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# Electrophysiological and Psychophysical Studies of Meridional Anisotropies in Children With and Without Astigmatism

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**PURPOSE.** We investigated the pattern of meridional anisotropies, if any, for pattern onset-offset visual evoked potential (POVEPs) responses and psychophysical grating acuity (GA) in children with normal letter visual acuity (20/20 or better).

**METHODS.** A total of 29 children (aged 3–9 years), nine of whom were astigmatic (AS), were recruited. Orientation-specific monocular POVEPs were recorded in response to sinewave grating stimuli oriented along the subjects' principal AS meridians. Horizontal and vertical gratings were designated Meridians 1 and 2, respectively, for nonastigmatic patients (Non-AS). Binocular POVEPs in response to the same stimuli, but oriented at 45°, 90°, 135°, and 180°, were recorded. Psychophysical GAs were assessed monocularly and binocularly along the same meridians using the same stimuli by a 2-alternative-forced-choice staircase technique. The C3 amplitudes and peak latencies of the POVEP and GAs were compared across meridians using linear mixed models (monocular) and ANOVA (binocular).

**RESULTS.** There were significant meridional anisotropies in monocular C3 amplitudes regardless of astigmatism status ( $P = 0.001$ ): Meridian 2 (mean  $\pm$  SE Non-AS,  $30.13 \pm 2.07$   $\mu$ V; AS,  $26.53 \pm 2.98$   $\mu$ V) was significantly higher than Meridian 1 (Non-AS,  $26.14 \pm 1.87$   $\mu$ V; AS,  $21.68 \pm 2.73$   $\mu$ V;  $P = 0.019$ ), but no meridional anisotropies were found for GA or C3 latency. Binocular C3 amplitude in response to horizontally oriented stimuli (180°,  $29.71 \pm 3.06$   $\mu$ V) was significantly lower than the oblique (45°,  $36.62 \pm 3.05$   $\mu$ V;  $P = 0.03$  and 135°,  $35.95 \pm 2.92$   $\mu$ V;  $P = 0.04$ ) and vertical (90°,  $37.82 \pm 3.65$   $\mu$ V;  $P = 0.02$ ) meridians, and binocular C3 latency was significantly shorter in response to vertical than oblique gratings ( $P \leq 0.001$ ).

**CONCLUSIONS.** Meridional anisotropy was observed in children with normal vision. The findings suggest that horizontal gratings result in a small, but significantly lower POVEP amplitude than for vertical and oblique gratings.

**Keywords:** astigmatism, refractive error, meridional anisotropy, oblique effect, horizontal effect

Astigmatism is a relatively common type of refractive error that affects approximately 20% of school-aged children.<sup>1</sup> If present with other refractive errors, it accounts for approximately 47%<sup>1</sup> of correctable visual impairments (defined as visual impairment that is correctable to 20/20 with optical correction). Although normally-developing infants have a relatively high prevalence of low-to-moderate astigmatism (1.00–2.00 diopters cylinder [DC]) with their principal meridians typically lying close to the cardinal orientations (i.e., vertical and horizontal),<sup>2–5</sup> they are unlikely to be negatively affected by the retinal blur caused by this degree of astigmatism.<sup>6</sup> In fact, retinal blur most likely contributes to the development of the accommodative feedback system.<sup>7</sup> Additionally, there is a sharp decline in the magnitude of astigmatism over the first year of life.<sup>2,3</sup>

High magnitudes of childhood astigmatism (>2.50 DC) are less common.<sup>8</sup> Previous studies indicated that only 5% to 20% of 4-year-old children have astigmatism between 1.00 to 2.00 DC<sup>9</sup> and fewer than 5% have  $\geq 2.00$  DC.<sup>9</sup> Astigmatism ( $\geq 1.50$  DC) at ages 5 to 6 years is approximately 11% in Singapore.<sup>10</sup> Some astigmatic children may suffer neural deficits corresponding to the astigmatic meridians,<sup>11</sup> a condition known as meridional amblyopia.<sup>12</sup> The onset of refractive amblyopia is approximately 3 to 4 years of age<sup>13</sup> and is less likely to develop for the first time beyond the age of 7 years.<sup>14,15</sup> Young children with astigmatism may be adapted to the optical aberration and may not actively complain about blurred vision, so astigmatism sometimes may be undetected without clinical examination or screening<sup>8</sup> leading to extended durations of uncorrected astigmatism. Thus, astigmatism may be an amblyogenic factor.



Factors thought to influence the development of meridional amblyopia include age at astigmatism onset,<sup>16</sup> duration of astigmatic blur,<sup>16</sup> magnitude of astigmatic blur,<sup>17,18</sup> type of astigmatism,<sup>19</sup> and the accommodative state that regulates astigmatic blur.<sup>20,21</sup>

A study of 1682 Singaporean children ages 30 to 72 months demonstrated that 85% of amblyopic cases were related to uncorrected refractive errors and only 15% were related to strabismus.<sup>10,22</sup> In addition, 29% of the amblyopes had isometric astigmatism  $>2.50$  DC and 42% had aniso-astigmatism  $\geq 1.50$  DC.<sup>22</sup> Meridional amblyopia also has been found previously in two small-scale experimental visual evoked potential (VEP) and psychophysical studies.<sup>20,23</sup> Freeman and Thibos<sup>20</sup> found that meridional amblyopes had reduced VEP amplitude at the meridian that experienced the greatest retinal blur and that this was not an optical effect. However, the number of subjects investigated was small ( $n = 9$ ) with no details about the age of or treatment undertaken by the subjects. Fiorentini and Maffei<sup>23</sup> reported meridional anisotropies along the astigmatic meridians in five of seven highly astigmatic children (defined as 3.00–4.00 DC) whereas low astigmatic children ( $n = 16$ ; defined as 0.50–1.50 DC) did not have significant meridional anisotropy. However, the report was confounded by mixed results in two subjects: one highly astigmatic subject who did not have meridional anisotropy and one who had highly irregular waveforms. Additionally, they were unable to establish whether the astigmatic children were previously amblyopic.

Another well-known meridional anisotropy is the oblique effect,<sup>24</sup> where stimuli oriented at the cardinal meridians (horizontal and vertical) tend to have stronger responses than those at the oblique meridians.<sup>25</sup> Other anisotropies observed in people with normal vision include two kinds of horizontal effect. One study found poorer contrast sensitivity to horizontal than vertical square-wave gratings of very low spatial frequencies (SF; 0.06–0.10 cycles per degree [cpd]) in newborn infants.<sup>26</sup> In that study, refractive errors, such as astigmatism, were not considered. It is unclear whether similar meridional anisotropies are expected in preschool and school-aged children. Another type of horizontal effect was found psychophysically in adults viewing natural scenes<sup>27–29</sup> containing broad SF and orientation content, whereby sensitivity was less for horizontal than for vertical and oblique stimuli. Studies have found that meridional anisotropies may be spatial frequency dependent<sup>30</sup> and may be dependent on: (1) contrast,<sup>31</sup> (2) type of stimulus (e.g., natural image<sup>32,33</sup> versus grating),<sup>34–38</sup> (3) mode of stimulus presentation (e.g., simultaneous or successive),<sup>39</sup> (4) time for neural adaptation (e.g., sustained or transient stimulus),<sup>40</sup> and (5) age of the subject.<sup>41</sup>

While individuals with meridional amblyopia are likely to have meridional anisotropy aligned with the astigmatic meridians, it is not clear whether nonamblyopic children with and without astigmatism will have any meridional anisotropy. It is important to understand the normal pattern of anisotropy of orientation-specific psychophysical and electrophysiologic responses in young children before evaluating children with amblyopia for the presence of meridional amblyopia. Therefore, we investigated whether meridional anisotropies exist in children with normal vision (letter acuity), using orientation-specific pattern onset–offset visual evoked potential (POVEP) and grating acuity (GA). We hypothesized that no meridional anisotropy would be demonstrated other than the oblique effect for the stimuli used.

## METHODS

Children with normal vision and no history of amblyopia were recruited from the refraction clinic at a children's hospital in

Singapore and by advertisement. Their visual system response to specifically oriented stimuli was evaluated using electrophysiologic and psychophysical methods at the visual electrophysiology laboratory at the Singapore National Eye Centre (SNEC). The research study adhered to the tenets of the Declaration of Helsinki and ethical approval was obtained from the centralized institutional review board (CIRB; Registration number: R1083/98/2013) at SingHealth and ratified by the human research ethics committees at the University of New South Wales, Sydney, NSW, Australia (Approval number: 09364). Parents and guardians gave their informed consent and children 6 years of age and above additionally provided assent.

## Subjects

Children of preschool and school age with normal letter visual acuity (VA; defined as  $\leq 0.05$  logMAR in each eye) were included in the study. Nonastigmatic children (Non-AS) were defined as having  $<0.50$  DC and astigmatic children (AS) were defined as having  $\geq 0.50$  DC. Spectacle correction, if required, was as prescribed by subjects' own attending clinicians to reflect real-life conditions. Children with amblyopia, strabismus, ocular diseases or abnormalities were excluded. All subjects underwent ocular health examination, logMAR VA (HOTV chart, Good-lite Co, Elgin, IL, USA), binocular vision, retinoscopy, autorefraction, and manifest subjective refraction assessments using age-appropriate refraction techniques. The decision to conduct cycloplegic refraction was made by the clinician, and not the researchers. Six out of 29 subjects did not have cycloplegic refraction. All subjects were able to read the English alphabet fluently due to education level.

## Orientation-Specific POVEP

Single-channel transient POVEPs were measured in response to a  $12^\circ$  field-size achromatic sinewave grating stimulus of 4 cpd oriented along the principal astigmatic meridians. The refractive power of each principal astigmatic meridian was considered in sphero-minus cylinder form. For example, for a refractive error of  $+0.50/-1.25 \times 180$ , Meridian 1 is  $180^\circ$ , where the refractive error is  $+0.50$  diopters (D), while Meridian 2 is  $90^\circ$  with refractive error  $-0.75$  D. As eight of nine AS subjects had with-the-rule (WTR) and either simple or compound myopic astigmatism, Meridian 1 typically was the most hyperopic or the least myopic meridian. Where astigmatism was absent, the horizontal and vertical gratings were arbitrarily assigned as the Meridian 1 and Meridian 2 stimuli, respectively. To check for the oblique effect, the POVEPs were recorded binocularly with the same stimuli orientated in four meridians ( $45^\circ$ ,  $90^\circ$ ,  $135^\circ$ , and  $180^\circ$ ). Two averages of 30 sweeps of 1-second duration were recorded in succession for each stimulus condition. The stimuli were presented with onset duration 100 msec, offset 400 msec, with Michelson contrast 54%; the latter was designed to reduce luminance artefacts from the monitor,<sup>42</sup> and at a temporal frequency of 2 Hz against a background of the same space-averaged luminance at a viewing distance of 1 meter. The order of stimulus presentation was randomized.

Subjects wore their full prescribed correction during recording, either using spectacles or trial lenses within a trial frame. The refraction was as prescribed by their clinician and was within 0.50 D of the subjective cycloplegic refraction in the majority of cases, except in one case where a hyperopic subject was undercorrected by 1.00 D. Subjects were encouraged to view a central fixation target (black dot with a 2-mm diameter) at 1 m during POVEP testing and their fixation was monitored visually. They were reminded regularly to look at the screen and to maintain the test

distance by leaning against the seat's backrest. Effects from any possible losses of fixation were minimized with the use of pattern-onset presentation mode with the suprathreshold stimulus (4 cpd) and accommodation was not controlled with addition lenses as the children were expected to have sufficient accommodation for the 1 m viewing distance. In situations where the subjects were excessively fidgeting or nonattentive, the recordings were paused and repeated, and those sweeps contaminated by artefacts were removed. Three gold-cup surface electrodes (9 mm) were used during VEP recording. The active recording electrode was located at Oz (occipital midline), the reference electrode at Cz and the ground electrode at Fz, using EEG conductance paste and micropore tape. The electrode montage was based on the International 10–20 configuration.<sup>43</sup>

## Equipment

The POVEPs were recorded using the Espion System (Diagnosys, Cambridge, UK) at a sampling rate of 5 kHz and a band-pass filter of 0.312–100 Hz and a recording window of 1 second per sweep. The stimuli were generated using the ViSaGe Mk II (Cambridge Research Systems, UK) and presented on a calibrated Sony CPD-G500 21-inch Trinitron cathode ray tube (CRT) monitor. The ViSaGe stimulus generator is a 14-bit system that was able to generate the stimulus specified at the viewing distances used and with the high-performance CRT monitor (Maximum Resolution, 2048 × 1536 at 75 Hz; horizontal and vertical scan range, 30–121 kHz and 48–160 Hz, respectively). It presented 35.2 cpd gratings without aliasing at the viewing distance of 2.2 m. If the resolution of the monitor was insufficient to present the stimulus without aliasing, the solution would have been to increase the viewing distance to increase the physical size of the stimulus while maintaining the angular size of the stimulus. Impedance was monitored to be below 8 kΩ before each recording.

## Grating Acuity (GA)

Psychophysical GA was measured monocularly using the same orientation-specific POVEP sine wave gratings with 54% contrast presented pattern-onset-offset (100 msec on and 400 msec off) for 2500 msec as described previously except a smaller field size of 3° was used to allow a spatial forced choice task within the display size. The stimulus was presented for 100 msec only five times and the task was to determine the location of the grating stimulus, on the left or right side of the screen, which were located either 2° left or right from the fixation target. Subjects indicated the location of the stimulus either verbally or by pointing at the stimulus location and they had ample time to make a decision, but usually within 5 to 10 seconds at most. If they were unable to detect the grating, they were encouraged to guess to make a decision. Threshold GA was estimated as the average of the last four reversals of a psychophysical staircase; two-alternative spatial forced-choice method with a 1 down 1 up staircase technique with 3-dB step size ranging from low to high SF (maximum presented at 35 cpd). Incorrect responses resulted in the SF being decreased and correct responses resulted in SF being increased. Custom-designed software (School of Optometry and Visual Science [SOVS]–Centre For Eye Health [CFEH] Psychophysical Testing Suite, Sydney, Australia) written using Matlab (Version R2017a, MathWorks, Inc., Natick, MA, USA) was used to generate the stimuli and assess threshold. Subjects were tested with room lights turned off at a viewing distance of 2.2 m.

## Analysis

The peak amplitudes and latencies of POVEP components C1, C2, and C3<sup>44</sup> of the AS and Non-AS groups were measured under masked conditions. The amplitude of each component was computed from the peak of the preceding wave and the latency of each component was calculated as the time taken from stimulus onset to each peak. As C1 and C2 were highly variable within subjects and were not measurable across all subjects and all stimuli,<sup>45</sup> these components were not analyzed further. In our study, as each POVEP sweep comprised two complete transient VEP waveforms due to the 1-second sweep recording window, to improve the estimate of C3 amplitude and latency further, averages of the first and second waveforms (60 sweeps) for each individual and stimulus condition were made.

Monocular results were assessed using linear mixed models (LMM) to account for right and left eye-related data and repeated measures ANOVA was used for the binocular data as there were no related right and left eye data to take into account. The statistical software package SPSS (version 23; IBM Corp, Armonk, NY, USA) was used for analysis. Monocular data from subgroups (AS, Non-AS) were analyzed using LMM with repeated measures on the individual subject and the two eyes<sup>46</sup> by running subject identifier as the subject variable, POVEP components (C3 amplitude, C3 latency) and GA as the dependent value, meridian (Meridian 1 or 2) and age as predictors in a linear model. Logarithmic (natural log) transformation was applied to C3 latency to satisfy normality assumptions of LMM. The binocular dataset was analyzed using ANOVA to compare the effect of meridian (45°, 90°, 135°, and 180°) on POVEP C3 amplitude, latency, and GA with age as a covariate and pairwise comparison was conducted for the four meridians with Bonferroni correction. The oblique effect was checked by comparing the average of the binocular 90° and 180° meridian responses with the average of the 45° and 135° responses. Meridional anisotropies were considered to exist if there were statistically significant differences between outcome measures for any meridians ( $P < 0.05$ ). Binocular latencies were analyzed using Friedman's test, with follow up pairwise comparisons and Bonferroni correction to correct family-wise errors.

## RESULTS

Twenty-nine subjects (mean age  $\pm$  SD,  $6.1 \pm 1.3$  years) with normal letter VA (right eye [OD]  $0.00 \pm 0.01$  and left eye [OS]  $0.00 \pm 0.01$  logMAR) were recruited. Twenty subjects were Non-AS (19 did not require refractive correction and one had bilateral myopia  $-1.75$  diopters sphere [DS]) and nine were AS (two did not have any history of spectacle wear and seven were current spectacle wearers). Mean age  $\pm$  SD of the AS and Non-AS groups was  $6.8 \pm 1.3$  (range, 4.6–9.2) and  $5.8 \pm 1.3$  (range, 3.9–8.2) years, respectively (Fig. 1). Effects due to age difference were accounted for in the analyses by including age as either a fixed variable or as a covariate, depending on the analysis.

Their refractive profiles are summarized in the Table. The group-averaged and each individual eye's POVEP waveforms and their main components (C1, C2, and C3 of the group averaged waveforms) are presented in Figure 2. Data from one Non-AS subject was thought to be an outlier as its peak latency was over 2 SD larger than the mean, but further investigation of that subject was unremarkable and the inclusion or exclusion did not affect the statistical analysis. For this reason, all data collected in this study were analyzed.



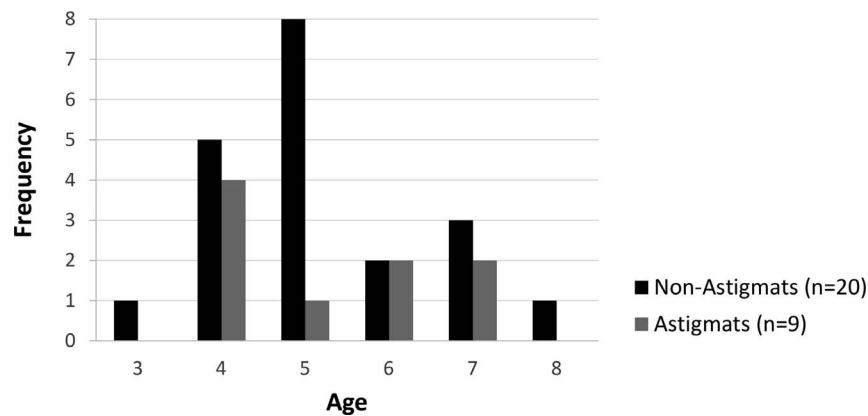


FIGURE 1. Frequency distribution of age in AS ( $n = 9$ ) and Non-AS ( $n = 20$ ) groups.

### Monocular Results

There was no significant effect of age on POVEP C3 amplitude or latency. However, age was a significant predictor for GA ( $P = 0.002$ ; 95% confidence interval [CI], 1.05–4.27); indicating a 0.22 octave (mean  $\pm$  SD,  $0.13 \pm 0.06$  log units; approximately equivalent to four letters on the logMAR chart) improvement for each additional year of age when considering AS and Non-AS in a single group (note that GA was tested at moderate contrast, not high contrast). No significant differences in POVEP C3 amplitude, latency, or GA were found between the AS and Non-AS groups despite the Non-AS group showing a trend of higher amplitudes (mean difference  $4.46 \pm 2.98$   $\mu$ V) and better GA (approximately 0.43 octaves or equivalent to nine letters on the logMAR chart; mean difference  $0.28 \pm 0.15$  log units or approximately) than the AS group (Fig. 3).

Overall, there was a significant effect of meridian for monocular POVEP C3 amplitudes, regardless of whether the subjects were AS or Non-AS ( $P = 0.001$ ;  $F_{1,27.10} = 15.00$ ). The C3 amplitude of Meridian 2 was statistically ( $B = 4.85 \pm 1.95$   $\mu$ V; degrees of freedom [df] = 28.79;  $t = 2.49$ ; 95% CI, 0.86–8.84;  $P = 0.019$ ) and clinically significantly higher than for Meridian 1 (Fig. 4a). There were no meridional anisotropies for monocular log(GA; Fig. 4b) or C3 latency.

### Binocular Results

There were no significant differences between the AS and Non-AS groups. Across the entire group of subjects, the average C3 amplitudes of the obliques (average of  $45^\circ$  and  $135^\circ$ ,  $34.62 \pm 2.11$   $\mu$ m; 95% CI, 30.28–38.95) were significantly ( $P = 0.017$ ) greater than the average cardinal meridians (average of  $90^\circ$  and  $180^\circ$ ,  $31.35 \pm 1.66$   $\mu$ m; 95% CI, 27.94–34.77) by a mean difference of  $3.27 \pm 1.28$   $\mu$ m (95% CI, 0.63–5.90).

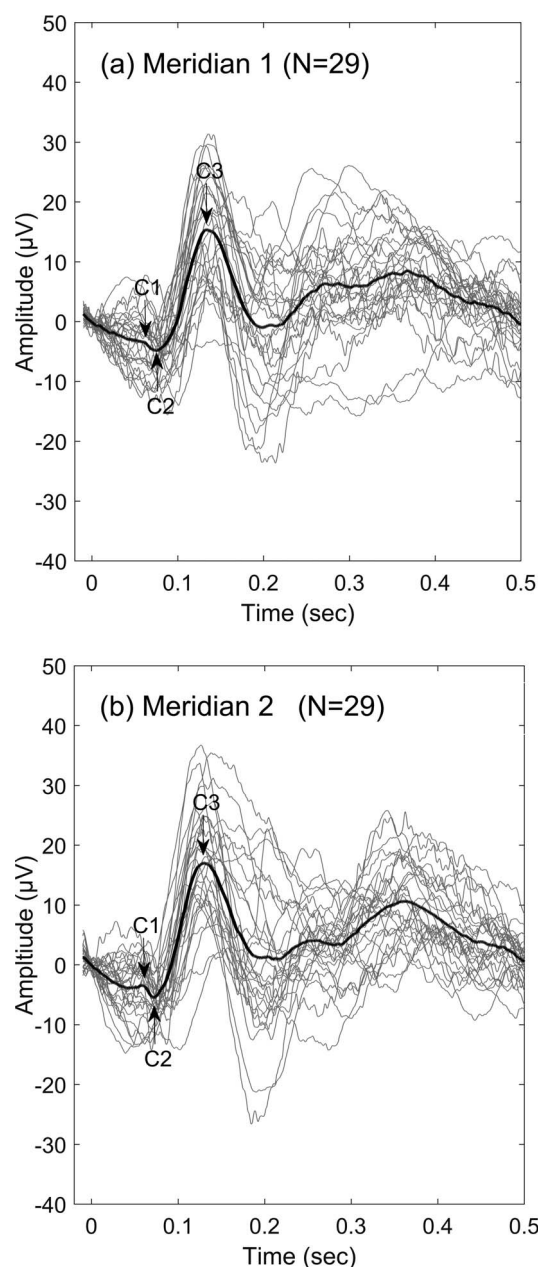
Additionally, there was a small but statistically significant effect of meridian on POVEP C3 log(amplitude;  $P = 0.03$ ;  $F_{3,24} = 3.56$ ). There was no effect of meridian or age on log(GA). Pairwise comparison of the binocular dataset shows that the horizontal ( $180^\circ$ ,  $29.71 \pm 3.06$   $\mu$ V; 95% CI, 3.00–3.48) was significantly lower in log(amplitude) compared to the rest of the meridians tested ( $45^\circ$ ,  $P = 0.030$ ;  $36.62 \pm 3.05$   $\mu$ V; 95% CI, 3.33–3.68;  $135^\circ$ ,  $P = 0.035$ ;  $35.95 \pm 2.92$   $\mu$ V; 95% CI, 3.27–3.66;  $90^\circ$ ,  $P = 0.02$ ;  $37.82 \pm 3.65$   $\mu$ V; 95% CI, 3.40–3.71). The mean differences between the horizontal and the rest of the meridians were  $6.90 \pm 1.53$   $\mu$ V (95% CI, 0.02–0.52),  $6.24 \pm 1.74$   $\mu$ V (95% CI, 0.01–0.45), and  $8.11 \pm 1.95$   $\mu$ V (95% CI, 0.03–0.59) for the  $45^\circ$ ,  $135^\circ$ , and  $90^\circ$  meridians, respectively (Fig. 5a).

C3 log(latency) was significantly shorter in response to vertical than oblique gratings ( $P \leq 0.001$ ; Fig. 5b).

TABLE. Summary of the Refractive Profile of AS and Non-AS Groups in This Study Showing the Mean Refractive Error (in DS and DC), Power Range (in DS and DC), Spherical Equivalent (in D), and the Refractive History of the Subjects

	AS	Non-AS
N	9 (8/9 WTR: Axis 15–160°; 1/9 oblique astigmatism: Axis 50° and 135° for each eye) (5/9 compound myopic astigmatism; 3/9 Simple myopic astigmatism [inclusive of 1 oblique astigmatism]; 1/9 compound hyperopic astigmatism)	20
Mean refractive error (DS/DC)	OD +0.83 DS/–1.59 DC OS –0.92 DS/–1.66 DC	OD –0.09 DS/0.00 DC OS –0.09 DS/0.00 DC
Power range (DS/DC)	OD +2.50 to –3.50 DS/–0.50 to –3.00 DC OS +3.00 to –3.75 DS/–0.50 to –3.50 DC	OD +0.25 to –1.75 DS/N.A. OS +0.75 to –1.75 DS/N.A.
Spherical equivalent (Mean $\pm$ SD)	OD –1.54 $\pm$ 1.31 D OS –1.65 $\pm$ 1.40 D	OD –0.09 $\pm$ 0.40 D OS –0.09 $\pm$ 0.40 D
Refractive history	7/9 Current spectacle wearers 2/9 New spectacles wearers (dispensed 10–20 minutes before POVEP and GA testing)	19/20 No refractive error 1/20 Myopic (–1.75 DS) and is a new spectacle wearer (just dispensed 10–20 minutes before POVEP and GA testing)

N, number; OD, right eye data; OS, left eye data; N.A., not applicable; WTR, with-the-rule astigmatism.



**FIGURE 2.** Monocular orientation-specific POVEP recordings made in response to sinewave grating stimuli oriented along (a) Meridian 1 and (b) Meridian 2. The main POVEP components (C1, C2, and C3) are indicated with arrows for the group average waveforms. Each subjects' monocular POVEPs (*thin lines*, average of 60 sweeps) and the group-averaged response (*thick line*) waveforms were plotted against time.

## DISCUSSION

We investigated whether meridional anisotropies exist in astigmatic and non-astigmatic children with normal vision using POVEP and psychophysical GA. It was hypothesized that no meridional anisotropy would be demonstrated other than the oblique effect. In the study, the only effect that might be similar to an oblique effect was for binocular C3 latency, in which longer latencies were observed for oblique stimuli compared to the vertical meridian ( $P \leq 0.001$ ). However, this may not be clinically significant if we consider 10% of the longest latency as being within the acceptable limits of repeatability.<sup>45,47</sup>

What could account for these findings? WTR astigmatism is known to have greater prevalence than other types (i.e., against-the-rule [ATR] or oblique astigmatism) in preschool/ kindergarten and school-aged children older than 4–5 years,<sup>48,49</sup> so the finding that eight of nine AS subjects in our study had WTR astigmatism is reflective of such a population trend. In this study, the POVEP grating stimuli for the monocular recordings were matched exactly to the principal astigmatic meridians of each child. Each meridian was considered separately in the AS cohort to identify which focal line lay closest to the retina when uncorrected for refractive error. AS patients may have to accommodate preferentially to one focal line, such that one orientation is imaged more clearly on the retina than the perpendicular orientation. Since the majority of the AS cohort had either simple (three of nine) or compound myopic (five of nine) WTR astigmatism (example:  $-1.00/-1.00 \times 180$ ), the more myopic focal line is horizontal. Given that accommodation tends to favor the situation in which one focal line lies on the retina,<sup>21</sup> it is expected that horizontal lines will be more frequently out-of-focus with distance viewing tasks. However, either line could become out-of-focus during near tasks (e.g., 40 cm).

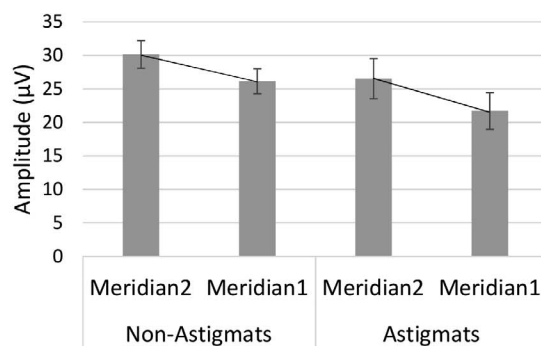
Consensual accommodation (equal for each eye) is the typical response to consensual accommodative stimuli,<sup>50</sup> with the qualifier that the binocular accommodative response is biased towards the dominant eye's response.<sup>51</sup> However, an aniso-accommodative stimulus of 1 D can generate 0.19 to 0.38 D of aniso-accommodation. This may act to partially or fully preserve binocular summation in contrast sensitivity, stereo acuity, and provide efferent feedback about each eye's refractive error that may guide isometropization.<sup>50</sup> In the chick model of myopia, induced astigmatic refractive error can result in complex compensatory changes to the retina that result in astigmatism when the inducing astigmatism is removed, despite the ability to accommodate. However, it is unclear how the human visual system may resolve accommodation in the case of bilateral astigmatic refractive errors or whether meridional amblyopia will arise.<sup>52</sup>

Meridional amblyopia may be one consequence if the astigmatic blur occurs during the critical period.<sup>20,21,53</sup> The degree of astigmatic blur is strongly dependent on its accommodative demand. Depending on the accommodative status of the individual,<sup>54</sup> there may be greater variability for either one of the focal planes to be clear when viewing a near object.<sup>15</sup> As there is no significant difference in the meridional anisotropies when comparing AS and Non-AS groups, it may be deduced that the meridional anisotropies in this AS cohort are not related to their principal astigmatic meridians.

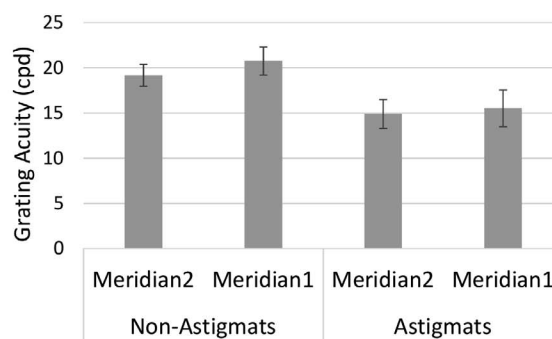
Alternatively, the finding of monocular meridional anisotropy may be attributed to a horizontal effect whereby the horizontal meridian is less sensitive than the rest of the meridians. The binocular POVEP data also supported this interpretation since the horizontal meridian's C3 amplitudes were significantly reduced compared to the oblique and vertical meridians. Furthermore, this phenomenon is unlikely to be induced by luminance artefacts from raster-scan CRT monitors, since such artefacts would have resulted in horizontal gratings being presented more precisely than vertical gratings.<sup>55–58</sup>

As our subjects were young children, it was postulated that these findings may be a continuation of the horizontal effect, as has been previously observed in infants in relation to contrast sensitivity to oriented gratings, but scaled to higher SF in line with improved spatial resolution acuity with increasing age.<sup>26</sup> Although horizontal effects have not been previously investigated electrophysiologically, data from a study by Arakawa et al.<sup>30</sup> in young adults ( $n = 9$ ) aged 19–25 years may be useful to review as they found higher VEP amplitudes in response to

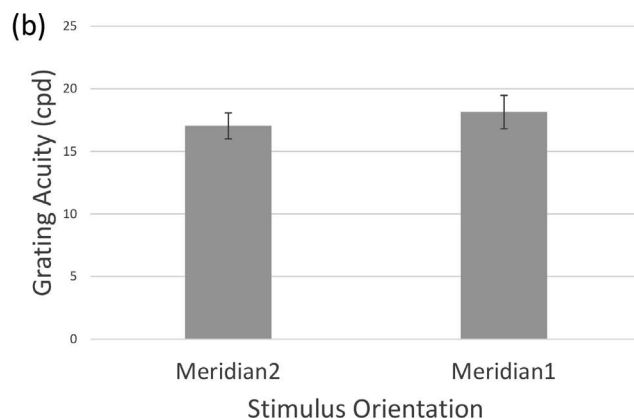
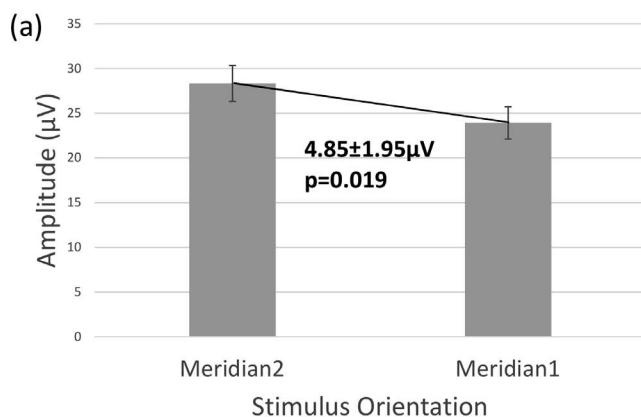
(a) POVEP C3 Amplitude



(b) Psychophysical Grating Acuity

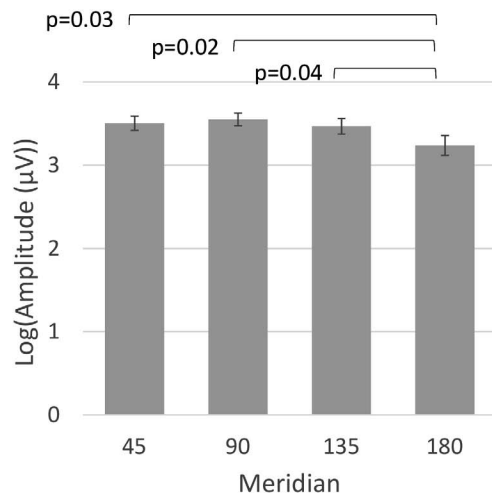


**FIGURE 3.** Estimated marginal means for the monocular measurements of orientation-specific (a) POVEP C3 amplitude and (b) psychophysical GA in AS and Non-AS groups. The C3 amplitudes (mean ± SE) for Meridian 2 are  $30.13 \pm 2.07$   $\mu$ V for Non-AS and  $26.53 \pm 2.98$   $\mu$ V for AS groups; and for Meridian 1 are  $26.14 \pm 1.87$   $\mu$ V for Non-AS and  $21.68 \pm 2.73$   $\mu$ V for AS groups. There was no significant difference in C3 amplitude and GA between AS and Non-AS groups and no significant within-subject differences in meridional measures of psychophysical GA (Meridian 1 vs. 2). Error bars: SEM for each parameter.

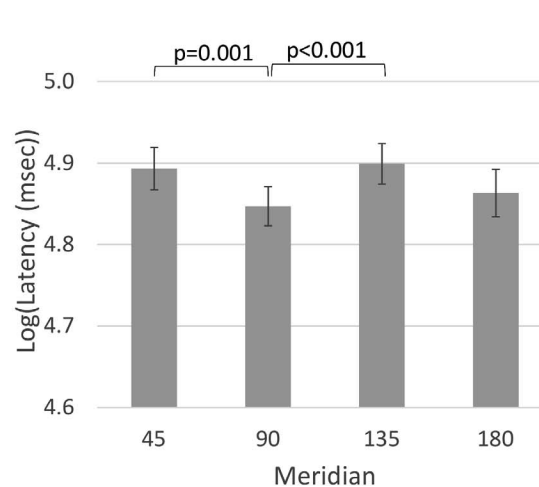


**FIGURE 4.** Estimated marginal means for the monocular measurements of (a) POVEP C3 amplitude and (b) psychophysical GA in AS and Non-AS groups. The POVEP C3 amplitude in Meridian 2 was significantly higher than the Meridian 1 ( $4.85 \pm 1.95$   $\mu$ V; 95% CI, 0.86–8.84;  $P = 0.019$ ). Error bars: SEM for each parameter.

(a) POVEP Log C3 Amplitude



(b) POVEP Log C3 Latency



**FIGURE 5.** Estimates for binocular measurements of POVEP (a) C3 log(amplitude;  $\mu$ V) and (b) C3 log(latency; msec), that were assessed along meridians 45°, 90°, 135°, and 180° with both subgroups combined. Pairwise comparison for C3 log (amplitude) in the horizontal (180°) was significantly lower compared to the oblique (45°:  $P = 0.03$ ; 135°:  $P = 0.035$ ) and vertical (90°:  $P = 0.021$ ) meridians. The mean differences between the horizontal and the rest of the meridians are  $6.90 \pm 1.53$   $\mu$ V (95% CI, 0.02–0.52),  $6.24 \pm 1.74$   $\mu$ V (95% CI, 0.01–0.45), and  $8.11 \pm 1.95$   $\mu$ V (95% CI, 0.03–0.59) for 45°, 135°, and 90° respectively. Pairwise comparison for C3 log (latency) was significantly shorter in response to vertical (90°) than oblique gratings (45° and 135°,  $P \leq 0.001$ ). Error bars: SEM for each parameter.



oblique rather than cardinal gratings at 4 cpd. Higher SF ( $>5$  cpd) tended to exhibit the oblique effect (oblique orientations were poorer than the horizontal orientation by approximately 1  $\mu$ V). Arakawa et al.<sup>30</sup> suggest a SF dependency of meridional anisotropies. Therefore, our finding of a horizontal effect may reflect normal, albeit immature, findings.

Young children may have more limited visual experiences than adults and, hence, less opportunity to develop biases against oblique meridians, which is perhaps why binocular latency findings are equivocal in relation to the oblique effect, and may reflect a developing oblique effect with respect to binocular C3 peak latency. The form of horizontal effect that has been described in response to viewing natural stimuli<sup>27–29</sup> is unlikely to explain our study data, as the stimuli used in our study were not broadband natural scenes. However, no meridional anisotropies were observed for psychophysical GA in either the AS or Non-AS groups.

While POVEP C3 amplitudes and psychophysical GA did not differ significantly between the AS and Non-AS groups, the Non-AS group had a trend for better GA, by 0.43 octaves (equivalent to approximately nine letters on the logMAR chart), than astigmatic children. Although childhood astigmatism was expected to have some deleterious effect on the visual resolution of the gratings, the astigmatic subjects in this cohort did not have as high magnitudes of astigmatism that have been described previously in other studies as causing negative effects on GA in nonamblyopic children  $<3$  years old.<sup>13</sup> Age improvements in GA may be related to improvements in contrast sensitivity with age as the gratings were presented at moderate, rather than high contrast.<sup>59</sup>

Our study established the presence of meridional anisotropies that are consistent with trends that have been found in other studies, specifically a horizontal effect. However, it is acknowledged that where no significant effects were found, this may be due to insufficient statistical power or low magnitudes of astigmatism. This is because the original sample size for the study was powered to detect the oblique effect, but not to assess the secondary exploratory aim of an effect due to astigmatic refractive error. While a larger sample size may help to clarify these observations, this would be a very small effect size based on the current study results. Other limitations of the study include: (1) not having a full history of the subject's refractive status, (2) being unable to track whether spectacles were worn regularly or consistently, (3) the assumption that vergence/accommodative demands were normal in this cohort, and (4) the results relate to the present sample and its generalizability to a larger population with a wider range of refractive errors or ages is unclear.

## CONCLUSIONS

In children aged 3.9 to 9.2 years, meridional anisotropy was observed for POVEP C3 amplitude where there is a small, but significantly lower amplitude with horizontal stimuli compared to vertical and oblique stimuli. C3 latency might have displayed a nascent oblique effect. The horizontal effect observed may be a physiologically normal phenomenon in immature visual systems, and binocular C3 latency may reflect an emerging oblique effect. It is unlikely that the meridional anisotropies reported in this study are related to the subjects' astigmatism. Future research may investigate refractive amblyopia with consideration of the presence of the horizontal effect, postulated to be a physiologically normal finding in young children with normal vision. Age effects were observed for GA, indicating continued neurodevelopmental maturation of the visual system.<sup>60,61</sup>

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