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The impact of asymmetrical accommodation on anisometropic amblyopia treatment outcomes

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ABSTRACT

Background:

Previous research revealed that the majority of children with anisometropic amblyopia have asymmetrical accommodation. Only 19% (5/26) had symmetrical accommodation, 58% (15/26) had aniso-accommodation and 23% (6/26) had anti-accommodation. The aim of this preliminary study was to determine if 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 (VA) in the amblyopic eye, post amblyopia treatment, was compared between those with symmetrical, aniso- and anti-accommodation.

Results:

There was a significant difference in final VA between the 3 accommodation groups ($p = 0.023$). The anisometropic amblyopes with anti-accommodation had the poorest final VA (0.42 ± 0.25 ($\pm 95\%$ CI) logMAR) with a statistically significant difference when compared to those with aniso-accommodation (0.14 ± 0.08 logMAR; $p = 0.023$). However the difference failed to reach significance when compared to those with symmetrical accommodation (0.20 ± 0.12 logMAR; $p = 0.234$), probably due to the small sample size. The initial VA in the amblyopic eye and the degree of anisometropia were also significantly positively correlated with final VA (both $p < 0.001$).

Conclusions:

The presence of anti-accommodation in anisometropic amblyopia was associated with a poorer amblyopia treatment outcome. The initial VA in the amblyopic eye and the degree of anisometropia were also associated with a poorer treatment outcome. It is possible that all these factors are associated but further research is required to determine causal relationships.

1 INTRODUCTION

2 Accommodation is considered to be a symmetrical process with an equal accommodative
3 response in both eyes[1-5]. However, research within our laboratory has provided strong
4 evidence for the presence of asymmetrical accommodation in a group of hyperopic
5 anisometropic amblyopes[6, 7].

6 A larger prospective study, following a single case report[6], revealed that asymmetrical
7 accommodation was widespread in uncorrected hyperopic anisometropic amblyopia[7]. Only
8 19% (5/26) of children with hyperopic anisometropia were found to have symmetrical
9 accommodation, whilst 81% (21/26) had asymmetrical accommodation to some extent. Of
10 those, 58% (15/26) demonstrated aniso-accommodation, where the amblyopic eye had lower
11 accommodative gain, and 23% (6/26) demonstrated “anti-accommodation”, where the
12 amblyopic eye accommodated more for distance than near.

13 The child with anti-accommodation in the initial case study had a poor response to amblyopia
14 treatment with a final VA in the amblyopic eye of 0.35 logMAR[6]. The success rate of
15 anisometropic amblyopia treatment varies between 47-95%. Although the degree of
16 anisometropia, initial VA and the depth of amblyopia have been implicated, there is no
17 general consensus on the factors that predict treatment success[8]. The poor response to
18 treatment of the child in the case study suggested to us that anti-accommodation could be an
19 additional factor that could indicate the likelihood of a poor outcome to amblyopia treatment.

20 The main aim of this preliminary study was to determine whether the type of accommodation
21 response, in particular, the presence of anti-accommodation, was associated with a poor
22 amblyopia treatment outcome.

23 **MATERIALS AND METHODS**

24 The study adhered to the Declaration of Helsinki, obtained University and UK National
25 Health Service Ethics Committee approval, and obtained fully informed consent from parents
26 and age-appropriate assent from children.

27 Twenty-six children aged between 4 and 8 years were recruited from a local hospital with a
28 primary diagnosis of hyperopic anisometropic amblyopia. They were assessed using
29 cycloplegic retinoscopy and a fundus and media check and full correction was given. They
30 completed an orthoptic investigation, which included VA testing using the Keeler (Keeler
31 Ltd, Windsor, UK) or Sonksen (Haag-Streit, Essex, UK) crowded LogMAR tests. All
32 participants had VA in the non-amblyopic/sound eye of at least 0.2 logMAR (6/9.5), with
33 >0.1 logMAR interocular difference. All had worn their spectacles for at least six weeks and
34 had undergone occlusion therapy, if this had been required, by the time of data collection.
35 Occlusion therapy was stopped after three consecutive visits of stable vision and this was
36 taken to be the final VA. The final VA of the amblyopic eye was extracted from the hospital
37 case notes during the laboratory study[7]. Successful treatment was defined as a final VA in
38 the amblyopic eye of 0.20 logMAR (6/9.5) or better. Other extracted information included the
39 presenting initial VA of the amblyopic eye, the degree of anisometropia (difference in
40 spherical equivalent) and the presence/absence of a microtropia, as these were considered to
41 be potential confounding variables.

42 In our previous report on this group[7], accommodation had been assessed over a range of
43 distances, simultaneously in both eyes, using a Plusoptix S04 photorefractor in PowerRef II

44 mode. Data was collected after spectacles had been worn for six weeks but at varying time
45 points during occlusion therapy. The mean accommodative gain of the sound eye was 0.86
46 ± 0.08 ($\pm 95\%$ confidence interval (CI)) and the mean accommodative gain of the amblyopic
47 eye was 0.41 (± 0.22). The 95% CI for the accommodation gain in the sound eye (± 0.08 ;
48 equivalent to 0.25D difference in accommodation between the eyes at 0.33m) was used as a
49 comparative value to define each individual's accommodative response. The study revealed
50 three types of accommodation response and the participants were grouped based on these
51 responses:

- 52 - 19% symmetrical accommodation (n = 5/26): the accommodative gain in the
53 amblyopic eye was within the 95% CI of the mean gain of the sound eye. The
54 amblyopic eye had a similar lag of accommodation to the sound eye at near and in the
55 distance.
- 56 - 58% aniso-accommodation (n = 15/26): asymmetrical accommodation, as the
57 accommodative gain in the amblyopic eye was greater than the upper boundary of the
58 95% CI of the mean gain of the sound eye. The accommodative gain was greater in
59 the sound eye due to the amblyopic eye under-accommodating.
- 60 - 23% anti-accommodation (n = 6/26): asymmetrical accommodation, as the
61 accommodative gain in the amblyopic eye was again greater than the upper boundary
62 of the 95% CI of the mean gain of the sound eye. The sound eye accommodated more
63 at near than in the distance but the amblyopic eye accommodated more in the distance
64 than at near (negative accommodative gain in the amblyopic eye).

65 The final VA of the amblyopic eye was compared between the three groups with SPSS v 24
66 software using a univariate analysis (final VA as the dependent variable and group as the
67 fixed factor). Further ANOVA analyses and Pearson correlations included the initial VA and
68 the degree of anisometropia. Post hoc t-tests were run as required and used Bonferroni

69 correction. Where assumptions of sphericity are violated, the Greenhouse-Geisser statistics
70 are quoted.

71 **RESULTS**

72 Across all 3 groups, the mean final VA in the amblyopic eye, post treatment, was 0.21 ± 0.09
73 ($\pm 95\%$ CI) logMAR (6/9.5; range -0.10 to 1.00 logMAR). The initial VA in the amblyopic
74 eye was 0.68 ± 0.12 logMAR (6/30; range 0.275 to 1.75 logMAR). The degree of
75 anisometropia was 3.03 ± 0.40 D (range 1.75 to 5.75 D).

76 Overall, 7 (27%) anisometropic amblyopes had no microtropia, 6 (23%) had a microtropia
77 without identity (minimal manifest deviation of less than 10 prism dioptres base out
78 observable on cover test) and 9 (35%) had a microtropia with identity (no movement seen on
79 cover test and central suppression, diagnosed using the 4 prism dioptre test or assessment of
80 fixation). The remaining 4 (15%) patients had no record of investigation of a microtropia
81 with identity within their case notes.

82 **Final VA**

83 Fifteen (58%) of the anisometropic amblyopes had a successful treatment outcome (VA of
84 0.2 logMAR or better in the amblyopic eye). Eight (31%) had a successful outcome following
85 refractive adaptation alone, with all these patients in the symmetrical or aniso-
86 accommodation group.

87 There was a significant difference in final VA between the 3 accommodation groups ($F(2,23)$
88 $= 4.31$, $p = 0.026$) (Figure 1). The anti-accommodation group had a mean final VA of 0.42
89 ± 0.25 logMAR and a significantly worse visual outcome compared to the aniso-
90 accommodation group (0.14 ± 0.08 logMAR, $p = 0.023$; mean difference of 0.28 logMAR
91 with 95% CI 0.03 - 0.54). Although the difference in final VA in the anti-accommodation
92 group failed to reach significance when compared to the symmetrical accommodation group

93 (0.20 ±0.12 logMAR, p = 0.234; mean difference of 0.22 logMAR with 95% CI -0.09 – 0.54)
94 the small participant numbers in both of these groups suggest the analysis could be under-
95 powered. There was no significant difference between the symmetrical and aniso-
96 accommodation groups (p = 1.00; mean difference of 0.06 logMAR with 95% CI -0.21 –
97 0.33).

98 **Initial VA**

99 The initial VA and final VA had a strong positive correlation (r=0.65, 95% CI 0.35 - 0.83, p
100 < 0.001), so a worse initial VA correlated with a worse final VA. On comparison of the 3
101 accommodation groups, the anti-accommodation group had a worse initial VA (anti-
102 accommodation: 0.92 ±0.34 logMAR; aniso-accommodation: 0.62 ±0.13 logMAR;
103 symmetrical accommodation: 0.58 ±0.17 logMAR) but this difference failed to reach
104 significance (F(2,23) = 2.55, p = 0.100). The data were re-analysed to compare the
105 improvement from initial to final VA (symmetrical accommodation: 0.39 ±0.25 logMAR;
106 aniso-accommodation: 0.49 ±0.13 logMAR; anti-accommodation: 0.50 ±0.13 logMAR) but
107 there was no significant difference between the groups (F(2,23) = 0.379, p = 0.690) (Figure
108 2).

109 **Degree of anisometropia**

110 In terms of the degree of anisometropia, there was a strong positive correlation with the initial
111 VA (r = 0.64, 95% CI 0.34 - 0.82, p < 0.001) and the final VA (r = 0.57, 95% CI 0.23 - 0.78 p
112 = 0.002). There was a significant difference on comparison of the 3 groups (F(2,23) = 15.38,
113 p < 0.001). The anti-accommodation group (4.42 ±0.76 D) had a significantly greater degree
114 of anisometropia in comparison to the symmetrical accommodation group (2.85 ±0.55 D; p =
115 0.004) and aniso-accommodation group (2.53 ±0.32 D; p < 0.001). There was no significant

116 difference in the degree of anisometropia between the symmetrical and aniso-accommodation
117 groups ($p = 1.00$).

118 **Microtropia**

119 The final VA in those with no microtropia, microtropia with identity and microtropia without
120 identity was $0.11 (\pm 0.08)$ logMAR, $0.28 (\pm 0.20)$ logMAR and $0.33 (\pm 0.15)$ logMAR
121 respectively. There was no significant difference in the final VA between these groups
122 ($F(2,19) = 1.592$, $p = 0.230$).

123 Two anisometropes in the symmetrical accommodation group, 3 in the aniso-accommodation
124 group and 4 in the anti-accommodation group had a microtropia with identity. One
125 anisometrope in the symmetrical accommodation group, 3 in the aniso-accommodation group
126 and 2 in the anti-accommodation group had a microtropia without identity. Due to the small
127 number of microtropes in each group, any analysis to determine if this is a potential
128 confounding variable would be inconclusive but it is interesting to note that both types of
129 microtropia were present in all groups.

130 **DISCUSSION**

131 This preliminary study revealed that the presence of anti-accommodation in anisometropic
132 amblyopes was associated with a poorer amblyopia treatment outcome. A greater degree of
133 anisometropia and possibly a poorer initial VA were also associated with a poorer visual
134 outcome.

135 The anisometropic amblyopia treatment success rate of 58% falls within the range of 47 to
136 95% cited in previous literature[9-14]. Similar to results of previous studies[15, 16], 31% of
137 patients resolved their amblyopia through refractive treatment alone. All of these children had
138 symmetrical or aniso-accommodation. None had anti-accommodation.

139 The anisometropic amblyopes with anti-accommodation had a significantly worse final VA
140 than those with aniso-accommodation (0.42 logMAR vs 0.14 logMAR). Those with anti-
141 accommodation had a worse final VA compared to those with symmetrical accommodation
142 (0.42 logMAR vs 0.20 logMAR) but this did not reach significance, likely due to the low
143 patient numbers in both these groups. We suggest that this association between anti-
144 accommodation and a poor treatment outcome could either be a sign of a more severe
145 primary defect or because poorer accommodation for near hinders treatment.

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

153 Potential confounding variables were investigated. As found in previous literature[9-11, 17-
154 20], a worse initial VA was associated with a worse final VA, but regardless of
155 accommodation type. Previous studies have also found a positive relationship between the
156 degree of anisometropia and the final VA[12, 17, 18]. Those with anti-accommodation had a
157 significantly higher degree of anisometropia. Therefore, although the presence of anti-
158 accommodation was associated with a worse final VA, there could be an association between
159 these two factors, the initial VA and the degree of anisometropia but causal relationships
160 cannot be resolved due to low participant numbers. The majority of researchers support the
161 finding that anisometropia causes amblyopia[11, 17, 21-23] so a greater degree of
162 anisometropia results in a worse initial VA. One possible theory is that the presence of anti-

163 accommodation is associated with a larger degree of anisometropia and hence a worse initial
164 VA, and in turn a worse final VA.

165 An important question is how these data might transfer to clinical practice. Although this is
166 yet to be studied, it might be possible to determine the presence of anti-accommodation in
167 patients by conducting dynamic retinoscopy at near and distance with both eyes open, and
168 comparing it to the anisometropia found on cycloplegic refraction. In aniso-accommodation,
169 there will be different amounts of anisometropia between the two distances, with a greater
170 degree of anisometropia at near, and in the case of anti-accommodation, less anisometropia in
171 the distance compared to the cycloplegic refraction.

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

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

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

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

205 **CONCLUSIONS**

206 The presence of anti-accommodation in hyperopic anisometropic amblyopia was associated
207 with a poorer treatment outcome. The initial VA and degree of anisometropia were also
208 associated with a worse response to amblyopia treatment. It is possible that all these factors
209 are associated but further research is required to determine causal relationships.

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267

268 LEGENDS

269 Figure 1. Mean final visual acuity ($\pm 95\%$ CI) in each group following treatment.

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