian ethnicity, and were less likely to have European Caucasian ethnicity.

Overall Distribution

Macular thickness was normally distributed (Fig. 1) and was least at the foveal minimum, followed by the central macula and outer macular ring (Table 2). The inner ring was the thickest macular region. Variability in macular thickness was significantly different ($P < 0.0001$) between the concentric macular regions and was greatest at the foveal minimum (SD 19.9 μm) and central macula (SD 18.7 μm). Variability in other regions was generally around 15 μm (SD). A global comparison of the thickness of inner macular regions found that they were significantly different from each other ($P < 0.0001$). The inner temporal region was thinner than other inner macular regions by approximately 10 μm, whereas differences for the outer regions were around 6 to 33 μm. Pair-wise comparison of inner macular regions, with Bonferroni correction for multiple comparisons, showed no significant difference in mean thickness between the inner nasal region with the inner inferior and inner superior regions ($P < 0.5$). The inner temporal region was significantly thinner ($P = 0.002$) than all other inner macular regions. Global and pair-wise comparison of outer macular regions showed that they were all significantly different from each other (all $P < 0.0001$). In 95% of children, the macula was within ±40 μm (2 SD) of the mean foveal minimum and central macular thickness, and within ±30 μm of the mean inner ring and outer ring average thickness.

The distribution of average NFL thickness was normal (data not shown), with a mean (SD) of 103.6 (10.6) μm. The variability of NFL thickness was significantly different between the four quadrants ($P < 0.0001$). NFL thickness followed a double-hump configuration around the optic nerve head, being thicker in the superior and inferior regions (Table 2, Fig. 2) than the temporal or nasal regions ($P < 0.0001$, global comparison). Pair-wise comparison of NFL quadrants found that they were all significantly different from each other ($P < 0.0001$), although the difference between inferior and superior NFL quadrants was not highly significant ($P = 0.034$). The superior quadrant was only 1.4 μm thicker than the inferior quadrant ($P = 0.01$). The mean ratio of superior maximum to inferior maximum thickness was 1.03. The nasal quadrant was significantly thicker (by 7.4 μm, $P < 0.0001$) than the temporal quadrant. The ratio of superior-to-temporal quadrant and inferior-to-temporal quadrant average thickness was around 1.7. This was similar to the vertical-to-horizontal thickness ratio (1.66). NFL thickness in 95% of children ranged from around 50 to 100 μm in the temporal quadrant and from around 50 to 115 μm in the nasal quadrant. Similarly, 95% of children had superior NFL thickness between 95 and 164 μm superiorly and between 92 and 164 μm inferiorly.

Almost all optic nerve head parameters were normally distributed (Fig. 3), apart from optic cup area (Fig. 3F), which was positively skewed so that most children had relatively small optic cup areas. Optic disc and optic cup shapes were mostly vertically oval. The mean vertical cup-to-disc ratio (0.39) was slightly smaller than the mean horizontal cup-to-disc ratio (0.44). The average thickness of the NFL at the optic disc margin (average nerve width) was greater along the vertical (0.38 ± 0.05 μm) than the horizontal meridian (0.29 ± 0.05 μm). In 95% of the children, the optic disc diameter ranged from 1.4 to 2.4 mm (vertical) and 1.2 to 2.0 mm (horizontal); the optic cup diameter ranged from 0.2 to 1.3 mm (vertical) and 0.2 to 1.2 mm (horizontal); the upper 95% limit of the cup-to-disc ratio was 0.7 (vertical) to 0.8 (horizontal). The correlation of neural rim area with average NFL thickness was 0.35 ($P = 0.0001$).

Sex differences in macular thickness and volume were statistically significant after adjusting for age, spherical equivalent refraction, height, ethnicity, and cluster sampling (Table 3). The results were similar when adjusted for axial length instead of spherical equivalent refraction. The foveal minimum, central macula, inner macula ring, and outer temporal quadrant were significantly thicker in the boys than in the girls ($P < 0.0001$), whereas the outer inferior quadrant was thicker in the girls ($P = 0.003$). Central and total macular volumes were significantly greater in the boys than in the girls, although the differences were marginal (not shown).

TABLE 2. Macular Thickness and NFL and Optic Disc Parameters in Right Eyes

Parameter	Mean	SD	Range	Kurtosis	Skew
Macular thickness, μm (n = 2068)					
Foveal minimum	161.6	19.9	115–266	1.8	1.0
Central macula	197.4	18.7	139–277	0.7	0.4
Inner ring average	271.9	15.0	199–318	1.1	−0.4
Inner temporal	263.0	15.5	184–316	1.9	−0.5
Inner superior	275.8	15.2	200–322	0.8	−0.3
Inner nasal	275.0	17.1	175–326	2.9	−0.8
Inner inferior	274.1	15.1	206–317	0.6	−0.3
Outer ring average	239.5	13.5	177–287	0.4	−0.1
Outer temporal	225.9	14.8	159–340	3.6	0.3
Outer superior	242.3	13.9	181–300	0.5	0.0
Outer nasal	258.4	16.4	157–309	2.1	−0.5
Outer inferior	231.5	14.4	167–277	0.3	0.0
NFL thickness, μm (n = 2132)					
Global average	103.6	10.6	57.5–165	1.0	0.1
Temporal average	74.6	12.8	40.7–149	1.4	0.7
Superior average	129.7	17.5	72.3–192	0.3	0.1
Nasal average	82.0	16.7	36.3–216	2.0	0.6
Inferior average	128.3	18.6	64.3–269	2.1	0.3
Superior maximum	165.7	19.9	100.3–264	0.7	0.3
Inferior maximum	163.8	22.6	88.3–395	6.0	0.9
Max-min difference	131.9	19.1	76.3–356	9.8	1.3
Other NFL parameters					
$Superior_{max}/inferior_{max}$ ratio	1.03	0.15	0.44–1.61	0.3	0.3
$Superior_{max}/temporal_{average}$ ratio	2.28	0.38	1.07–4.00	0.6	0.5
$Inferior_{max}/temporal_{average}$ ratio	2.26	0.42	1.24–6.37	5.6	1.1
$Superior_{max}/nasal_{average}$ ratio	2.12	0.50	0.81–7.79	9.6	1.7
Vertical/horizontal thickness ratio	1.66	0.36	0.93–2.46	0.7	0.4
Optic disc parameter (n = 2054)*					
Horizontal disc diameter (mm)	1.61	0.20	1.05–2.53	0.4	0.5
Vertical disc diameter (mm)	1.88	0.25	0.85–3.00	0.5	0.2
Horizontal cup diameter (mm)	0.70	0.28	0.03–1.86	0.3	0.4
Vertical cup diameter (mm)	0.73	0.28	0.01–1.70	−0.1	0.2
Disc area (mm^2)	2.34	0.41	1.18–4.67	1.0	0.6
Cup area (mm^2)	0.46	0.32	0.003–2.30	2.2	1.3
Neuroretinal rim area (mm^2)	1.93	0.42	0.92–4.67	1.5	0.7
Horizontal cup-to-disc ratio	0.44	0.16	0.02–0.88	−0.2	0.0
Vertical cup-to-disc ratio	0.39	0.14	0.02–0.78	−0.4	−0.1
Cup-to-disc area ratio	0.21	0.14	0.009–0.84	1.7	1.2

* Optic disc parameters were magnification-corrected.

After adjusting for age, spherical equivalent refraction, height, ethnicity, and cluster sampling, NFL thickness was similar between the boys and the girls, with differences of less than 1.3 μm between corresponding quadrants (Table 3). When examined in clock hours (30° sectors), NFL thickness was significantly greater in the boys at 9 (temporal, by 0.9 μm) and 12 (by 4.2 μm) o'clock, and in the girls at 10 (by 2.0 μm), 4 (by 2.9 μm), and 7 (by 2.2 μm) o'clock.

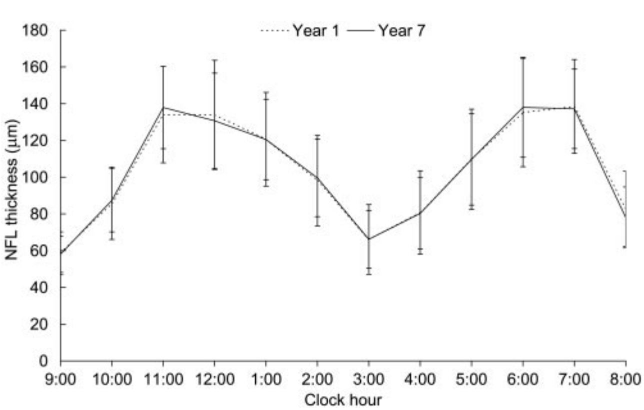

FIGURE 2. Comparative distribution of peripapillary nerve layer thickness by clock hour in right eyes between year 1 (n = 1369) and year 7 (n = 2132) students. Error bars, standard deviations.

After adjustment for age, ethnicity, axial length, and cluster sampling, the optic disc diameter, optic disc area, and neural rim area were significantly greater in the girls than in the boys, whereas the cup-to-disc ratios were significantly smaller in the girls. These differences, however, were marginal.

The comparative distribution of macular thickness in the year 1 and 7 students is shown in Figure 1. Overall, the year 1 students[1] (age range, 11.1–14.4 years) had slightly thinner central (mean ± SD, 193.6 ± 17.9 μm, $P < 0.0001$; Fig. 1A), inner (264.3 ±15.2 μm, $P < 0.0001$; Fig. 1B), and outer macular (236.9 ±13.6 μm, $P < 0.0001$; Fig. 1C) regions than did the year 7 students (Table 2). The foveal minimum thickness in the year 1 students[1] (161.1 ± 19.4 μm) was significantly thinner than in the year 7 students ($P = 0.009$), although only marginally so.

In Figure 2, the distribution of peripapillary NFL thickness was not significantly different between the year 1 and 7 students ($P = 0.4$). The mean ± SD NFL thickness in the year 1 students was 103.7 ± 11.4 μm, which was not significantly different from values of 103.6 (10.6) μm for the year 7 students ($P = 0.9$).

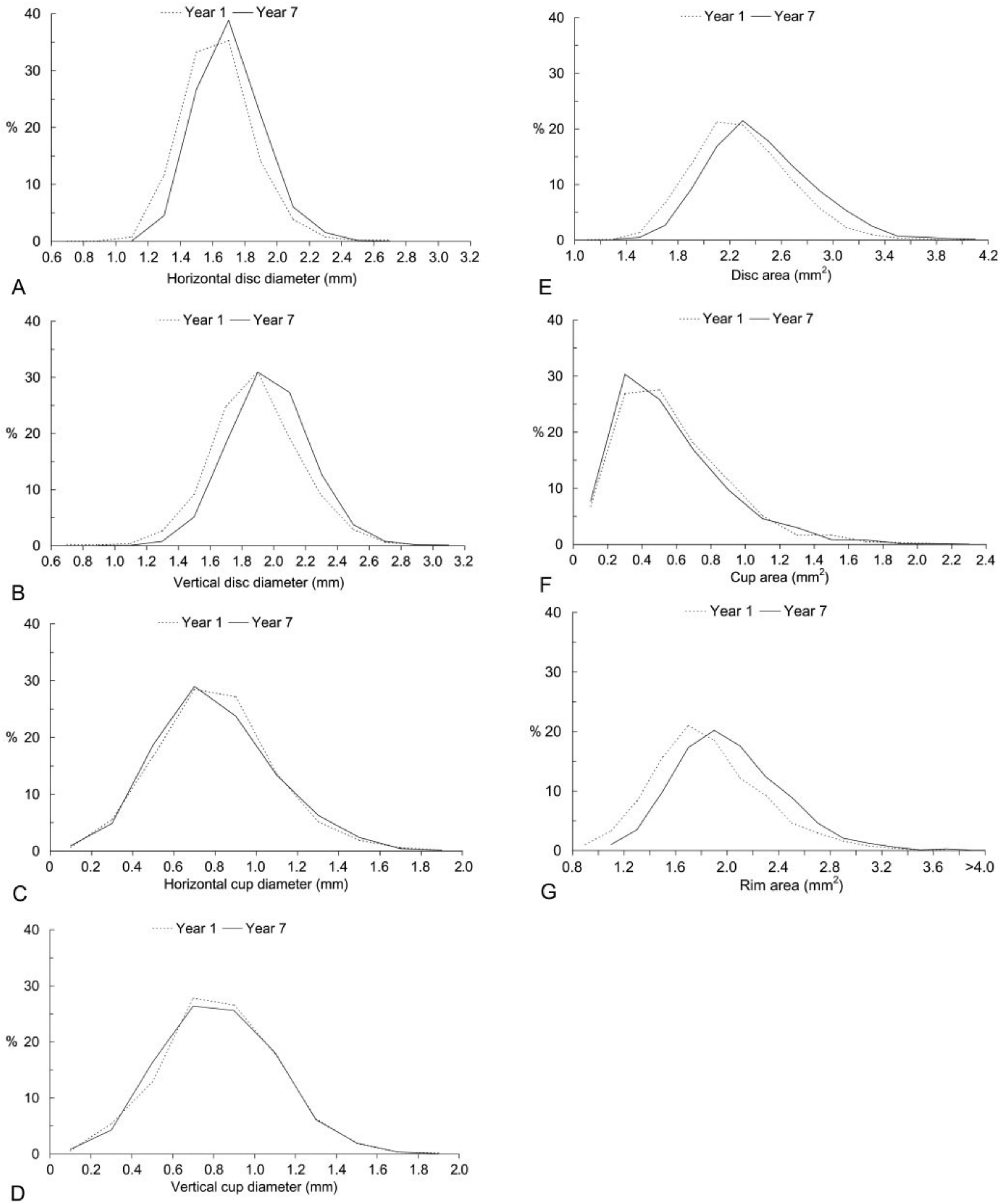

FIGURE 3. Comparative distribution in right eyes of (**A**) horizontal disc diameter, (**B**) vertical disc diameter, (**C**) horizontal cup diameter, (**D**) vertical cup diameter, (**E**) optic disc area, (**F**) optic cup area, and (**G**) neural rim area. All parameters were adjusted for magnification (year 1, $n = 1309$; year 7, $n = 2054$).

Optic disc diameter and area were slightly larger in the year 7 than in the year 1 students (Figs. 3A, 3B, 3E, all $P < 0.0001$). Horizontal and vertical optic cup diameters were not significantly different between the year 1 and year 7 students (Figs. 3C–D, $P = 0.3$ and $P = 0.2$, respectively); however, the optic cup area was slightly smaller in the year 7 students (Fig. 3F, $P =$

Table 3. Sex-Specific Distribution of Selected Macular, NFL, and Optic Disc Parameters

	Girls	Boys	Difference (Girls − Boys)	
	Mean ± SD*	Mean ± SD*	Mean (95% CI)	*P*
Macular thickness, μm†	*n* = 997	*n* = 1071		
Foveal minimum	158.7 ± 18.8	164.2 ± 20.5	−4.2 (−6.4 to −2.0)	0.0001
Central macula	193.0 ± 17.7	201.5 ± 18.6	−7.1 (−9.3 to −5.0)	<0.0001
Inner ring average	268.8 ± 15.0	274.9 ± 14.3	−5.0 (−6.6 to −3.5)	<0.0001
Inner temporal	259.4 ± 15.8	266.3 ± 14.6	−5.8 (−7.4 to −4.3)	<0.0001
Inner superior	273.0 ± 15.3	278.5 ± 14.6	−4.6 (−6.1 to −3.0)	<0.0001
Inner nasal	271.5 ± 17.5	278.2 ± 16.1	−5.6 (−7.3 to −3.8)	<0.0001
Inner inferior	271.2 ± 15.0	276.7 ± 14.7	−4.2 (−5.8 to −2.6)	<0.0001
Outer ring average	238.9 ± 14.0	240.1 ± 13.0	−0.3 (−1.4 to 0.8)	0.6
Outer temporal	224.0 ± 15.0	227.6 ± 14.5	−2.6 (−3.8 to −1.4)	<0.0001
Outer superior	242.0 ± 14.4	242.6 ± 13.3	0.1 (−1.3 to 1.5)	0.9
Outer nasal	257.6 ± 17.2	259.1 ± 15.6	−0.5 (−2.0 to 1.0)	0.5
Outer inferior	231.8 ± 14.8	231.2 ± 14.1	1.7 (0.6 to 2.8)	0.003
NFL thickness, μm†	*n* = 1026	*n* = 1106		
Average	103.9 ± 10.5	103.4 ± 10.7	−0.4 (−1.3 to 0.5)	0.2
Temporal average	74.7 ± 13.0	74.4 ± 12.7	1.3 (0.1 to 2.5)	0.4
Superior average	129.6 ± 17.4	129.8 ± 17.7	−1.3 (−2.7 to 0.05)	0.4
Nasal average	82.4 ± 17.2	81.7 ± 16.1	−0.5 (−1.8 to 0.9)	0.04
Inferior average	129.0 ± 18.7	127.7 ± 18.5	−1.2 (−2.8 to 0.5)	0.07
Optic disc parameters‡§	*n* = 983	*n* = 1071		
Horizontal disc diameter, mm	1.60 ± 0.20	1.61 ± 0.20	0.02 (0.002 to 0.03)	0.02
Vertical disc diameter, mm	1.88 ± 0.24	1.87 ± 0.26	0.02 (0.0002 to 0.04)	0.048
Horizontal cup diameter, mm	0.62 ± 0.33	0.66 ± 0.34	−0.02 (−0.05 to 0.005)	0.1
Vertical cup diameter, mm	0.65 ± 0.33	0.68 ± 0.34	−0.03 (−0.05 to 0.005)	0.1
Disc area, mm^2	2.34 ± 0.41	2.34 ± 0.42	0.04 (0.02 to 0.07)	0.002
Cup area, mm^2	0.40 ± 0.33	0.43 ± 0.34	−0.03 (−0.06 to 0.004)	0.09
Neuroretinal rim area, mm^2	1.94 ± 0.42	1.91 ± 0.43	0.07 (0.03 to 0.1)	0.001
Horizontal cup-to-disc ratio	0.39 ± 0.19	0.41 ± 0.20	−0.02 (−0.04 to −0.003)	0.02
Vertical cup-to-disc ratio	0.35 ± 0.17	0.36 ± 0.17	−0.02 (−0.04 to −0.004)	0.02
Cup-to-disc area ratio	0.19 ± 0.14	0.20 ± 0.15	−0.02 (−0.03 to −0.005)	0.005

Sex differences were adjusted for multiple variables.
* Unadjusted values.
† Sex differences adjusted for age, ethnicity, height, refraction, and cluster sampling.
‡ Sex differences adjusted for age, ethnicity, axial length, and cluster sampling.
§ Optic disc parameters were magnification-corrected.

0.005). Neural rim area was significantly larger in the year 7 students (Fig. 3G, $P < 0.0001$).

Discussion

In this study, we found that the macular, NFL, and most of the optic disc parameters in early-adolescence children were normally distributed. This finding is consistent with our observation of these parameters in younger children[1–3] and with other ocular biometric variables such as corneal curvature and axial length.[22]

Variability in Retinal and Optic Disc Parameters

These data also reveal that there is marked variability in macular and NFL thickness, as well as in optic disc parameters. Within 2 standard deviations of the mean thickness (equivalent to 95% of the children), the foveal minimum thickness differed by ~160%, whereas central macular thickness differed by ~150%, between the higher and the lower limits. In contrast, inner and outer macular ring thickness measures were less variable (~125%). NFL thickness in quadrants varied by around 170%, 180%, 200%, and 230% for the inferior, superior, temporal, and nasal quadrants, respectively. Average NFL thickness, however, varied by ~150%. Similarly, optic disc diameter varied by up to 160% to 170%, whereas optic disc area varied by ~200%. Optic cup parameters were markedly more variable (up to eightfold). Neural rim area, which reflects the amount of neural tissue within the optic nerve,[23] varied by ~250%, which is much greater than the variability of average NFL thickness. We speculate that this difference is due to increased glial tissue in larger discs. Alternatively, reflectivity of the nerve fibers may also be reduced around the region of the optic cup,[24] because of the sloped orientation of nerve fibers relative to the scanning beam as they enter the optic nerve. This decrease in reflectivity potentially increases error in determining the vitreoretinal boundary in steeper optic cups, although it should be explored in studies directly comparing OCT versus photographic methods. Of interest, the correlation between neural rim area and average NFL thickness was lower than expected ($r = 0.35$), perhaps because of a difference in the amount of glial tissue between the two regions. Finally, variables that show lower variability in the population, such as NFL thickness compared with neural rim area, are likely to be better indicators of abnormality.

Comparison with Other Studies

Few studies have been conducted to explore retinal and optic disc parameters in children and adolescents,[1–3,8–10,25] only three of which were population-based.[1–3] In comparing our data with those in other studies, therefore, it is important to note differences in sample characteristics such as sample size, age, ethnicity, refractive error, axial length, and the instrument used.

Hess et al.[9] measured the macula of 104 young and early-adolescence children (aged 3–17 years) with the Stratus OCT3 (Carl Zeiss Meditec, Inc.). They reported outer macular thickness (228 ± 17.7–245.9 ± 16.3 μm) similar to the measures from our study, although the thickness of other macular subregions were not reported. Kee et al.[26] also measured foveal thickness in children (mean age, 8.5 years) and found this to be 157.4 μm, which is comparable to our findings. In early histological studies, foveal thickness was reported by Hogan et al.[27] to be 130 μm. This slightly thinner macula is possibly due to tissue shrinkage associated with histologic preparation. As found in our previous study of younger children,[1] there were subtle sex differences in various parameters in this early-adolescence group. In both samples, the inner macula was significantly thicker in the boys than in the girls, whereas outer macular thickness was similar in both sexes, consistent with findings by others.[28]

Our findings on NFL thickness in early-adolescence children compare closely to results in previous studies in children[9,10] and adults.[29] NFL thickness is taken to be greater inferiorly than superiorly in clinical practice,[30] but several studies have shown that NFL thickness is more or less equal between the inferior and superior quadrants.[2,6,9,10] The average NFL thickness also compares closely to adult values.[7] In our studies, average NFL thickness was significantly greater in the younger group of boys than in the girls, although only marginally so, whereas there were no significant differences in the early adolescence group. These marginal-to-nonsignificant differences between the sexes in average NFL thickness are in keeping with previous studies.[6,10,18,31–33]

Comparative data for optic disc parameters in children are limited.[8,25] Mansour et al.[8] examined optic disc stereophotographs of younger volunteer children (age range, 2 to 10 years; $n = 66$) and reported optic discs sizes that were larger in both horizontal (~1.8 mm) and vertical (~2.0 mm) diameters. The cup-to-disc ratios were smaller (~0.30) than in our study; in white children, the cup-to-disc ratio was 0.15. Tong et al.,[25] however, found similar mean vertical (0.38, SD 0.10) and horizontal (0.45, SD 0.13) cup-to-disc ratios in a sample of 100 emmetropic children aged 8 to 13 years. These children, however, were not examined by using stereophotographs. The difference between our findings and those of Mansour[8] may be due to a difference in age and instrument used. Optic disc parameters showed statistically significant, but only slight, differences between the sexes in our study sample. There were no significant differences between the sexes in optic disc parameters in the younger group of children examined.[3] This finding is consistent with those in previous studies.[8,18,23,34,35]

Developmental Perspective

Although there are numerous studies of the effects of age on retinal and NFL thickness in adults, few studies have examined age-related changes in retinal parameters in young children.[16,17,29] Alamouti and Funk[16] examined 100 subjects cross-sectionally and found that retinal thickness at the temporal disc margin, measured by OCT, decreased by 0.53 μm per year ($P = 0.0002$). The ages of their subjects, however, ranged from 0 to 80 years, and the number of subjects in each age group was small (~6% were aged <20 years), which could have increased measurement variability in each age group. Furthermore, changes in retinal thickness at the temporal disc margin, do not necessarily affect macular thickness. In our study, mean foveal minimum thickness was not different between the early-childhood and -adolescence groups of children. However, the thickness of the central, inner, and outer macula was all slightly greater in the adolescents than in the younger children (Fig. 1). This suggests that foveal minimum thickness remains essentially unchanged in early childhood, although other macular areas become slightly thicker. An increase in macular thickness up until early adulthood is also suggested by findings in the study by Chan et al.[36] ($n = 37$), which reported a mean central macular thickness of 212 ± 20 μm and a foveal minimum thickness of 182 ± 23 μm, although their study sample was relatively small. Longitudinal data are needed to confirm these findings.

Thinning of the peripapillary NFL with age has been more consistently reported.[16–18,29] In the study by Poinoosawmy et al.,[29] 150 normal volunteers aged 5 to 90 years were examined with a scanning laser polarimeter. The NFL was found to become thinner with age (by 0.38 μm/year, $P < 0.001$). NFL thinning was more marked in the inferior and superior quadrants. A similar rate of NFL thinning (0.44 μm/year, P = 0.0019) was found by Alamouti and Funk[16] in their study of 100 healthy subjects (age range, 6–79 years) examined using an OCT2. Bowd et al.[18] also reported OCT NFL thinning with age in a sample of 155 Caucasian subjects (age range, 23– years). Thinning was greater in the nasal, inferior, and superior quadrants. Kanamori et al.,[17] however, found age-related NFL thinning in the inferior, superior, and temporal quadrants, but no correlation with the nasal quadrant. In our two cross-sectional studies,[2] the mean NFL thickness was not different between the two age groups, suggesting that NFL thickness remains constant in early childhood and adolescence.

The human optic disc appears to enlarge with age. According to Rimmer et al.[37] in a study of 95 histologic specimens obtained at autopsy of patients ranging in age from 4.8 months gestation to 21.9 years, 95% of the growth of the optic disc occurs before the age of 1 year. They suggested that a small amount of optic disc growth occurs during adolescence. Bengtsson[38] found a small increase in optic disc diameter between the ages of 25 and 75 years. Rimmer et al.[37] also found that the optic disc diameter in their 10- to 22-year-old patients was around 10% less than previously found for adults.[23,39,40] This apparent enlargement of the optic disc from childhood is most likely due to an increase in glial and septal elements rather than in neural tissue. The age-related differences in optic disc size between childhood and adulthood may also be confounded by concurrent changes in refraction and axial length, differences in magnification of the fundus cameras used, and racial differences and differences between the sexes in the different samples.

The main strengths of this study are its large, population-based sample, uniformity of examination procedures, high participation rate, and low rate of ocular disease.[41] A potential weakness was that macular and NFL scans were performed without adjusting the size of the scan pattern for magnification due to nonstandard axial length and refraction. Potentially, this could have resulted in scans being performed in noncorresponding areas of the macula or peripapillary NFL. In a previous study,[21] we reported that macular and NFL measurements performed without adjustment for magnification at the time of scanning did not deviate significantly from measurements performed with adjustment for magnification. This may not apply to eyes that are very long or very short or those that have high refractive errors, and so data from the present study should be accepted with caution in these circumstances.

In summary, we found that almost all macular, NFL, and optic disc parameters as measured by OCT in this population-based sample of early-adolescence children were normally distributed. We have also established a population-based normative database of these parameters in children. Slight increases in macular and optic disc parameters, the lack of difference in NFL parameters between the early-childhood and -adolescence groups, and the similarity of these parameters to that found in adults, suggest that the growth of these parameters is almost complete at or soon after birth, and certainly by early childhood. Ideally, though, age-related changes will be better shown in large, longitudinal studies.

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