The effect of asymmetrical accommodation on anisometropic amblyopia treatment outcomes

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BACKGROUND Previous research has revealed that the majority of children with anisometropic amblyopia have asymmetrical accommodation. The aim of this preliminary study was to determine whether the type of accommodation response was associated with a poor amblyopia treatment outcome in the same patients.

METHODS The type of accommodation response of 26 children with anisometropic amblyopia was determined in a previous study. The final visual acuity in the amblyopic eye, after treatment, was compared between those with symmetrical, aniso-, and anti-accommodation.

RESULTS The difference in final visual acuity between the three accommodation groups was significant ($P = 0.023$). Subjects with anisometropic amblyopia with anti-accommodation had the poorest final visual acuity (0.42 ± 0.25 logMAR) with a statistically significant difference compared with those who had aniso-accommodation (0.14 ± 0.08 logMAR; $P = 0.023$). However, the difference failed to reach significance compared to those with symmetrical accommodation (0.20 ± 0.12 logMAR; $P = 0.234$), probably due to the small sample size. The initial visual acuity in the amblyopic eye and the degree of anisometropia were also significantly positively correlated with final visual acuity ($P < 0.001$ for both).

CONCLUSIONS In this study cohort, the presence of anti-accommodation in anisometropic amblyopia was associated with a poorer amblyopia treatment outcome. The initial visual acuity in the amblyopic eye and the degree of anisometropia were also associated with a poorer outcome. It is possible that all these factors are associated, but further research is required to determine causal relationships. (J AAPOS 2019;23:203.e1-5)

Accommodation is generally considered to be a symmetrical process, with an equal accommodative response in both eyes.[1-5] However, research within our laboratory has provided strong evidence for the presence of asymmetrical accommodation in a group of hyperopic anisometropic amblyopic subjects.[6,7] A larger, prospective study,[7] following a single case report,[6] revealed that asymmetrical accommodation was widespread in uncorrected hyperopic anisometropic amblyopia. Only 19% of children (5/26) with hyperopic anisometropic amblyopia were found to have symmetrical accommodation, whereas 81% (21/26) had asymmetrical accommodation to some extent. Of those, 58% (15/26) demonstrated aniso-accommodation, where the amblyopic eye had lower accommodative gain, and 23% (6/26) demonstrated "anti-accommodation," where the amblyopic eye accommodated more for distance than near.

The child with anti-accommodation in the initial case study[6] had a poor response to amblyopia treatment, with a final visual acuity in the amblyopic eye of 0.35 logMAR. The success rate for treatment of anisometropic amblyopia is between 47% and 95%. Although degree of anisometropia, initial visual acuity, and depth of amblyopia have been implicated, there is no general consensus on the factors predictive of success.[8] The poor response to treatment of the child in the case study suggested to us that anti-accommodation could be an additional factor that could indicate the likelihood of a poor outcome to amblyopia treatment. The main aim of this preliminary study was to determine whether the type of accommodation response, in particular, the presence of anti-accommodation, was associated with a poor amblyopia treatment outcome.

Subjects and Methods

This study adhered to the tenets of the Declaration of Helsinki and was approved by the University of Reading and the UK National Health Service Ethics Committee. Fully informed consent was obtained from parents; age-appropriate assent, from children.

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In a previous study,[7] 26 children aged 4–8 years with a primary diagnosis of hyperopic anisometropic amblyopia were recruited from the Royal Berkshire Hospital. They were assessed using cycloplegic retinoscopy and a fundus and media check. Full correction was provided. Subjects received a completed orthoptic investigation, which included visual acuity testing using the Keeler (Keeler Ltd, Windsor, UK) or Sonksen (Haag-Streit, Essex, UK) crowded logMAR tests. All participants had visual acuity in the nonamblyopic of at least 0.2 logMAR (6/9.5), with >0.1 logMAR interocular difference. All had worn spectacles for at least 6 weeks and had undergone occlusion therapy, if required, by the time of data collection. Occlusion therapy was stopped after 3 consecutive visits of stable vision, and this was considered the final visual acuity. Successful treatment was defined as a final visual acuity in the amblyopic eye of at least 0.20 logMAR (6/9.5). Other extracted information included the presenting initial visual acuity of the amblyopic eye, degree of anisometropia (difference in spherical equivalent), and presence or absence of a microtropia, because these were considered to be potential confounding variables.

As previously reported,[7] accommodation was assessed over a range of distances, simultaneously in both eyes, using the plusoptiX S04 photorefractor in PowerRef II mode (Plusoptix GmbH, Nuremberg, Germany). Data was collected after spectacles had been worn for 6 weeks but at varying time points during occlusion therapy. The mean accommodative gain (with 95% confidence interval) of the sound eye was 0.86 ± 0.08 and the mean accommodative gain of the amblyopic eye was 0.41 ± 0.22. The 95% CI for the accommodation gain in the sound eye (±0.08; equivalent to 0.25 D difference in accommodation between the eyes at 0.33 m) was used as a comparative value to define each individual's accommodative response. The study revealed three types of accommodation response and the participants were grouped based on these responses: (1) symmetrical accommodation (5/26 [19%]); (2) aniso-accommodation (15/26 [58%]); and anti-accommodation (6/26 [23%]). In the first, accommodative gain in the amblyopic eye was within the 95% CI of the mean gain of the sound eye. The amblyopic eye had a similar lag of accommodation to the sound eye at near and in the distance. In the second, accommodative gain in the amblyopic eye was greater than the upper boundary of the 95% CI of the mean gain of the sound eye. The accommodative gain was greater in the sound eye due to the amblyopic eye under-accommodating. In the third, accommodation was asymmetrical, because the accommodative gain in the amblyopic eye was again greater than the upper boundary of the 95% CI of the mean gain of the sound eye. The sound eye accommodated more at near than in the distance, but the amblyopic eye accommodated more in the distance than at near (negative accommodative gain in the amblyopic eye).

The final visual acuity of the amblyopic eye was compared between groups using SPSS v 24 software (IBM Corp, New York) using a univariate analysis, with final visual acuity as the dependent variable and group as the fixed factor. Further ANOVA analyses and Pearson correlations included the initial visual acuity and the degree of anisometropia. Post hoc *t* tests were performed as required and used Bonferroni correction. Where assumptions of sphericity are violated, the Greenhouse-Geisser statistics are quoted.

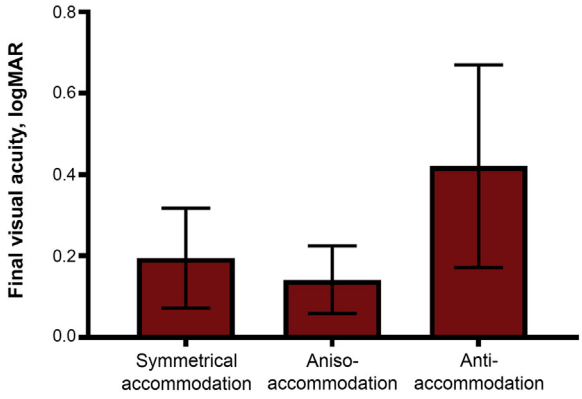

FIG 1. Mean final visual acuity (with 95% confidence intervals) in each group following treatment.

Results

Across all three groups, the mean final visual acuity in the amblyopic eye after treatment was 0.21 ± 0.09 logMAR (6/9.5; range, −0.10 to 1.00 logMAR). The initial visual acuity in the amblyopic eye was 0.68 ± 0.12 logMAR (6/30; range, 0.275–1.75 logMAR). The degree of anisometropia was 3.03 ± 0.40 D (range, 1.75–5.75 D).

Overall, 7 anisometropic amblyopic subjects (27%) had no microtropia, 6 (23%) had a microtropia without identity (minimal manifest deviation of $<10^{\Delta}$ base-out observable on cover test), and 9 (35%) had a microtropia with identity (no movement seen on cover test and central suppression, diagnosed using the 4^{Δ} test or assessment of fixation). In the remaining 4 cases (15%), there was no record of investigation of a microtropia with identity within their medical records.

Final Visual Acuity

Of the anisometropic amblyopic subjects, 15 (58%) had a successful treatment outcome; 8 (31%) had a successful outcome following refractive adaptation alone, with all of these patients in the symmetrical or aniso-accommodation group. The difference in final visual acuity between the three accommodation groups was significant ($F[2,23] = 4.31$; $P = 0.026$). See Figure 1. The anti-accommodation group had a mean final visual acuity of 0.42 ± 0.25 logMAR and a significantly worse visual outcome compared to the aniso-accommodation group (0.14 ± 0.08 logMAR; $P = 0.023$; mean difference of 0.28 logMAR, with 95% CI, 0.03–0.54). Although the difference in final visual acuity in the anti-accommodation group failed to reach significance compared to the symmetrical accommodation group (0.20 ± 0.12 logMAR, $P = 0.234$; mean difference of 0.22 logMAR, with 95% CI, −0.09 to 0.54), the small participant numbers in both of these groups suggest that the analysis could be underpowered. The difference between the symmetrical and aniso-accommodation groups was not significant

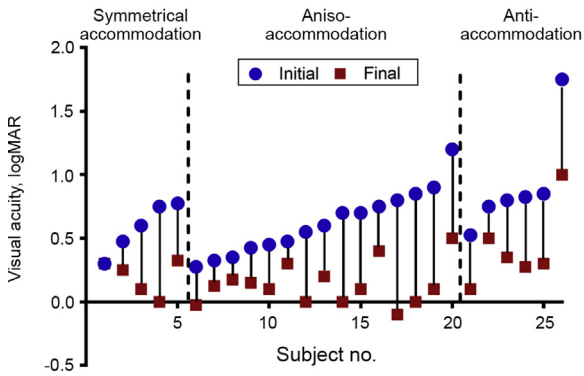

FIG 2. The change from initial (circles) to final (squares) visual acuity for each participant in each group.

($P = 1.00$; mean difference of 0.06 logMAR, with 95% CI, −0.21 to 0.33).

Initial Visual Acuity

Initial and final visual acuity had a strong positive correlation ($r = 0.65$; 95% CI, 0.35–0.83; $P < 0.001$); thus, a worse initial visual acuity correlated with a worse final visual acuity. On comparison of the three accommodation groups, the anti-accommodation group had a worse initial visual acuity (anti-accommodation, 0.92 ± 0.34 logMAR; aniso-accommodation, 0.62 ± 0.13 logMAR; symmetrical accommodation, 0.58 ± 0.17 logMAR), but this difference failed to reach significance ($F[2,23] = 2.55$; $P = 0.100$). The data were reanalyzed to compare the improvement from initial to final visual acuity (symmetrical accommodation, 0.39 ± 0.25 logMAR; aniso-accommodation, 0.49 ± 0.13 logMAR; anti-accommodation, 0.50 ± 0.13 logMAR), but there was no significant difference between groups ($F[2,23] = 0.379$; $P = 0.690$). See Figure 2.

Degree of Anisometropia

In terms of the degree of anisometropia, there was a strong positive correlation with the initial visual acuity ($r = 0.64$; 95% CI, 0.34–0.82; $P < 0.001$) and the final visual acuity ($r = 0.57$; 95% CI, 0.23–0.78; $P = 0.002$). There was a significant difference on comparison of the three groups ($F[2,23] = 15.38$, $P < 0.001$). The anti-accommodation group (4.42 ± 0.76 D) had a significantly greater degree of anisometropia in comparison to the symmetrical accommodation group (2.85 ± 0.55 D; $P = 0.004$) and aniso-accommodation group (2.53 ± 0.32 D; $P < 0.001$). There was no significant difference in the degree of anisometropia between the symmetrical and aniso-accommodation groups ($P = 1.00$).

Microtropia

The final visual acuity in subjects with no microtropia, microtropia with identity, and microtropia without identity was 0.11 ± 0.08 logMAR, 0.28 ± 0.20 logMAR, and 0.33 ± 0.15 logMAR, respectively. There was no significant difference in the final visual acuity between these groups ($F[2,19] = 1.592$; $P = 0.230$). Two anisometropic subjects in the symmetrical accommodation group, 3 in the aniso-accommodation group, and 4 in the anti-accommodation group had a microtropia with identity. One anisometropic subject in the symmetrical accommodation group, 3 in the aniso-accommodation group, and 2 in the anti-accommodation group had a microtropia without identity. Due to the small number in each group, any analysis to determine whether this is a potential confounding variable would be inconclusive, but it is noteworthy that both types of microtropia were present in all groups.

Discussion

In our study cohort, the presence of anti-accommodation in anisometropic amblyopic subjects was associated with a poorer treatment outcome. A greater degree of anisometropia and possibly a poorer initial visual acuity were also associated with a relatively poor visual outcome. The anisometropic amblyopia treatment success rate of 58% falls within the range of 47%–95% cited in previous literature.[9-14] Similar to previous studies,[15,16] in 31% of subjects, amblyopia was resolved through refractive treatment alone. All of these children had symmetrical or aniso-accommodation; none had anti-accommodation.

The anisometropic amblyopic subjects with anti-accommodation had a significantly worse final visual acuity than those with aniso-accommodation (0.42 logMAR vs 0.14 logMAR). Those with anti-accommodation had a worse final visual acuity compared with those with symmetrical accommodation (0.42 logMAR vs 0.20 logMAR), but this did not reach statistical significance, probably because of the low patient numbers in both groups. We suggest that this association between anti-accommodation and poor outcome could either be due to a more severe primary defect or because poorer accommodation for near hinders treatment.

In our previous report on this group, accommodation had also been assessed with spectacles.[7] There was no evidence of optical overcorrection in the anti-accommodation group at distance where visual acuity is tested. At a distance of 2 m, where 0.5 D of accommodation should be exerted, only a mean of 0.044 D over accommodation had occurred. However, in the anti-accommodation group, we have evidence of possible overcorrection at distance under other viewing conditions (mean, 0.27 D), which might affect visual acuity assessment.

Potential confounding variables were investigated. As in previous literature,[9–11,17-20] a worse initial visual acuity was associated with a worse final visual acuity, but regardless of accommodation type. Previous studies have also found a positive relationship between the degree of anisometropia and the final visual acuity.[12,17,18] Those with anti-accommodation had a significantly higher degree of anisometropia. Therefore, there could be an association between the presence of anti-accommodation, final visual acuity, initial visual acuity, and degree of anisometropia, but causal

relationships cannot be resolved because of the low participant numbers. The majority of researchers support the finding that anisometropia causes amblyopia,[11,17,21-23] so a greater degree of anisometropia results in a worse initial visual acuity. One possible theory is that the presence of anti-accommodation is associated with a larger degree of anisometropia and hence a worse initial visual acuity and, in turn, a worse final visual acuity.

The clinical relevance of our findings has yet to be determined. It might be possible to demonstrate the presence of anti-accommodation in patients by conducting dynamic retinoscopy at near and distance with both eyes open and comparing it to the anisometropia found on cycloplegic refraction. In aniso-accommodation, there will be different amounts of anisometropia between the two distances, with a greater degree of anisometropia at near and, in the case of anti-accommodation, less anisometropia at distance compared to the cycloplegic refraction.

The presence of anti-accommodation means that more accommodation occurs at distance and could result in the full cycloplegic refraction overcorrecting the hypermetropia. However, with spectacles, these patients no longer demonstrated anti-accommodation, although they still demonstrated some milder aniso-accommodation.[7] Even if accurate dynamic retinoscopy is not possible to reveal subtle differences in anisometropia, we suggest that every child returning for visual acuity assessment with their first pair of glasses should have their visual acuity tested with a pinhole or small minus lens to confirm that the tested vision is not affected by a small overcorrection for distance.

The findings from this research might enable clinicians to predict which children with anisometropic amblyopia might have poorer response to treatment. Because anti-accommodation was associated with a worse treatment outcome, it could be argued that occlusion therapy should be started sooner. None of these patients had a successful outcome following refractive treatment alone. Whether refractive adaptation is of benefit in those with anti-accommodation or whether patching should be started immediately is a topic for further study.

Of note, the child from the initial case study[6] learned to accommodate symmetrically after 5 years of full correction and continuing monocular activity encouraged by her parents (after prescribed occlusion had been stopped 4 years earlier). On the other hand, we have seen cases of persistent anti-accommodation in adults. Future research will be aimed at determining whether those with anti-accommodation can be taught to accommodate symmetrically and whether this consequently improves amblyopia treatment outcomes.

This preliminary laboratory-based study is limited by the small sample size. Sufficient participants were not available to perform an adjusted statistical analysis; therefore, it was not possible to separate the effects of final visual acuity and type of accommodation response from the effects of initial visual acuity and the degree of anisometropia. Each accommodation group might have differed before treatment had started. In addition, instead of a full assessment conducted at the time of testing, information regarding the participants was extracted from the medical record. Although this was necessary for some information, it prevented a full diagnosis in some cases. Fifteen percent of patients had no recorded assessment for the presence of a microtropia with identity. Those diagnosed with a microtropia with identity did not all have the presence of eccentric fixation confirmed using the visuoscope. Further research is required to address these confounding variables in relation to the found association between the presence of anti-accommodation and a poor amblyopia treatment outcome.

References

1. Koh LH, Charman WN. Accommodative responses to anisoaccommodative targets. Ophthalmic Physiol Opt 1998;18:254-62.
2. Bharadwaj SR, Candy TR. The effect of lens-induced anisometropia on accommodation and vergence during human visual development. Investig Ophthalmol Vis Sci 2011;52:3595-603.
3. Flitcroft DI, Judge SJ, Morley JW. Binocular interactions in accommodation control: effects of anisometropic stimuli. J Neurosci 1992; 12:188-203.
4. Ball EA. A study of consensual accommodation. Am J Optom Arch Am Acad Optom 1952;29:561-74.
5. Campbell FW. Correlation of accommodation between the two eyes. J Opt Soc Am 1960;50:738.
6. Horwood AM, Riddell PM. Independent and reciprocal accommodation in anisometropic amblyopia. J AAPOS 2010;14:447-9.
7. Toor S, Horwood AM, Riddell P. Asymmetrical accommodation in hyperopic anisometropic amblyopia. Br J Ophthalmol 2018;102: 772-8.
8. Toor SS, Horwood AM, Riddell PM. Anisometropic amblyopia: factors influencing the success or failure of its treatment. Br Ir Orthopt J 2012;9:9-16.
9. Flynn JT, Schiffman J, Feuer W, Corona A. The therapy of amblyopia: an analysis of the results of amblyopia therapy utilizing the pooled data of published studies. Trans Am Ophthalmol Soc 1998;96:431-53.
10. Flynn JT, Woodruff G, Thompson JR, et al. The therapy of amblyopia: an analysis comparing the results of amblyopia therapy utilizing two pooled data sets. Trans Am Ophthalmol 1999;97:373-95.
11. Hussein MA, Coats DK, Muthialu A, Cohen E, Paysse EA. Risk factors for treatment failure of anisometropic amblyopia. J AAPOS 2004; 8:429-34.
12. Scott WE, Kutschke PJ, Keech RV, Pfeifer WL, Nichols B, Zhang L. Amblyopia treatment outcomes. J AAPOS 2005;9:107-11.
13. de Vries J. Anisometropia in children: analysis of a hospital population. Br J Ophthalmol 1985;69:504-7.
14. Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. Arch Ophthalmol 2002;120:268-78.
15. Stewart CE, Moseley MJ, Fielder AR, Stephens DA; MOTAS Cooperative. Refractive adaptation in amblyopia: quantification of effect and implications for practice. Br J Ophthalmol 2004;88:1552-6.
16. Cotter SA; Pediatric Eye Disease Investigator Group, Edwards AR, et al. Treatment of anisometropic amblyopia in children with refractive correction. Ophthalmology 2006;113:895-903.
17. Cobb CJ, Russell K, Cox A, MacEwen CJ. Factors influencing visual outcome in anisometropic amblyopes. Br J Ophthalmol 2002;86: 1278-81.
18. Chen PL, Chen JT, Tai MC, Fu JJ, Chang CC, Lu DW. Anisometropic amblyopia treated with spectacle correction alone: possible factors predicting success and time to start patching. Am J Ophthalmol 2007;143:54-60.
19. Kutschke PJ, Scott WE, Keech RV. Anisometropic amblyopia. Ophthalmology 1991;98:258-63.

20. Woodruff G, Hiscox F, Thompson JR, Smith LK. Factors affecting the outcome of children treated for amblyopia. Eye (Lond) 1994;8:627-31.
21. Wu C, Hunter DG. Amblyopia: diagnostic and therapeutic options. Am J Ophthalmol 2006;141:175-84.
22. Weakley DR. The association between anisometropia, amblyopia, and binocularity in the absence of strabismus. Trans Am Ophthalmol Soc 1999;97:987-1021.
23. Fielder AR, Moseley MJ. Anisometropia and amblyopia—chicken or egg? Br J Ophthalmol 1996;80:857-8.