Is there meridional anisotropy in children with normal visual acuity and different astigmatic refractive errors?

An electrophysiology and psychophysical study.

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Purpose:

Astigmatism is an amblyogenic factor that may be important when monitoring recovery in response to treatment. Given that little is known about orientation-specific cortical processing in children with amblyopia, it is important to first establish normative findings in children with normal visual acuity (VA) before checking for meridional effects in amblyopes.

The aim of the study was to determine the effects of astigmatic refractive error on orientation-specific pattern-onset visual evoked potentials (POVEP) in children with normal vision.

Methods:

Inclusion criteria: Children age 3–9 years old with normal VA (≤0.05 logMAR in each eye). Non-astigmats have <0.50 Dioptre Cylinder (DC). Astigmats have ≥0.50DC as low degrees of astigmatism can limit neural sensitivities[1,2,3,4]

Exclusion criteria: Amblyopia (defined by VA of either eye ≥0.30), strabismus, ocular diseases or abnormalities as determined from ocular health examination, binocular vision, ETDRS VA (HOTV logMAR chart) and refraction assessments

Orientation-specific POVEP: Sinewave grating stimuli of 4.00 cycles per degree (cpd) oriented along and perpendicular (on- and against- axes) to the subject's aided principal astigmatic meridians of each eye were tested in random order (onset 100msec, offset 400msec, contrast 70%, 2Hz). Horizontal grating was arbitrarily assigned as on-axis in non-astigmats.

Grating acuity: Same meridians of each eye were tested (same settings) using two-alternative forced-choice preferential-looking with a 2 down 1 up staircase technique with 3-dB step size (Matlab R2017a, MathWorks Inc, Massachusetts, USA).

Equipment: Espion system (Diagnosys, Cambridge, UK) ViSaGe stimulus generator (Cambridge Research Systems, UK), calibrated monitor (Sony CPF-G500 21" Trinitron CRT)

Analysis: Each subgroup (astigmats, non-astigmats) was analysed by running subject identifier as the subject variable, POVEP components (C3 amplitude, C3 latency; Fig. 3) and GA as the dependent value, meridional anisotropies (on- or against- axes) and age as predictors in a linear model. Generalised estimating equations (GEE) was used to assess its average response changes and a follow-up analysis was conducted using linear mixed models (LMM) to assess the changes of individual responses over time by taking into account of inter-individual heterogeneity (multiple random effects for each variable)[5]. Logarithmic transformation was applied to C3 latency to satisfy normality assumptions of LMM.

Declaration: The research study adheres to the tenets of Helsinki. Informed consent was taken from parents of the child. Ethics approval was obtained from the Centralized Institutional Review Board (CIRB: R1083/98/2013). No financial interest.

Results:

Subjects: n=29; mean(SD) age=6.1(1.3)years

- 9/29 were astigmats (mostly with-the-rule); the rest were non-astigmats (excluded 1 subject due to poor recording)
- Mean(SD) VA: OD 0.00(0.01) and OS 0.00(0.01) logMAR
- Mean spherical/cylindrical (sph/cyl) refractive errors (Astigmats: OD+0.83/-1.59 OS-0.92/-1.66 axes 5–180 degrees ; Non-astigmats: OD-0.09/0.00 OS-0.09/0.00)

Normal maturation:

- Age was a significant predictor for GA (Exp(B)=7.45, p<0.0001; Estimate=2.66cpd; p=0.002); i.e. 2.66cpd improvement every year (95%CI:1.06–4.27)
- No effect of age for POVEP C3 amplitude (p=0.83) and log-latency (p=0.49)

Astigmats vs non-astigmats:

- Non-astigmats has significantly better GA compared to astigmats by about 5.25cpd (95%CI: 0.34–10.17; p=0.04; Exp(B)=252.24, p=0.004) (Fig. 1)
- No significant difference between astigmats and non-astigmats for POVEP C3 amplitude (p=0.14) and log-latency (p=0.51) even though non-astigmats tend to have higher amplitudes than astigmats (Fig. 2)

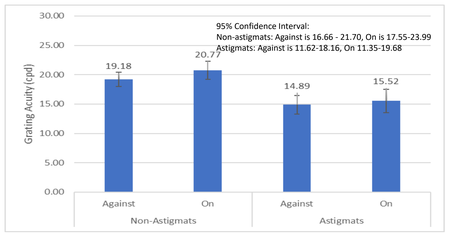

Figure 1: Estimated marginal means of psychophysical grating acuity in astigmats and non-astigmats (corrected for age 6.32 years old). Non-astigmats has a significantly better psychophysical grating acuity compared to astigmats by about 5.25cpd (95%CI: 0.34-10.17; p=0.04) and there are no significant differences between on-axis and against-axis measures of psychophysical grating acuity. The error bars indicate the standard errors of each parameter.

Meridional anisotropies:

- Significant meridional anisotrophies on POVEP C3 amplitudes regardless of whether the subjects were astigmats or non-astigmats (p=0.001): Against-axis were associated with higher C3 amplitudes (p=0.019; Estimate 4.85μV; 95%CI: 0.86 – 8.84) than on-axis (Fig. 2 and 3)
- Based on GEE, meridian was a significant predictor of C3 amplitude (Exp(B)=61.56, p=0.003) in the non-astigmats, but not the astigmats.
- No meridional effect on GA, latency or log-latency when analysed using GEE and LMM.

Discussion:

- This study suggests that GA is a sensitive test to demonstrate an effect on age and that non-astigmats have significantly better GA compared to astigmats. The absence of an association with POVEP may be attributed to poorer sensitivity from suprathreshold stimulus setting
- The improvement of GA with age reflects the continual maturation of GA beyond the age of three years old[6]. Psychophysical GA differs from VA testing because: (1) GA reflects the neural sensitivity according to the subject's principal astigmatic meridians, (2) GA was tested in pattern-onset mode where subjects have limited time to make a two-alternative forced-choice decision compared to a paper-based VA chart, (3) letter-recognition in VA testing necessitates higher cognitive processing than GA[7,8], (4) GA uses sinusoidal gratings instead of square-waves as in the case of VA testing, and (5) the contrast of VA chart was 100% compared to 70% in psychophysical GA testing to avoid artefacts from the monitor.
- The presence of early-onset astigmatism may have a deleterious influence on vision development[9]. The findings in this study is consistent with previous work on astigmatic children<3 years old (>2.00DC) which similarly found reduced GA in both horizontal and vertical orientations even though they did not have meridional amblyopia[9].

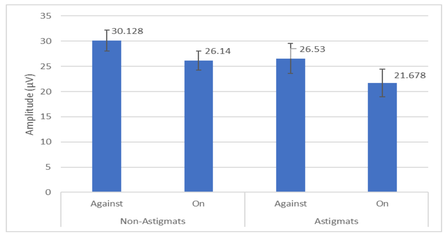

Figure 2: Estimated marginal means for POVEP C3 amplitude (μV) in astigmats and non-astigmats (corrected for age 6.12 years old). There is no significant difference in amplitude between astigmatic and non-astigmatic groups (p=0.14). When considering both groups, their against-axis were associated with higher C3 amplitudes (p=0.019; Estimate 4.85μV; 95%CI: 0.86 – 8.84) than on-axis. The error bars indicate the standard errors of each parameter.

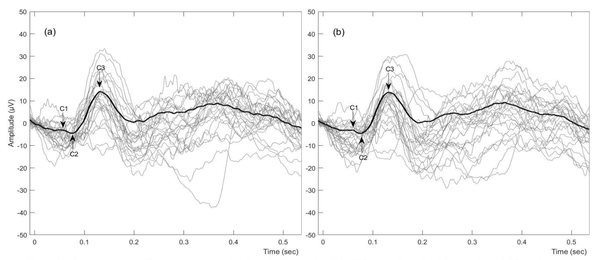

Figure 3: Orientation-specific pattern-onset visual evoked potential (POVEP) recordings for (a) on-axis and (b) against-axis. The averaged amplitude (μV) waveform is plotted (thick line) against time (seconds) together with the individual waveforms (thin lines) for each eye of each subject. The main POVEP components (C1, C2 and C3) are indicated on the graphs. Amplitude is computed from the peak of preceding wave and latency is calculated as the time taken to each peak.

- Meridional anisotropies are present in young children with greater C3 amplitude response to against-axis than on-axis stimuli regardless whether they are or are not astigmatic
- Horizontal effect occurs where horizontal stimuli are worse than oblique stimuli[10,11] – a normal phenomenon that is observed when viewing natural visual scenes[10,11]. This is contrary to well established knowledge that the human visual resolution to oblique gratings tends to be diminished compared to the cardinal orientations (i.e. oblique effect)[12,13] due to reduced high spatial frequency exposure to oblique meridians compared to the cardinal meridians[14,15,16,17].
- It is possible that young children may have more limited visual experiences than adults to develop these biases, while the horizontal effect may be a physiologically normal feature of an immature visual system which tends to process the salient aspects of objects whilst discounting visual contents (i.e. the horizontal orientations) that are already dominating natural visual scenes[10,11]

Conclusion:

Age effects were observed for GA during the normal maturation of young children and non-astigmats have better VA than astigmats, but these effects were not statistically significant in POVEP. Meridional anisotropy was observed for C3 amplitude where there is greater response with vertical stimuli than horizontal stimuli. This suggests that C3 amplitude is better at indicating meridional anisotropy than C3 latencies and GA. This horizontal effect may be physiologically normal in immature visual systems and these effects may extend beyond 9 years old.

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