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Eye size and shape in newborn children and their relation to axial length and refraction at 3 years

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Abstract

Purpose: To determine if eye size and shape at birth are associated with eye size and refractive error 3 years later.
Methods: A subset of 173 full-term newborn infants from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort underwent magnetic resonance imaging (MRI) to measure the dimensions of the internal eye. Eye shape was assessed by an oblateness index, calculated as 1 − (axial length/width) or 1 − (axial length/height). Cycloplegic autorefraction (Canon Autorefractor RK-F1) and optical biometry (IOLMaster) were performed 3 years later.
Results: Both eyes of 173 children were analysed. Eyes with longer axial length at birth had smaller increases in axial length at 3 years ($p < 0.001$). Eyes with larger baseline volumes and surface areas had smaller increases in axial length at 3 years ($p < 0.001$ for both). Eyes which were more oblate at birth had greater increases in axial length at 3 years ($p < 0.001$). Using width to calculate oblateness, prolate eyes had smaller increases in axial length at 3 years compared to oblate eyes ($p < 0.001$), and, using height, prolate and spherical eyes had smaller increases in axial length at 3 years compared to oblate eyes ($p < 0.001$ for both). There were no associations between eye size and shape at birth and refraction, corneal curvature or myopia at 3 years.
Conclusions: Eyes that are larger and have prolate or spherical shapes at birth exhibit smaller increases in axial length over the first 3 years of life. Eye size and shape at birth influence subsequent eye growth but not refractive error development.

Introduction

Myopia is an increasingly prevalent public health problem, with particularly high rates amongst Chinese East Asian populations such as those in Taiwan and Singapore.[1–3] Pathological myopia is associated with potentially blinding complications,[4–8] and considerable lifetime socioeconomic costs.[9–11] Understanding the pathogenesis of myopia is important for formulating preventive strategies, whether pharmacological or optical.[12–21]

Several risk factors for myopia in children have been identified in large-scale epidemiologic studies. These include a genetic basis for myopia susceptibility,[22,23] and a diverse range of environmental factors such as near-work,

outdoor activity, socio-economic background and nutrition.[24–29] However, the pathogenetic mechanisms underlying myopia development remain poorly understood, with the relative contributions of genetic and environmental influences being an unresolved issue.

The shape of the eyeball has been receiving increasing attention as a possible biomarker, descriptor or risk factor for myopia. Myopia has traditionally been regarded as a mismatch between the refractive power of the eye and the axial length (AL) of the eyeball. However, it is increasingly being recognised that the anatomical deviations in myopia involve more complex three-dimensional changes than are captured in a single-dimension axial measurement.[30–35] The shape of the eyeball is a variable that can now be investigated with high-resolution *in vivo* imaging techniques such as magnetic resonance imaging (MRI) and computer software for three-dimensional modelling. It has been suggested that the shape of the eyeball may determine future refractive development. Experiments in both chicks and primates have shown that peripheral defocus and regional form deprivation[36–41] lead to localised compensatory alterations in eye growth and shape. Conversely, variations in peripheral image quality resulting from different eye shapes could lead to image-dependent eye growth and refractive error. In a prospective study of Dutch trainee pilots, the presence of peripheral hyperopic astigmatism at baseline predicted future myopic shift, suggesting that a prolate eyeball shape was a risk factor for subsequent myopia.[42] Similarly, a prospective study in children found that children who became myopic had more hyperopic relative peripheral refractive errors than emmetropes.[43,44] More recently, based on MRI data, Gilmartin has proposed that a spherical posterior chamber shape may constitute a biomechanical limitation on further axial elongation in myopia while eyes with oblate shapes may be predisposed to further myopia progression.[45]

We have previously reported on the distribution and variability of ocular dimensions and shape in the normal infant.[46] Evaluating ocular dimensions and shape in infancy provides information on the baseline shape of the globe, before any extrauterine environmental stimuli can have an effect. The aim of this study is to determine if measures of eye size and shape in the newborn are correlated with subsequent AL and refractive changes.

Methods

This study was conducted on a subset of the birth cohort study termed GUSTO: Growing Up in Singapore Towards healthy Outcomes. This is Singapore's largest and most comprehensive birth cohort study and is designed to adopt a life course approach to define the importance of foetal and developmental factors in early pathways to metabolic diseases.

The study population consists of the children of all pregnant women aged 18 years and above attending the first trimester antenatal dating ultrasound scan clinic at the two major public maternity units in Singapore, namely the National University Hospital and the KK Women's and Children's Hospital. These subjects are Singapore citizens or permanent residents who are Chinese, Malay or Indian with homogenous parental ethnic background and have the intention to reside in Singapore for the next 5 years. Mothers on chemotherapy, psychotropic drugs or with Type I Diabetes Mellitus were excluded. Only women who agreed to donate birth tissues such as cord, placenta and cord blood at delivery were included. Out of the 3335 screened, 1163 (35%) pregnant women were recruited from June 2009 to September 2010.

A key feature of the GUSTO study is to have body fat measures on all participants. After delivery, the children of enrolled subjects underwent whole body magnetic resonance imaging (MRI), including brain imaging, at 5–17 days to accurately document body fat.

Written informed consent from the parents of subjects was obtained. Most of the children had returned home by the time of the MRI, and many parents were unwilling to return to the hospital for the scan. Also, as we did not sedate the babies, many children who were unable to sleep through the scan had to be excluded. As such, only approximately 15% of the total cohort provided data for this study.

The study was approved by the Centralized Institutional Review Boards of the Singapore Health Services and Domain Specific Review Board of National Health Care Group.

MRI acquisition and eye shape analysis

Data acquisition

At 5–17 days of life, neonates underwent fast spin-echo T2-weighted MRI (TR = 3500 ms; TE = 110 ms; FOV = 256 mm × 256 mm; matrix size = 256 × 256; 50 axial slices with 2.0 mm thickness) scans using a 1.5-Tesla GE scanner with an 8-channel head coil at the Department of Diagnostic and Interventional Imaging of the KKH. Two T2-weighted images were acquired per subject. The image resolution was $1 \times 1 \times 2$ mm^3. The scans were acquired when subjects were sleeping in the scanner. No sedation was used and precautions were taken to reduce exposure to the MRI scanner noise. A neonatologist was present during each scan. A pulse oximeter was used to monitor heart rate and oxygen saturation throughout the entire scans. One-hundred and eighty-nine neonates underwent the T2-weighted MRI scans. Through visual inspection, 173 neonates with at least one good T2-weighted MRI scan were included in the analyses.

Segmentation

We developed an atlas-based segmentation approach to automatically delineate the left and right eyes from the T2-weighted image.[46] We manually delineated the eye from one subject's image. Segmenting the eye of other subjects was a matter of extrapolating from this manually labelled training image, referred as an atlas. This method is typically referred as atlas-based segmentation. It requires the use of image registration in order to align the atlas image to the other subjects' images. We then constructed the three-dimensional shape of the eye.[47–49]

Three-dimensional eye coordinate system

We constructed a three-dimensional coordinate system for each eye by determining the transverse, sagittal and coronal axes. We fitted the eye shape using two ellipsoids: one modelled on the corneal region and the other modelled on the vitreous humour. One ellipsoid encompassed the whole of the corneal region and the other encompassed the whole of the vitreous chamber. We employed the least-square optimisation method to fit the eye ball shape using these two ellipsoids. The geometric centre of the eye was then represented by the centre of the ellipsoid containing the vitreous chamber. The long axis of the eye ball was defined as the line passing through the centres of the aforementioned two fitted ellipsoids. The length, width, and height were measured automatically by the software. The traditional AL was computed as the distance between the most anterior and posterior points of the long axis, representing the length from the posterior corneal surface to the retinal surface. The vertical axis was then determined as the cross product between the long axis of the eye and the line passing through the centres of the left and right eyes. The cross product is a binary operation on two vectors in three-dimensional space and results in a vector which is perpendicular to both of the vectors being multiplied and therefore normal to the plane containing them. The height of the eye was then calculated as the distance between the most superior and inferior points along the vertical axis. Finally, the horizontal axis of each eye was determined as the cross product of the long and vertical axes. The width of the eye was computed as the distance between the most temporal and nasal points along the horizontal axis. The length, width, and height described above were the measurements for the internal eye.[33] The term 'globe' in this paper refers to the internal surface of the eye.[46]

Eye volume, surface area, and shape measurements

The volume of the eye was computed as the number of voxels labelled as part of the eye in the T2-weighted image multiplied by the image resolution, and the surface area of the eyeball was approximated as the area of the triangulated mesh.

We have used these scanning and analysis techniques in a previous study on older children.[34] In that study, we evaluated the accuracy of the MRI segmentation by comparing the longitudinal axial length obtained from MRI with the axial length using partial coherence interferometer (PCI), with no significant differences found.

Eye examination and clinical assessment at 3 years of age

Eye measurements were conducted by trained optometrists when the children were approximately 36 months old ($\pm$1 month). Cycloplegic objective refraction was performed using the Canon Autorefractor RK-F1 (http://www.usa.canon.com/). Cycloplegic objective refraction was assessed approximately 30 min after instillation of topical proparacaine (0.5%) and three drops each of 1% cyclopentolate and 2.5% phenylephrine each, given 5 min apart. A total of five consecutive readings was obtained. Each autorefractor was calibrated prior to testing on a daily basis, and the same two auto-refractors were used for all subjects throughout the study. Autorefractor readings were within $\leq$0.25 dioptres (D) of each other. If auto-refraction could not be performed (e.g. due to poor child cooperation), streak retinoscopy (Welch Allyn, http://www.welchallyn.com/) was performed by a trained study optometrist. Non-cycloplegic autorefraction was performed on the parents with the Canon RK-F1 autorefractor to assess parental myopia. Corneal curvature (CC) at 3 years was measured using the Canon Autorefractor as well. The child's height (measured without shoes) and age at testing (in months) were recorded during the clinic visit. Ethnicity and parental risk factors were captured by interviewer administered questionnaires during antenatal visits. Axial length measurements were obtained using an optical biometer (IOLMaster; Carl Zeiss-Meditec, http://www.zeiss.com/). The reliability of each axial length measurement was assessed using signal-to-noise ratio (SNR), and the reading was accepted if SNR $\geq$ 2.0.

Statistical analysis and definitions

A summary index of eye shape was given by oblateness,[34,46,50] defined as 1 $-$ (axial length/equatorial diameter). Oblateness was determined using both the width and height alternately as the equatorial diameter. A prolate eye was defined as oblateness <-0.01, while an oblate eye was defined as oblateness $>+0.01$. A spherical eye was defined as oblateness between -0.01 and $+0.01$.[46] Myopia was defined as spherical equivalent refraction (SER) < -0.5 D.

Mixed linear models were constructed to account for inter-eye correlations, with AL at 3 years, change in AL at 3 years, CC, AL/CC ratio, SER and myopia, respectively, as the dependent variable and the other ocular measurements

as the independent variables, with adjustments for the child's age, sex, race, maternal educational attainment and parental myopia.[29,51,52] Descriptive statistics was presented as the mean (±standard deviation). All probabilities quoted were two-sided and all statistical analyses were undertaken using IBM SPSS (http://www-01.ibm.com/software/sg/analytics/spss/) 20.0. A Bonferroni correction was applied with $p < 0.006$ required for statistical significance.

Results

The analyses included both eyes of 173 newborn children (Days 5–17). The mean gestational age at the time of MRI examination was 38.4 ± 1.1 weeks and the mean birth weight was 3125 ± 409 g. There were 74 Chinese children (43%), 75 Malay children (43%) and 24 Indian children (14%). The slight majority were male (94 children, 54%).

Measurements were obtained from all the MRI images. The mean AL, width and height were 17.3 ± standard deviation (S.D.) 0.9 mm (range 14.0–19.6), 16.3 ± 0.8 mm (13.7–18.4), and 17.1 ± 1.0 mm (14.3–20.3), respectively, while the mean volume and surface area of the globe were 2428 ± 272 mm^3 (1653–3744) and 898 ± 70 mm^2 (677–1217), respectively. The mean oblateness in relation to width was −0.06 ± 0.05 (−0.23 to 0.08), and the mean oblateness in relation to height was −0.01 ± 0.04 (−0.19 to +0.13). The distribution of globe shapes based on oblateness is as follows: for width, most eyes were prolate (294 eyes, 85%), followed by spherical (27 eyes, 8%) and oblate (25 eyes, 7%); for height, the largest proportion of eyes was also prolate (163 eyes, 47%), followed by oblate (128 eyes, 38%) and spherical (55 eyes, 16%).

At 3 years, the mean AL was 21.74 ± 0.68 mm (19.77–23.84). The mean AL increased from birth by 4.47 ± 0.94 mm (1.71–7.20), and the mean SER was +0.91 ± 0.80 D (−2.40 to +3.47) (*Table 1*). The mean CC was 7.75 ± 0.27 mm (7.23–8.50) and the mean AL/CC ratio was 2.81 ± 0.07. Only a small proportion of eyes was myopic (eight eyes, 4%).

Table 2 shows the associations between AL at 3 years and eye measurements at birth. After multivariate adjustment, only a prolate shape (using width) was significantly associated with the AL at 3 years. Compared to oblate eyes (using width), prolate eyes were longer axially by a mean of 0.09 mm [95% confidence interval (CI) 0.02–0.16]. Compared to oblate eyes (using height), spherical eyes were longer axially by a mean of 0.06 mm (0.01–0.12). However, these associations were not significant with Bonferroni correction.

The associations between change in AL at 3 years and eye measurements at birth are shown in *Table 3* and the *Figure 1*. After multivariate adjustment, eyes with longer AL at birth had smaller increases in AL at 3 years [mean difference −0.99 mm (95% CI −1.02 to −0.95) per mm increase, $p < 0.001$] (*Figure 1a*). Eyes with larger baseline volumes and surface areas had smaller increases in AL at 3 years [mean difference −0.001 mm (95% CI −0.002 to −0.007) per mm^3 increase, $p < 0.001$; and mean difference −0.006 mm (95% CI −0.007 to −0.005) per mm^2 increase,

Table 1. Means and distributions of eye measurements

Variables	Side	*N*	Range	Mean	Standard deviation	Inter-eye correlation
Axial length	Left	173	15.29–19.56	17.48	0.87	0.77
	Right	173	14.04–18.93	17.06	0.78	
Width	Left	173	13.74–17.70	16.09	0.70	0.64
	Right	173	14.09–18.35	16.48	0.75	
Height	Left	173	14.35–20.27	16.94	1.04	0.60
	Right	173	14.32–20.00	17.30	0.96	
Volume	Left	173	1674.00–3432.00	2393.17	260.38	0.93
	Right	173	1653.00–3744.00	2462.82	279.75	
Surface area	Left	173	676.51–1217.09	906.31	72.41	0.93
	Right	173	679.94–1130.27	890.50	67.28	
Oblateness by height	Left	173	−0.19 to 0.10	−0.03	0.06	0.46
	Right	173	−0.16 to 0.13	0.01	0.05	
Oblateness by width	Left	173	−0.23 to 0.02	−0.09	0.04	0.22
	Right	173	−0.16 to 0.08	−0.04	0.04	
Axial length at 3 years old	Left	130	19.93–23.70	21.74	0.68	0.98
	Right	130	19.77–23.84	21.73	0.69	
Change in axial length at 3 years old	Left	130	1.71–6.86	4.23	0.97	0.81
	Right	130	2.82–7.20	4.67	0.87	
Spherical equivalent refraction at 3 years old	Left	110	−2.40 to 3.47	0.96	0.83	0.84
	Right	115	−2.18 to 2.75	0.87	0.78	

Table 2. Associations between axial length (AL) at 3 years and axial length, width, height, volume, surface area and shape of the globe at birth

	Axial length at year 3					
	Unadjusted			Multivariate adjusted*		
	p-value	Estimate	95% CI	*p*-value	Estimate	95% CI
AL at birth	0.60	0.01	−0.03 to 0.05	0.47	0.01	−0.02 to 0.05
Width	0.61	−0.01	−0.04 to 0.02	0.65	−0.01	−0.04 to 0.03
Height	0.74	0.00	−0.02 to 0.03	0.80	0.00	−0.02 to 0.03
Volume	0.10	0.00	−0.00 to 0.00	0.10	0.00	−0.00 to 0.00
Surface area	0.06	0.00	−0.00 to 0.00	0.07	0.00	−0.00 to 0.00
Oblateness (1−AL/width)	0.56	−0.10	−0.44 to 0.24	0.50	−0.12	−0.46 to 0.23
Oblateness (1−AL/height)	0.96	0.01	−0.31 to 0.33	0.90	−0.02	−0.34 to 0.30
Shape of eye (by width)						
Prolate	0.02	0.09	0.02 to 0.16	0.01	0.09	0.02 to 0.17
Spherical	0.13	0.07	−0.02 to 0.16	0.10	0.07	−0.02 to 0.17
Oblate	Reference			Reference		
Shape of eye (by height)						
Prolate	0.77	0.01	−0.03 to 0.05	0.66	0.01	−0.03 to 0.05
Spherical	0.02	0.06	0.01 to 0.12	0.03	0.06	0.01 to 0.12
Oblate	Reference			Reference		

*Multivariate adjusted for age at month 36, sex, race, child's height M36, mother education levels and parental myopia.

$p < 0.001$, respectively] (*Figure 1b,c*). Eyes which were more oblate at birth had greater increases in AL at 3 years [mean difference 7.29 mm (6.14–8.43) per unit increase, $p < 0.001$ using width; and mean difference 5.67 mm (4.49–6.84) per unit increase, $p < 0.001$ using height respectively]. Using width to calculate oblateness, prolate eyes had smaller increases in AL at 3 years compared to oblate eyes [mean difference −0.72 mm (−1.03 to −0.40), $p < 0.001$], and, using height, prolate and spherical eyes had smaller increases in AL at 3 years compared to oblate eyes [mean difference −0.61 mm (−0.77 to −0.45), $p < 0.001$ and −0.25 mm (−0.47 to −0.04), $p < 0.001$; respectively] (*Figure 1d,e*).

No significant associations were found between the eye measurements at birth and SER at 3 years. No significant associations were found between the eye measurements at birth and myopia at 3 years in unadjusted analyses. Meaningful multivariate adjusted models could not be constructed for myopia at 3 years due to the small proportion of eyes with myopia. Neither CC nor the AL/CC ratio was significantly associated with any of the baseline measurements.

Discussion

Our study provides data on the relationships between ocular dimensions and shape at birth and the changes in AL and refraction 3 years later in a cohort of Asian children. Prolate eyes and spherical eyes at birth had longer AL at 3 years than oblate eyes. Eyes with longer AL, larger volumes and larger surface areas at birth had smaller increases in AL over 3 years. Eyes which were more prolate at birth had smaller increases in AL at 3 years. However, the size and shape of the eye at birth were not associated with the refractive status 3 years later.

The concept that peripheral refraction, and, by extension, eye shape, could determine future refractive development was first described in 1971 by Hoogerheide.[42] In their study, 400 young adult trainee pilots had their peripheral refraction measured over the central 60° of their horizontal visual fields. Subjects who were initially axially emmetropic or mildly hyperopic but had relative peripheral hyperopia at baseline had a high chance of developing myopia later (40%). In contrast, subjects who were relatively emmetropic or myopic in the periphery had only a low likelihood of becoming myopic later (4%). More recently, Mutti evaluated the relative peripheral refractive error in children enrolled in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study.[44] Six hundred and five children aged 6 years and above who became myopic over the course of follow-up were compared with 374 who remained emmetropic. Children who became myopic consistently had more hyperopic relative peripheral refraction than emmetropes from 2 years before through to 5 years after the onset of myopia. Myopia progression was greater per dioptre of more hyperopic relative peripheral refractive error by a small amount (−0.024 D per year).[53] These results suggest that a more prolate eye shape may be a risk factor for subsequent myopia. Experimental studies have established that local defocus due to the relative peripheral refraction can influence eye growth.[15,40,41,54–56] For example, Smith *et al.*[41]

Table 3. Associations between change in axial length (AL) at 3 years and axial length, width, height, volume, surface area and shape of the globe at birth

	Change in axial length at 3 years (axial length at 3 years – axial length at birth)					
	Unadjusted			Multivariate adjusted*		
	p-value	Estimate	95% CI	*p*-value	Estimate	95% CI
AL at birth	<0.001	−0.99	−1.03 to −0.96	<0.001	−0.99	−1.02 to −0.95
Width	0.48	−0.05	−0.18 to 0.08	0.15	−0.10	−0.23 to 0.04
Height	0.43	−0.04	−0.14 to 0.06	0.20	−0.07	−0.16 to 0.04
Volume	<0.001	−0.00	−0.00 to −0.00	<0.001	−0.00	−0.00 to −0.00
Surface area	<0.001	−0.01	−0.01 to −0.00	<0.001	−0.01	−0.01 to −0.01
Oblateness (1−AL/width)	<0.001	7.34	6.19 to 8.49	<0.001	7.29	6.14 to 8.43
Oblateness (1−AL/height)	<0.001	5.71	4.53 to 6.90	<0.001	5.67	4.49 to 6.84
Shape of eye (by width)						
Prolate	<0.001	−0.73	−1.05 to −0.41	<0.001	−0.72	−1.03 to −0.41
Spherical	0.08	−0.36	−0.76 to 0.05	0.09	−0.33	−0.73 to 0.06
Oblate	Reference			Reference		
Shape of eye (by height)						
Prolate	<0.001	−0.60	−0.76 to −0.44	<0.001	−0.61	−0.77 to −0.45
Spherical	0.046	−0.22	−0.44 to −0.00	0.02	−0.25	−0.47 to −0.04
Oblate	Reference			Reference		

*Multivariate adjusted for age at month 36, sex, race, child's height M36, mother education levels and parental myopia.

have recently demonstrated that the effects of local myopic defocus on refractive development in rhesus monkeys. Monkeys which were reared with monocular +3 D lenses that produced relative myopic defocus across the entire field of view developed compensating hyperopic anisometropia to a constant degree across the horizontal meridian. Monkeys that were exposed to hyperopic defocus in the nasal field experienced hyperopic changes in the nasal field selectively. Consistent with these observations, Charman *et al.*[57] have proposed a model in which an axially emmetropic eye with relative peripheral hyperopia undergoes global expansion to bring the peripheral image into focus, and, in so doing, leads to axial myopia. The structural correlate of relative peripheral hyperopia is a prolate shape, although it is still not clear if the prolate shape is merely associated with myopia or causative. Thus, it has been suggested that it is 'the subset of hyperopic and emmetropic eyes which have a more prolate (or less oblate) shape that might be at risk of becoming myopic'.[57]

Our study results support the notion that eye shape is related to subsequent eye growth, but also contrast with the work of Hoogerheide and Mutti. Eye shape is a parameter that is determined at birth, possibly by as yet unidentified genetic factors. Blomdhal[58] has shown that axial length and corneal power at birth are related to birth weight and height in neonates. The growth of the different refractive components of the eye are thus likely to all be coordinated during prenatal life by genetically modulated processes similar to those that induce ocular differentiation during embryonic life. These genetic programs are possibly influenced by the general growth of body size, which may in turn have both genetic and environmental aspects. As such, the determination of eye shape at birth might have both genetic and environmental factors. Unknown alterations in the embryonic or foetal environment could explain rare cases of congenital, non-progressive myopia, in which the eye grows excessively before birth but maintains a normal rate of growth after birth.[59] In our cohort, subjects with larger eyes and more prolate shapes at birth showed smaller increases in AL over the first 3 years of life. As the gestational ages and birth weights of the newborns were all within a fairly narrow range, differences in maturity at birth are unlikely to account for our findings. Flitcroft has published a synthesis of the interactions between retinal, optical and environmental factors in myopia pathogenesis.[60] A key component of this is the dioptric uniformity or three dimensional structure of the environment. The dioptric uniformity of the environment is dependent both on the setting (indoors or outdoors), and on the visual task. The extent of peripheral defocus produced by dioptric non-uniformity of the environment is in turn modified by the baseline off-axis refraction or shape of the eye. The resultant peripheral hyperopic defocus is maximal in prolate eyes for reading tasks and minimal for outdoor viewing or distance viewing indoors. The children in our cohort were generally below the age of literacy. As such, most of them would have had minimal peripheral hyperopic defocus if they had prolate eyes at baseline, and maximal peripheral hyperopic defocus if they had oblate eyes at baseline. The

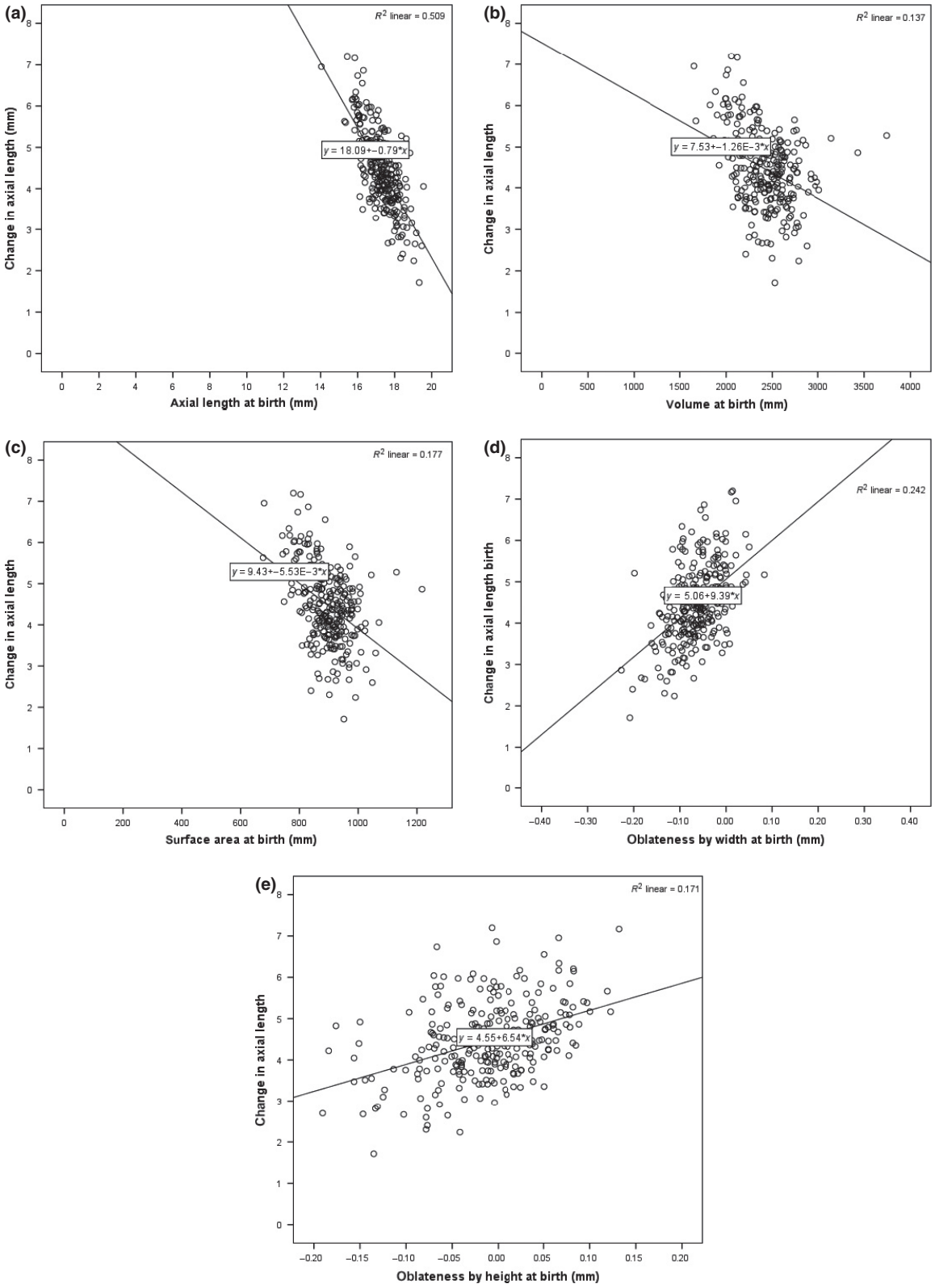

Figure 1. Scatterplot of change in axial length at 3 years vs (a) baseline axial length, (b) baseline volume, (c) baseline surface area, (d) baseline oblateness by width and (e) baseline oblateness by height.

greater peripheral hyperopic defocus in oblate eyes would be a likely stimulus for the greater axial growth seen.

Mutti *et al.*[61] has reported that the distribution of refractive errors at 9 months of age is tighter than at 3 months of age. This was related to a greater rate of axial elongation in more hyperopic eyes at baseline, and is consistent with a report by Saunders *et al.*[62] that emmetropisation occurs more rapidly in the presence of higher hyperopic refractive errors at baseline. The principal mechanism that leads to a tighter distribution of refractive errors in the first years of life may be the modulation of the rate of axial elongation by the amount of imposed hyperopic defocus in hyperopic eyes. Our results suggest that this modulation of axial growth could be based on peripheral hyperopic defocus and not only on axial hyperopic defocus. We were unable to demonstrate associations between eye size and shape at birth and refraction at age three, consistent with the fact that neonatal high hyperopia should have been lost in this 3 year period. Eye shape at birth could have been associated with refractive error at birth, but once the eyes had undergone emmetropisation, this association would have been lost. Prolonged exposure to myopiagenic stimuli such as extended periods of near work or lack of outdoor time that usually occur in older children may subsequently overwhelm the compensatory mechanisms of the eye, at which point an oblate shape may predispose to further axial elongation. These findings may be consistent with those of Gilmartin, in which oblate eyes are biomechanically predisposed to enlargement. Longer follow-up is likely to yield subjects with larger degrees of myopia, and may allow us to determine if eye size and shape are associated with subsequent ametropia in addition to differences in eye growth patterns. However, our longitudinal data in 3 year old children provides important information on early compensatory mechanisms in very young children before excessive exposures to the external environment.

One of the strengths of our study design is a relatively large, population based sample. We were able to capture baseline data on eye size and shape in very young children with no exposure to environmental influences on refractive development. This allowed us to isolate the effects of eye size and shape. MRI scans in young children are difficult to obtain due in no small part to the need for subject cooperation and parental consent, and our study is the first to provide data on this population. The accuracy of our measurements was partly limited by the acquisition time afforded to us. General limitations include the cross-sectional nature of our study which limits inferences of causation, and the relatively small proportion of myopic children. Although we did not systematically select a subset for analysis, there may also have been unavoidable selection bias as only children whose parents consented underwent MRI shortly after birth. Most of the children had returned home by the time of the MRI, and many parents were unwilling to return to the hospital for their children to undergo the scan. Also, as we did not sedate the babies, many children who were unable to sleep through the scan had to be excluded. Other studies using MRI to analyse eye shape have also had higher resolution images than we had. These are however non-differential errors that should not affect the relationships we found. Overall, the proportion of children who were myopic by definition was very small, making it hard to analyse this group meaningfully.

In conclusion, our study has shown that the size and shape of the newborn eye are linked to subsequent eye growth. Eyes that are larger and have prolate or spherical shapes at birth exhibit smaller increases in AL over the first 3 years of life. Eye size and shape at birth influence subsequent eye growth but not the development of refractive error, suggesting adequate compensatory mechanisms to maintain mild hyperopia for at least the first 3 years of life. Longer follow-up will allow us to determine if these factors are also linked to subsequent ametropia, potentially allowing us to identify eyes with at-risk shapes for early interventions to prevent or retard myopia onset.

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