Refractive adaptation in amblyopia: quantification of effect and implications for practice

C E Stewart, M J Moseley, A R Fielder, D A Stephens, and the MOTAS cooperative

Aim: To describe the visual response to spectacle correction (“refractive adaptation”) for children with unilateral amblyopia as a function of age, type of amblyopia, and category of refractive error.

Method: Measurement of corrected amblyopic and fellow eye logMAR visual acuity in newly diagnosed children. Measurements repeated at 6 weekly intervals for a total 18 weeks.

Results: Data were collected from 65 children of mean (SD) age 5.1 (1.4) years with previously untreated amblyopia and significant refractive error. Amblyopia was associated with anisometropia in 18 (5.5 (1.4) years), strabismus in 16 (4.2 (0.98) years), and mixed in 31 (5.2 (1.5) years) of the study participants. Mean (SD) corrected visual acuity of amblyopic eyes improved significantly (p<0.001) from 0.67 (0.38) to 0.43 (0.37) logMAR: a mean improvement of 0.24 (0.18), range 0.0–0.6 log units. Change in logMAR visual acuity did not significantly differ as a function of amblyopia type (p=0.29) (anisometropia 0.22 (0.13); mixed 0.18 (0.14); strabismic 0.30 (0.24)) or for age (p=0.38) (“under 4 years” 0.23 (0.18); “4–6 years” 0.24 (0.20); “over 6 years” 0.16 (0.23)).

Conclusion: Refractive adaptation is a distinct component of amblyopia treatment. To appropriately evaluate mainstream therapies such as occlusion and penalisation, the beneficial effects of refractive adaptation need to be fully differentiated. A consequence for clinical practice is that children may start occlusion with improved visual acuity, possibly enhancing compliance, and in some cases unnecessary patching will be avoided.

Amblyopia is the commonest childhood vision disorder with an estimated prevalence of 1.6–3.5%. This developmental anomaly is characterised by a loss of spatial vision (usually unilateral) in the presence of strabismus, refractive error (bilateral anisometropia or anisometropia), and/or form deprivation. The defining loss of resolution in amblyopia cannot immediately be alleviated by refractive correction even when the sole amblyopic association is anisometropia. None the less, it is accepted that correction of refractive error, particularly in those with anisometropic amblyopia, can, over a period of weeks, reduce the visual deficit—a phenomenon we have termed refractive adaptation. The mechanism which underpins this period of improvement remains unclear although a non-competitive, activity dependent process may be implicated.

Refractive correction is a necessary component of most cases of amblyopia therapy and, where indicated, it is typically prescribed together with mainstream therapies such as occlusion and penalisation. Perhaps because of the presumed urgency of treating the condition, both therapeutic components tend to be prescribed simultaneously or in close temporal proximity. Yet there is evidence that a successful period of refractive adaptation may fully correct the visual deficit and pre-empt the need for further treatment, and, even where this is not the case, limited improvement may still enhance concordance with occlusion therapy. From the perspective of treatment evaluation, prescribing a refractive correction at the same time as another therapy militates against differentiating their relative contributions to the eventual visual outcome.

The present study examines the phenomenon of refractive adaptation, specifically with regard to its influence as a function of age, type of amblyopia, and refractive error. The analysis utilises the dataset of the Monitored Occlusion Treatment of Amblyopia Study—a recently reported investigation of the dose-response function of amblyopia therapy that included non-overlapping phases of refractive adaptation and occlusion therapy.

**METHODS**

**Study design**

The Monitored Occlusion Treatment for Amblyopia Study (MOTAS) sought to determine the dose-response function of occlusion therapy for the treatment of amblyopia in childhood. The design and principal findings have been reported separately elsewhere. Children were recruited from two London hospitals between January 2000 and December 2001. Ethical approval was sought and obtained from the two local research ethics committees. Inclusion eligibility criteria were 3–8 years of age; anisometropia and/or strabismus; an interocular acuity difference of at least 0.1 logMAR; and no history of previous amblyopia treatment (includes spectacle wear or occlusion), or ocular pathology or learning difficulties. Rationale for inclusion criteria are discussed elsewhere. Anisometropia was defined as 1.00D or more difference in refractive error between the two eyes. A diagnosis of strabismus was given in all cases of manifest strabismus for near and/or distance fixation including those with microtropia with identity where the presence of eccentric fixation was the only sign of strabismus.

The principal design components of MOTAS were a phase of refractive adaptation (for those children with refractive error) followed by a phase of occlusion. The duration of the former was of a fixed 18 week duration: a period adopted on the basis of a recent study indicating that no clinically significant gains (that is, >0.10 logMAR) occurred beyond this time. The occlusion phase was of variable duration depending upon an algorithm to detect “stability” of visual outcome (that is, the best visual outcome likely to have been achieved for any given child). Here, we report only upon
visual outcome at the end of the refractive adaptation phase.

Prescription of spectacle correction was based on a strict refraction protocol (table 1). Refractive adaptation began approximately 14 days after the initial assessment and determination of stable baseline measures (allowing for delivery of spectacles from the child’s own dispensing optician). At the first visit of the refractive adaptation phase (week 0), visual performance was recorded with and without refractive correction. Previous instruction had been given that spectacles were not to be worn in the intervening period between delivery and clinic attendance. Children and parents were advised of the need for spectacles to be worn full time and a schedule of three vision assessments at 6 weekly intervals instigated (weeks 6, 12, and 18).

The primary visual function outcome measure was logMAR visual acuity. Three logMAR visual acuity charts were employed: ETDRS (manufacturer precision vision), crowded (Keeler Ltd), and uncrowded (Keeler Ltd) logMAR charts. Standard protocols for visual acuity testing were used and were scored by letter. The type of chart used depended on the reading ability of the child, and was generally age dependent.

Kruskal-Wallis one way analysis of variance on ranks was provided in table 5. The number of data sets at the 0, 6, 12, and 18 weeks assessment were 49, 50, 47, and 52, respectively.

RESULTS

With parental written consent, 65 children of mean (SD) age 5.1 (1.4) years with previously untreated amblyopia and significant refractive error were recruited. Amblyopia was associated with anisometropia in 18 (mean age 5.5 (1.4) years) participants, strabismus in 16 (mean age 4.2 (0.98) years), and both anisometropia and strabismus in 31 (mean age 5.2 (1.5) years). For amblyopic eyes, mean (SD) visual acuity at recruitment was 0.77 (0.41) and ranged from 0.1 to 1.6 logMAR. Mean (SD) visual acuity in the fellow eyes was 0.15 (0.1) and ranged from −0.05 to 0.4. The number of data sets at the 0, 6, 12, and 18 weeks assessment were 49, 50, 47, and 52, respectively.

Distribution of refractive errors

Mean (SD) (spherical error (dioptres)) for the amblyopic and fellow eyes was +4.0 (2.1) and +2.7 (1.8), respectively. Astigmatism was present in 41 (63%) with a mean (SD) cylindrical error of −0.91 (1.00) for amblyopic eyes and −0.45 (0.62) for fellow eyes. Distribution of refractive error according to amblyopic type is shown in table 2. Mean (SD) anisometropia was 1.47 (1.56) for the whole group and 1.97 (1.03), 0.32 (0.34) and 1.66 (2.11) for amblyopia associated with anisometropia, strabismus, and mixed amblyopia, respectively.

Participants were categorised according to type of refractive error: anisometropic hypermetropia, anisometropic astigmatism, isometropic. Details of the classification scheme are shown in table 3, and the mean refractive error of each group is provided in table 4.

Distribution of strabismus

Details of the classification of strabismus for those in the strabismic amblyopia and mixed amblyopia groups are provided in table 5.

Response to spectacle wear

Amblyopic eyes

The mean (SD) uncorrected vision of amblyopic eyes at week 0 refractive adaptation was 0.77 (0.40). Mean (SD) corrected visual acuity of amblyopic eyes improved significantly (p<0.001) from 0.67 (0.40) at week 0 to 0.43 (0.37) after 18 weeks of spectacle wear: a mean improvement of 0.24 (0.18), range 0.00 to 0.60 log units (fig 1 and table 6). Eight
(12%) children demonstrated less than 1 log line (0.1) of improvement (six mixed; one anisometropic; one strabismic).
Five of the eight children had worn spectacles (range 8–14 weeks) before study entry, although significantly different
prescriptions were ordered at the start of the refractive
adaptation phase of the study.
Mean (SD) interocular difference reduced significantly
(p = 0.01) from 0.15 (0.13) to 0.07 (0.07)
in visual acuity of 0.09 (0.08) log units. Children with less
significant refractive errors in the fellow eye (1.5D or less)
demonstrated a 0.04 (0.05) log unit improvement. Those with
significant refractive errors (1.75D or more) demonstrated a
0.16 (0.20) log unit improvement.

Resolution of amblyopia with spectacles alone
During refractive adaptation the mean (SD), visual acuity of
the amblyopic eye in 14 study participants (mean age 5.49
(1.46) years) improved from 0.48 (0.20) to 0.1 (0.08). These
children had an average interocular difference of 0.02 (0.05)
at the end of refractive adaptation and therefore no longer
met the study entry inclusion criteria. On this basis they left
the study (that is, did not progress to the occlusion phase). Of
these 14, nine did not require any further treatment; five had
strabismus, five anisometropia, and four had both strabismus
and significant refractive errors.

Fellow eyes
Mean (SD) visual acuity in the fellow eyes improved
significantly (p<0.001) from 0.15 (0.13) to 0.07 (0.07)
logMAR during refractive adaptation, a mean (SD) change
in visual acuity of 0.09 (0.08) log units. Children with less
significant refractive errors in the fellow eye (1.5D or less)
demonstrated a 0.04 (0.05) log unit improvement. Those with
significant refractive errors (1.75D or more) demonstrated a
0.1 (0.07) log unit improvement.

Table 4 Mean (SD) refractive error and cylinder axis range for refractive error categories

<table>
<thead>
<tr>
<th>Amblyopic eye</th>
<th>All groups</th>
<th>Anisometropic hypermetropia (n = 29)</th>
<th>Anisometropic astigmatism (n = 19)</th>
<th>Isometropia (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean sphere</td>
<td>4.0 (2.1)</td>
<td>4.51 (1.9)</td>
<td>4.34 (2.7)</td>
<td>3.69 (1.64)</td>
</tr>
<tr>
<td>Range sphere</td>
<td>+9.00 to 4.00</td>
<td>+9.00 to 2.00</td>
<td>+7.75 to 4.00</td>
<td>+6.50 to 0.75</td>
</tr>
<tr>
<td>Mean cylinder</td>
<td>−0.91 (1.0)</td>
<td>−0.45 (0.29)</td>
<td>−1.4 (0.87)</td>
<td>−1.1 (0.85)</td>
</tr>
<tr>
<td>Range cylinder</td>
<td>0 to 3.50</td>
<td>0 to 0.50</td>
<td>0.75 to 3.25</td>
<td>0 to 3.50</td>
</tr>
<tr>
<td>Mean sphere</td>
<td>2.7 (1.8)</td>
<td>2.19 (1.19)</td>
<td>2.67 (1.35)</td>
<td>3.37 (1.65)</td>
</tr>
<tr>
<td>Range sphere</td>
<td>+6.50 to 0.00</td>
<td>+6.00 to 0.00</td>
<td>+6.50 to 0.00</td>
<td>+6.00 to 0.75</td>
</tr>
<tr>
<td>Mean cylinder</td>
<td>−0.45 (0.62)</td>
<td>−0.13 (0.19)</td>
<td>−0.71 (0.33)</td>
<td>−0.71 (0.88)</td>
</tr>
<tr>
<td>Range cylinder</td>
<td>0 to 3.00</td>
<td>0 to 0.50</td>
<td>0.75 to 1.25</td>
<td>0 to 3.00</td>
</tr>
</tbody>
</table>

Table 5 Classification of subjects with manifest strabismus (includes those with mixed
amblyopia). Mean (SD) of angle of deviation at near and distance fixation with and
without correction at week 0

<table>
<thead>
<tr>
<th>Classification of subjects with manifest strabismus</th>
<th>Corrected PCT (near)</th>
<th>Corrected PCT (distance)</th>
<th>Uncorrected PCT (near)</th>
<th>Uncorrected PCT (distance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully accommodative esotropia (n = 3)</td>
<td>9 (4) △ BO</td>
<td>7 (3) △ BO</td>
<td>20 (9) △ BO</td>
<td>16 (8) △ BO</td>
</tr>
<tr>
<td>Partially accommodative esotropia (n = 21)</td>
<td>20 (12) △ BO</td>
<td>15 (12) △ BO</td>
<td>29 (14) △ BO</td>
<td>22 (14) △ BO</td>
</tr>
<tr>
<td>Microtropia with identity (n = 5)</td>
<td>1 (2) △ BI</td>
<td>1 (1) △ BI</td>
<td>1 (2) △ BI</td>
<td>1 (1) △ BI</td>
</tr>
<tr>
<td>Microtropia without identity (n = 5)</td>
<td>5 (2) △ BO</td>
<td>4 (2) △ BO</td>
<td>8 (3) △ BO</td>
<td>6 (4) △ BO</td>
</tr>
<tr>
<td>Acquired non-accommodative esotropia (n = 7)</td>
<td>35 (12) △ BO</td>
<td>30 (9) △ BO</td>
<td>40 (12) △ BO</td>
<td>34 (11) △ BO</td>
</tr>
<tr>
<td>Non-specific exotropia (n = 1)</td>
<td>8 △ BI</td>
<td>4 △ BI</td>
<td>8 △ BI</td>
<td>6 △ BI</td>
</tr>
<tr>
<td>Distance exotropia (n = 1)</td>
<td>6 △ BI</td>
<td>18 △ BI</td>
<td>8 △ BI</td>
<td>20 △ BI</td>
</tr>
<tr>
<td>Total (n = 47)</td>
<td>19 (15) △ BO</td>
<td>15 (13) △ BO</td>
<td>25 (17) △ BO</td>
<td>19 (13) △ BO</td>
</tr>
</tbody>
</table>

BO, base out; BI, base in.
*SD, not applicable (n = 1).

Figure 1 Change in mean (SD) logMAR visual acuity of the amblyopic eye during refractive adaptation.
Table 6  Mean (SD) logMAR visual acuity during refractive adaptation by amblyopia type

<table>
<thead>
<tr>
<th></th>
<th>All groups</th>
<th>Anisometropic (n = 18)</th>
<th>Strabismus (n = 16)</th>
<th>Mixed (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncorrected VA start</td>
<td>5.1 (1.4)</td>
<td>5.5 (1.5)</td>
<td>4.2 (1.0)</td>
<td>5.2 (1.5)</td>
</tr>
<tr>
<td>Corrected VA week 0</td>
<td>0.77 (0.41)</td>
<td>0.74 (0.37)</td>
<td>0.78 (0.36)</td>
<td>0.75 (0.52)</td>
</tr>
<tr>
<td>Corrected VA week 6</td>
<td>0.67 (0.38)</td>
<td>0.66 (0.32)</td>
<td>0.70 (0.50)</td>
<td></td>
</tr>
<tr>
<td>Corrected VA week 12</td>
<td>0.56 (0.38)</td>
<td>0.59 (0.40)</td>
<td>0.61 (0.40)</td>
<td>0.40 (0.42)</td>
</tr>
<tr>
<td>Corrected VA week 18</td>
<td>0.45 (0.37)</td>
<td>0.47 (0.38)</td>
<td>0.62 (0.39)</td>
<td>0.31 (0.24)</td>
</tr>
<tr>
<td>Best VA</td>
<td>0.43 (0.41)</td>
<td>0.48 (0.43)</td>
<td>0.51 (0.40)</td>
<td>0.45 (0.43)</td>
</tr>
<tr>
<td>Change in VA</td>
<td>0.24 (0.18)</td>
<td>0.24 (0.14)</td>
<td>0.15 (0.19)</td>
<td>0.25 (0.22)</td>
</tr>
<tr>
<td>Weeks to best VA (within study duration)</td>
<td>13.4 (5.7)</td>
<td>14.8 (3.86)</td>
<td>13.1 (5.8)</td>
<td>14.0 (4.0)</td>
</tr>
</tbody>
</table>

Table 7  Mean (SD) logMAR visual acuity during refractive by category of refractive error

<table>
<thead>
<tr>
<th></th>
<th>All groups</th>
<th>Anisometropic hypermetropia (n = 29)</th>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>0.31 (0.24)</td>
</tr>
<tr>
<td>Improvement in VA</td>
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<td>0.48 (0.43)</td>
<td>0.51 (0.40)</td>
<td>0.45 (0.43)</td>
</tr>
<tr>
<td>Weeks to best VA (within study duration)</td>
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<td>14.8 (3.86)</td>
<td>13.1 (5.8)</td>
<td>14.0 (4.0)</td>
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</tbody>
</table>

and anisometropia; 13 of the 14 had a significant refractive error in their fellow eye.

DISCUSSION

This study has quantified the gains in visual acuity attributable to refractive correction and a subsequent period of refractive adaptation as a function of amblyopia type and age of child.

Clinically and statistically significant improvements in the acuity of amblyopic eyes were observed subsequent to 18 weeks of refractive adaptation, which did not differ as a function of type of amblyopia or age (3–8 years). Our study does not allow us to rule out the possibility of further improvement beyond 18 weeks. A significant proportion of children attained acuity in their amblyopic eye such that occlusion therapy was not required. Acuity gains accrued gradually over time taking, on average, 14 weeks and were slightly less (by around one line) than we reported in a much smaller (n = 12) cohort. In contrast, a recent randomised controlled trial of the treatment of unilateral visual impairment reported similar gains in the spectacle only group to those of our present study but only from an initially smaller (n = 12) cohort. In children, this is the first time that the visually sensitive period around 6–7 years the evidence is 8 years of age. This is the first time that the visually sensitive period around 6–7 years the evidence is 8 years of age. This is the first time that the visually sensitive period around 6–7 years.18,19

The pathophysiological mechanisms contributing to the amblyopic deficit differ according to amblyopia type. In anisometropic amblyopia unilateral blur causes visual deprivation and reduced cortical neuronal sensitivity. In strabismic amblyopia there is cortical inhibition of impulses from the fovea of the deviating eye.11 For anisometropic amblyopia the correction of refractive error eliminates the unilateral blur which should improve neuronal sensitivity and therefore stimulate visual recovery (see above). However, in the case of the strabismic amblyope with identical refractions in each eye, correction of refractive error may reduce the angle of strabismus but this is unlikely to change cortical inhibition and therefore the mechanism(s) of improvement is unclear. Possibly, in-focus peripheral visual input has a part to play.

Significant gains were also seen in the fellow eyes of children; however, in most participants this was predictable given the presence of a significant refractive error in their fellow eye. Those with none or insignificant refractive errors showed a minimal change within the limits of normal test-retest variability.14

Although it is a long held clinical belief that amblyopia therapy is more successful in the earlier stages of visual development (in accord with the presumed end of the visual sensitive period around 6–7 years18,19), the evidence is not conclusive. Recent ATS studies of the Pediatric Eye Investigator Group demonstrated greater gains in visual acuity of those less than 5 years of age for children with severe amblyopia17 but no difference for children of another study that had moderate amblyopia.16 However, here we demonstrate equal gains for all age groups between 3 and 8 years of age. This is the first time that the visually sensitive period for refractive correction has been examined.
Authors' affiliations
C E Stewart, M J Moseley, A R Fielder, Department of Visual Neuroscience, Imperial College London, UK
D A Stephens, Department of Mathematics, Imperial College London, UK

REFERENCES

The Lighter Side

Mr Beadle’s episode of Bell’s palsy could not have come at a worse time. © Michael Balis.
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