

Two Case Studies: Eccentric Fixation and Amblyopia - A Challenge to the Treating Practitioner

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ABSTRACT

Two cases of eccentric fixation in the presence of strabismic and anisometropic amblyopia are presented, both of which failed to respond to therapeutic efforts. A brief account of past and present treatment modalities used in the management of eccentric fixation is provided, including a discussion as to the limitations and efficacy of each. Analysis of the literature reveals that regardless of the treatment method employed, a population of "incurable" patients exist who fail to improve despite treatment efforts.

Treatment outcome is dependent upon a multitude of factors and the potential reasons as to why this sub-group of patients with eccentric fixation fail to show improvement are discussed. This paper serves to highlight the challenges that such cases pose to the treating eye care practitioner and encourages the need for further research in this area; an area where little is known even today.

Keywords: eccentric fixation, amblyopia, strabismus, anisometropia, visual outcome

INTRODUCTION

Amblyopia is a leading cause of monocular vision impairment.¹ Known causes of amblyopia include ocular misalignment (strabismus) and a difference in uncorrected refractive error between the two eyes (anisometropia).² Mixed strabismus and anisometropia is reported as the cause of amblyopia in 37% to 43% of cases.³⁻⁷ In the majority of instances, amblyopia can be successfully treated via means of occlusion therapy, atropine penalisation, spectacle correction or a combination of these.^{4,6,8-10} However, not infrequently the treatment of amblyopia is made challenging by the presence of non-central fixation in the amblyopic eye. Eccentric fixation has been reported by Cüppers (1958) and Von Noorden (1970) to exist in as many as 35% to 44% of cases of amblyopia and thus constitutes a considerable factor in the management of this condition.¹¹

Fixation typically involves the purposeful imaging of an object of interest on the fovea - the part of the retina in most individuals that possesses the highest resolving power and holds principal visual direction.¹²⁻¹⁴ However,

in individuals with eccentric fixation a reorganisation of retinal motor values occurs such that a retinal point other than the fovea assumes principal visual direction.^{11,15,16} This occurs despite a reduction in the level of visual acuity achievable with the eccentric retinal locus compared to that permitted by the fovea.^{13,15,16} The visuscope, born out of earlier improvements in diagnostic armamentarium, made possible the identification of such anomalies in fixation and upon its invention contributed to eccentric fixation no longer being considered a rare phenomenon in amblyopic eyes.¹⁷ The visuscope is still commonly used by practitioners today and represents an invaluable tool in the diagnosis and classification of eccentric fixation.¹⁸

Despite the therapeutic management of eccentric fixation being the subject of much controversy in the past, the restoration of central fixation and subsequent reversal of amblyopia is generally achieved in most cases today.¹ However, a minority of patients still remain unresponsive to treatment.¹⁹ In such cases, an investigation as to the factors impinging upon the prognosis is warranted and can aid in making a clinical decision about when to cease treatment.

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CASE REPORTS

Case Report 1

Master C presented at age 2 years and 3 months with a right esotropia present since birth. No known family history was reported and general health was otherwise unremarkable. Cover testing confirmed a constant right esotropia, with RSO-- and RIO++ revealed on ocular movement testing. Unaided visual acuity was assessed and no response to any of the single Kay Pictures could be elicited from the right eye at 0.5 metres, with marked objection to left cover. Visual acuity in the left eye was 3/5 unaided. Non-central fixation of the right eye was diagnosed on visuoscopy, wandering in the area of the disc. Left fixation was central. Cycloplegic refraction revealed hypermetropic anisometropia and glasses were prescribed, RE +4.50 DS and LE +2.50 DS. No other clinically significant findings were apparent.

In a three-month follow-up visit, right amblyopia was seen to persist, with no improvement in vision. Left occlusion was then prescribed for four to six hours per day for one month. Over the following nine months, when left occlusion was prescribed for six hours per day, the family reported that he mostly wore it for four to five hours a day, with generally good compliance. Regular review showed right fixation remained eccentric midway between the fovea and disc, with a negligible improvement in vision, stabilising at LE 3/30 and RE 3/4.5. The esotropia remained stable at 25 to 30 prism dioptres.

At this stage of the treatment, Master C began demonstrating social withdrawal, becoming uncharacteristically solemn and lacking motivation to play or venture outdoors. Master C's parents were advised to taper occlusion and strabismus surgery was to be considered.

Case Report 2

Miss D presented at age 4 years and 3 months with a right esotropia present since birth. General health was otherwise unremarkable. Past ocular history included weekly atropine penalisation for eight months and no prior surgery or occlusion therapy. Cover testing revealed a moderate right esotropia not taking up fixation, measuring 25 prism dioptres by Krinsky reflections. Ocular movements were full. Visual acuity with glasses was RE 2/60 (Sheridan Gardiner singles) and LE 3/4.8 (matching logMAR). Visuoscopy revealed unsteady eccentric fixation in the amblyopic eye and central fixation in the left. Hypermetropic anisometropia was present and spectacle prescription was increased to RE +9.00/-1.25 x 180° and LE +2.50/-1.25 x 175° at this visit.

Minimal change in vision was noted in a subsequent examination three months later. Left atropine penalisation was then prescribed twice per week with one hour of left occlusion per day. Over the following 11 months, poor treatment compliance was reported and Miss D failed to attend several visits. Despite the family being advised on

consecutive occasions as to the importance of occlusion therapy, the patient completed irregular and ill-sustained periods of patching and atropine occlusion.

Upon regular review, right fixation remained eccentric and unsteady, midway between fovea and disc. At age 5 years and 5 months limited improvement in visual acuity was observed, RE 3/18 (Sheridan Gardiner singles) and LE 3/3 (logMAR chart). Only one letter on the 3/30 line was seen when visual acuity in the right eye was tested using the crowded chart. At this stage, the patient was advised to increase left occlusion to four or more hours per day and continue left atropine twice per week until no further improvement in vision could be attained.

DISCUSSION

Despite eccentric fixation representing a common phenomenon in young patients with strabismus or severe unilateral retinal image blur, little is known about the exact aetiology of this fixation anomaly. Some have proposed that a causal relationship exists between abnormal retinal correspondence (ARC) and eccentric fixation, whereby the facultative change in principal visual direction that occurs under binocular conditions in ARC can progress to become obligatory under monocular viewing and thus manifests as eccentric fixation.²⁰ However, this theory has been refuted on the basis that the angle of anomaly and angle of eccentricity are not always equal.^{13,21} Others suggest that eccentric fixation is the direct result of a non-organic defect in foveal function brought about by sensory inhibition.^{20,22} Allegedly, the reduction in foveal function experienced through suppression is occasionally carried to such an extent that the resolving power of the fovea is reduced to a level below that of the surrounding retina.²³ The incentive is then for the amblyopic eye to fixate eccentrically. However, this mechanism remains questionable as frequently the visual acuity at the fovea remains superior to that at the locus of eccentric fixation in amblyopic eyes.^{24,25}

Many different treatment modalities for eccentric fixation have been employed in the past, including pleoptics, red filter treatment, inverse prisms, inverse occlusion and direct occlusion. All reported success, with 60% to 98% of cases showing improvement,^{17,18,26-33} however, none were without their limitations.^{26,29,30,34,35} Pleoptics involved dazzling the peripheral retina of the amblyopic eye with a high intensity light, then stimulating the fovea with prolonged sessions of intermittent flashing, followed by exercises to restore foveal straight-ahead projection.¹⁶ Generally only suitable in children aged 7 years or older, it was popular following its initiation but later abandoned due to inconsistent results and the treatment proving both expensive and arduous.^{16,36-38} Similarly, others reporting on the efficacy of red filter treatment, where the sound eye was occluded and a red filter placed over the amblyopic

eye to preferentially stimulate the cone photoreceptors,²⁶ noted that central fixation could be restored to normal in some instances but that maximum visual acuity was not usually obtained.^{27,37} Inverse prisms, designed to force the eye to make a fixation movement so that the fovea is in a straight-ahead position, were used in conjunction with hand-eye activities to retrain the principal visual direction.³⁹ However, this method demanded significant patience and adherence to detail on behalf of the patient, and successful results often required up to nine or ten months in difficult cases.³⁹ Inverse occlusion was advocated by Bangerter (1953) and Cüppers (1958) on the premise that occlusion of the eccentrically fixing eye could disrupt the links connecting the fovea of the sound eye with the eccentric retinal locus of the deviated eye. However, this method has been largely replaced by conventional occlusion; with the aim that occlusion of the normally fixing eye will result in a re-establishment of central fixation and improvement of vision in the amblyopic eye.^{17,19,36}

On researching the literature, the authors have found minimal reported studies or mention of eccentric fixation since the 1970s, a fact also noted by others.³ Mainstream treatments used in contemporary practice aim to promote the function of the amblyopic eye and encourage central fixation by restricting, usually through direct occlusion or atropine penalisation, the competitive advantage of the fellow eye.^{1,19} These methods are commonly preceded by spectacle correction, with the aim of first minimising retinal image blur owing to uncorrected refractive error.¹ Recently, the valuable role of refractive correction in the treatment of amblyopia was reported.^{4,9,40,41} Refractive correction alone has been reported to improve visual acuity an average of 2.9 lines and result in resolution of amblyopia in at least one-third of 3 to 7 year-old children with untreated anisometropic amblyopia.⁴

In modern practice, direct occlusion for the treatment of severe amblyopia is now advised regardless of the type of fixation, provided that the patient is still within the plastic age of visual development.¹⁹ It has been demonstrated that six hours of occlusion per day produces a similar outcome to full-time occlusion in severe amblyopia,⁵ or even two hours occlusion with atropine penalisation.⁶ Two hours of daily patching combined with one hour of near activities has also been shown to modestly improve amblyopia associated with strabismus, anisometropia, or both, in children aged 3 to 7 years old.¹⁰ Earlier studies of children with eccentric fixation who were successfully treated, reported that central fixation and maximal visual acuity was generally achieved within three to four months of full-time occlusion, with a small number of children being occluded for up to nine months.^{17,30,31,35} More recently, dose-response studies have shown that vision improvement reaches a plateau around 100 cumulative hours,⁷ or at 200 hours, with minimal improvement after 400 hours.³ Maximum improvement occurs within the first three to four months,^{3,5,6} but further

improvement can be demonstrated up to six months.⁶ It has also been suggested that strabismus surgery disrupts the eccentric fixation due to proprioceptive and innervational influences, but that this seldom results in a spontaneous improvement in vision.^{17,18}

Despite being the treatment method of choice, occlusion therapy is not without its limitations. The implications of occlusion on the psycho-social well-being of patients, including peer victimisation,^{42,43} social stigma and subsequent alterations in self-concept,⁴⁴ have been documented. The ill effects of which were beginning to manifest in Master C following prolonged and intensive treatment. For this reason, atropine penalisation is often favoured over occlusion for the decreased social burden inflicted and has been shown to produce similar treatment outcomes to patching.^{8,45}

Regardless of the treatment modality employed, a minority of patients fail to improve in spite of therapeutic efforts,^{26,29,30,34,35} as in the cases of Master C and Miss D. These patients, referred to in the literature as "lost cases," are only revealed when no positive response to considerable attempts at management can be elicited.¹⁹ Historically, red filter treatment had a non-responder rate of 13% to 53%,^{26,27,37} with one study reporting that 80% of cases did not maintain any gain in visual acuity.³⁸ However, of note is that all of these studies employed small sample sizes. Studies involving pleoptics reported a non-responder rate of between 28% and 35%,^{18,32} with one study finding no long-term benefit in 45% of patients.⁴⁶ Furthermore, 10% to 33% of subjects undergoing direct occlusion, either with or without a preparatory period of inverse occlusion, failed to achieve central fixation.^{17,35,37} Inverse occlusion was found to be ineffective and not recommended for young children^{30,35} and it has even been suggested that it represents a waste of valuable time, detracting from the critical treatment period.¹⁷ Comparison of treatment outcomes is complicated by the lack of definition of the eccentric fixation and the vague and varied definitions of cure or improvement. However, analysis of the reported cases showed that those with peripheral, steady eccentric fixation were the least likely to improve.^{17,18,28,32} Herein, in apparent non-responders the dilemma lies in determining whether further treatment would prove futile and thus a clinical decision about when to discontinue treatment must be made. In such instances, an investigation as to the factors affecting treatment outcome is warranted.

The restoration of central fixation and success of amblyopia treatment is contingent upon several factors. Final visual outcome is dependent upon the type of fixation present, with central wandering fixation holding a better functional prognosis than steady, well-entrenched eccentric fixation.^{19,34,38} Visual acuity potential is greater if fixation is nearer the fovea,⁴⁷ with the hypothesis that occlusion improves the amblyopia component but that residual visual

acuity is dependent on the eccentric retinal point.⁷ The severity of amblyopia can also dictate treatment success, with well-established amblyopia and those with poor visual acuity at diagnosis often proving more treatment-resistant.^{5,7,48,49} Best-corrected vision of less than 6/12 at the time of initial treatment and a difference in visual acuity between the two eyes of four or more lines have been identified as risk factors for treatment failure.⁴⁸ The degree of anisometropia is also highly significant in predicting final visual outcome in patients, with higher degrees of anisometropia having a negative effect on treatment outcome.^{4,7,48,49} Stewart et al found that children with eccentric fixation responded significantly less to refractive correction, and that those with severe mixed amblyopia and eccentric fixation had significantly greater residual amblyopia after six hours per day of occlusion therapy.⁷ Owing to each of the above factors, the success of treatment in both of the current patients may have been compromised.

The success of treatment is not only limited to factors pertaining to the patient's visual status, but extends to include more readily modifiable influences. A long interval between the onset of squint and the implementation of effective treatment can negatively affect prognosis.^{16,28} Thus, prompt diagnosis and early treatment is imperative.³⁴ In addition, non-compliance is a known and frequently reported influence on treatment outcome, with poor compliance leading to a reduction in treatment success.^{7,48} Miss D in particular was diagnosed much later and demonstrated reduced compliance which could have contributed, at least in part, to poor treatment outcome. The reasons for non-compliance are infinitely broad but poor parental cooperation is often a key factor underlying non-compliance in children.¹⁹ Thus, it is recommended that a full and detailed explanation of the importance and reasoning behind treatment be consistently issued to parents in an effort to gain their cooperation and understanding if therapy is to be effective.^{28,48}

In reviewing the given cases, Master C was compliant with occlusion over a ten-month period and has certainly received the optimal dose of occlusion with minimal change. It would appear that surgery is the next option and atropine penalisation could be attempted as this would avoid the psycho-social problems now in evidence. In the same way Miss D, who has never been compliant is at least continuing with atropine as maintenance occlusion. Given that they are both non-responsive to occlusion, this level of maintenance occlusion may give some benefit with minimal side-effects during the sensitive period.

Indeed, eccentric fixation remains an area where knowledge is limited and further research is required in order to understand its mechanisms and why this sub-group of patients fail to improve despite concerted treatment efforts. The authors hypothesise that there may be some sub-clinical foveal pathology present in these patients which drives the

incentive for them to fixate eccentrically. However, evidence to support this theory has not yet been found.

CONCLUSION

Whilst eccentric fixation in accompaniment with amblyopia is not uncommon, the pathogenesis of this fixation anomaly remains unclear. A myriad of treatments have been implemented in the past, each carrying specific limitations and different levels of efficacy. Whilst the treatment methods of choice used today are often effective in restoring central fixation and ameliorating amblyopia, they do not guarantee success in every patient. Ultimate success is contingent upon many factors, some of which are known and can be easily identified in a given case, and others which may not be immediately apparent. The latter makes the decision about when to cease treatment difficult and a clinical judgement must be made about whether maximum vision is likely to have been achieved and thus any continued treatment futile. Until such a time when more is known, in patients who fail to respond to conventional treatment, the clinician can at best conduct a thorough examination into the factors potentially impinging upon prognosis; be it non-compliance, well-established eccentric fixation or otherwise. These factors can then help guide the clinician in making an appropriate decision about when to cease treatment. Indeed, further research in this field is necessary and encouraged; as currently it still stands to represent an area about which relatively little is known.

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