Recovery in microtropia: implications for aetiology and neurophysiology

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Abstract

Aims/Background—The basis of binocular single vision in microtropia remains a matter of contention. This paper discusses the implications of recovery, in a group of primary microtropes following treatment, in relation to current concepts on the aetiology of the condition and proposed retinocortical correspondence.

Methods—Nine previously untreated primary microtropes whose condition resolved, were reviewed in detail to assess the patterns of change in retinal correspondence, uniocular fixation, stereacuity, and visual acuity in response to treatment.

Results—Anomalous retinal correspondence (ARC), a central scotoma, reduced or absent stereacuity, amblyopia, and uniocular eccentric fixation were present in all patients before treatment. Following treatment, all cases attained normal retinal correspondence (NRC), elimination of the central scotoma, stereo acuity levels of between 20 and 40 seconds of arc, 6/5 Snellen visual acuity in both eyes, and foveal fixation in both eyes.

Conclusion—A hypothesis is put forward that for the patients described, a period of normal development is likely to have preceded the onset of microtropia, during which the retinocortical “foundations” for NRC were established. Precise pairing of foveo-foveal receptive fields was not abolished by the presence of amblyopia and a central scotoma, but this relation was temporarily suspended and binocular single vision was sustained via the neural substrate of paired receptive fields over a wide retinocortical area.

Microtropia was diagnosed according to Lang’s classification,1 on the basis of the findings on cover-uncover test, alternate prism and simultaneous prism and cover test with full refractive correction worn while fixation was maintained on an accommodative target at 1/3 and 6 metres. Binocular status was assessed using Bagolini striated glasses,2 fusional amplitudes were measured with prisms, the Irvine V test3 was employed to aid differentiation of bifoveal BSV and a central scotoma, and stereo acuity was measured with the Frisby stereotest4 while wearing appropriate spectacle correction. Detailed assessment of uniocular fixation was undertaken using an Oculus visuscope which has a scale calibrated to allow 0.5° accuracy. Position, pattern, percentage foveation, primary visual direction (PVD), and zero retinomotor point (ZRP) were recorded.5 Percentage foveation was measured while the subject was instructed to fixate steadily on the fixation graticule during a 30 second period. The ZRP was assessed by moving the fixation graticule away from the initial fixation area to the peripheral retina, while the subject looked...
The subject was then instructed to re-fixate the graticule and the initial point of reflex fixation was recorded as the ZRP. The PVD was assessed by asking the patient to state whether he or she felt they were looking directly at the fixation target in order to see and whether it seemed to lie straight ahead. The retinal locus which was aligned with the fixation target when this sensation was appreciated was recorded as being associated with the PVD. Snellen visual acuity was assessed in all cases and was converted to a log scale for the purpose of analysis.

All patients were prescribed full time wear of their full cycloplegic (cyclopentolate hydrochloride 1%) retinoscopy result (less only the spherical allowance for working distance) for 6 to 8 weeks, before initiation of total occlusion of between 4 and 7 hours daily for residual amblyopia. Amblyopia was defined as 6/9 or poorer Snellen crowded visual acuity or two or more lines difference between the two eyes. The quantity of occlusion was related to the initial degree of amblyopia, with a greater number of hours prescribed in patients with poorer acuity. Initial review was after 2–4 weeks, and subsequently at 4–6 week intervals until 6/5 Snellen visual acuity was achieved in both eyes. At this stage occlusion was stopped in five patients, and was gradually reduced to 1 hour maintenance level in the remaining four patients, before discontinuing after 1–3 months. Two patients (A and C) were given full time partial occlusion (Blenderm) when compliance with total occlusion waned. This was worn constantly for 4–6 weeks, then reduced to 3 hours for a further 4–6 weeks before discontinuing. Parents were warned to stop occlusion should diplopia be reported, but this was never the case.

Results
The recovered group comprised five males and four females. The age at presentation ranged from 4.5 years to 7.8 years (mean 5.6 (SD 1.2) years; median 5.25 years). The laterality distribution of the microtropic eye was right eye four: left eye five. A positive family history of strabismus, hypermetropia, or amblyopia in the parent and/or sibling was noted in four patients.

The pretreatment diagnosis was microtropia “with identity” in six patients (four micro esotropes and two micro exotropes), and “without identity” in three patients (two micro esotropes and one micro exotrope). No patient spontaneously converted to bifoveal fixation before occlusion therapy by solely wearing their refractive correction. Following occlusion all patients demonstrated a heterophoria on cover test with and without spectacles. In four patients, there was a change in the direction of deviation from micro esotropia to exophoria.

Figure 1 shows the change in deviation for all nine patients (A–I) before and after treatment. Following occlusion, all patients were heterophoric on cover test (seven exophoria, two esophoria). The pretreatment angle of deviation ranged from 8° base in (BI) to 4° base out (BO). After treatment, the angle of deviation ranged from 2° BI to 2° BO. In the four patients (B, D, F, H) in whom the direction of deviation changed, the magnitude of change was also greatest (range 4–8°, mean 5.5° (SD 1.8°), median 5°) compared with 0–2° in the remaining five patients (mean 0.6° (0.9°), median 1°).

Before treatment ARC was apparent in all nine patients on the basis of a binocular single vision (BSV) response with Bagolini striated glasses (two striations of light seen at 135° and 45° in the form of an “X”) in the presence of a heterotropia, a central scotoma on the 4° test, and unioocular eccentric fixation on visuscopy. Following treatment, perception of an “X” response on Bagolini striated glasses confirmed normal BSV and NRC in all patients, the 4° test (BO and BI) indicated bifoveal fixation, and the fovea of the amblyopic eye adopted the ZRP and PVD on visuscopy.

Figure 2 demonstrates the change in stereopsis from pre- to post-treatment for each patient in relation to age. Before occlusion, five patients had stereocuities of 85–170 seconds of arc with the Frisby stereo test, with a mean of 131 seconds of arc, and median of 120 seconds of arc.
Table 1 shows the fixation patterns before and after treatment for the seven patients who allowed sequential visuscopy assessment (inadequate cooperation with visuscopy precluded fixation assessment in patients G and H). Before treatment all seven patients demonstrated a degree of eccentric fixation on repeated assessment in the microtropic eye (range 0.5°–1.5°; mean 0.7°(0.4°); median 0.5°), with steady foveal fixation in the non-microtropic eye in five patients and unsteady foveal fixation in the remaining two patients. The eccentric area was the ZRP, and was always associated with the PVD. The direction of eccentric fixation was nasal in five patients, two having an additional superior component, and temporal in two patients. The percentage foveation was 0% in five of the seven tested, 20% in one case, and 40% in the remaining case. Following treatment, fixation became steady or slightly unsteady foveal in both eyes in all cases, with the fovea resuming the PVD and becoming the ZRP. The final percentage foveation ranged from 75 to 100%.

Figure 3 shows the initial and final corrected Snellen visual acuities. Before treatment, the visual acuity levels in the microtropic eye ranged from 6/9 to 6/60 Snellen (mean 0.45 (0.26) log units, median 0.52 (Snellen 6/18)). The pretreatment interocular log acuity difference ranged from 0.18 to 1, with a mean of 0.44 (0.27), and median of 0.30. Following treatment, 6/5 Snellen acuity either eye was achieved in all patients, thereby eliminating any discriminable interocular acuity difference. While visual acuity in the microtropic eye remained 6/9 or poorer, all patients remained microtropic: recovery of normal BSV only occurred when 6/5 Snellen acuity was achieved in seven cases, and 6/6 in two cases.

Table 2 shows the refractive status of the nine patients. Eight patients were hypermetropic or hypermetropic astigmats, and the ninth patient was a unilateral mixed astigmat. Anisometropia (1° spherical equivalent refraction (SER) or 1° dioptre cylinder (DC)) was present in four of the nine patients, including the two patients with a high unilateral astigmatic component (3DC). The SER difference in these four patients ranged from 1.5 to 3.5, mean 2.84 (0.92), median 3.19: two were microtropes “with identity” and two were “without identity”. The overall mean SER difference for the whole group was 0.99 (1.29); median 0.38. There was no significant correlation between the SER difference and corrected interocular acuity difference pretreatment (y = 0.284 + 0.159x, r² = 0.57, p = 0.019).

Table 1

<table>
<thead>
<tr>
<th>Subject</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Unsteady nasal 0.5–1°; 0% foveation; nasal drift; temporal saccade; nasal 1°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>B</td>
<td>Unsteady nasal 0.5°; superior 0.5°; 20% foveation; nasal–superior drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>C</td>
<td>Unsteady nasal 0.5°; superior 0.5°; nasal 0.5°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>D</td>
<td>Unsteady nasal 1°, superior 0.5°; nasal–superior drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>E</td>
<td>Steady temporal 0.5°; nasal–superior drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>F</td>
<td>Unsteady temporal 0.5–1°; nasal drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Steady foveal; fovea=ZRP</td>
</tr>
<tr>
<td>G</td>
<td>Unsteady nasal 0.5°; 40% foveation; nasal drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Unsteady foveal; random saccades; fovea=ZRP</td>
</tr>
<tr>
<td>H</td>
<td>Unsteady nasal 0.5°; 0% foveation; nasal drift; nasal–superior drift; temporal saccade; nasal 0.5°=ZRP</td>
<td>Unsteady foveal; 75% foveation; random saccades; fovea=ZRP</td>
</tr>
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ZRP = zero retinomotor point.

Figure 3 Initial and final corrected Snellen visual acuities (n = 9).
The recovery period from microtropia to heterophoria ranged between 2 and 29 months, with a mean of 9 months and median of 5 months. The number of hours of occlusion to restoration of normal binocular function was also calculated and ranged between 56 and 953 hours (mean 320 (270) hours; median 252 hours). The compliance levels were calculated as the percentage of hours of occlusion prescribed against the hours worn, based on a parental verbal report at each visit. Recovery in six patients was achieved within 7 months; in the remaining three patients recovery took 11, 19, and 29 months. Reported compliance levels for the former group was 100% in five patients and 79% in the remaining patient, and in the latter group were 43%, 80%, and 63% respectively. The range for the whole group was 43 to 100%; mean 85, median 100%. The time to recovery in months was correlated neither with the age at presentation (y = 67.5 + 0.041x, r² = 0.001, p = 0.93) nor with the number of hours of occlusion to cure (y = 20.92 + 0.007x, r² = 0.032, p = 0.65). There was no significant correlation between the number of hours of occlusion to cure and the pre-occlusion interocular acuity difference (y = 352.6 + 77.62x, r² = 0.005, p = 0.85) or the degree of anisometropia (y = 334.7 + 14.81x, r² = 0.005, p = 0.86).

The total follow-up period ranged from 4 to 34 months. The range of follow up after recovery was 0 to 27 months, with a mean of 9 (SD 8) months, and a median of 7 months. One patient (F) was lost to follow up after 5 months (2 months occlusion), and the findings of recovery from microtropia were confirmed on one occasion only. In another patient (C), vision dropped to 6/6 in both eyes following a period of non-compliance with spectacle wear, and recurrence of an occasional micro esotropia was noted on cover test. Snellen acuity of 6/5 and an exophoria were restored with reinstatement of full time spectacle wear. Unilateral fixation remained unsteady foveal with 80% foveation and stereoeuity was maintained at 30 seconds of arc. In the remaining seven patients, NRC, high grade stereo acuity, uniocular foveal fixation, and 6/5 Snellen visual acuity were maintained throughout the entire follow up period. The number of consecutive visits with static findings ranged from one to seven, with a mean of three and median of four visits.

Discussion

The recovery of bifoveal binocular single vision in nine patients with primary microtropia following full time wear of the appropriate spectacles and a period of occlusion strongly suggests plasticity in the retinocortical connections in some patients with this condition.

It is commonly stated that the sensory status of microtropia is irreversible, and stereoeuity of 60 seconds of arc is unachievable, although a few cases of recovery of microtropia have been reported previously. Von Noorden observed recovery in three patients following intensive treatment but no details were given. “Spontaneous” recovery has been described in a single report of seven cases of microtropia but as visuoscopy examination was not carried out, microtropia with identity cannot be excluded as a normal clinical condition.

Binocular single vision in microtropia is generally believed to occur on the basis of ARC although some authors favour the concept of NRC facilitated via an expanded Panum’s fusional area. The debate has been confounded by inconsistency of responses to different clinical tests with varying degrees of dissociation, as well as the findings of coexisting NRC and ARC both in different parts of the visual field, and in intermittent or decompenasing strabismus. The exact neurophysiological basis of ARC remains uncertain. NRC and high grade random dot stereopsis are known to be based on maximal precision of binocular interaction fields at the foveas, whereas cortical representation is greatest (at area 17 of the striate cortex). In ARC, projection to inferotemporal cortex has been suggested, and to an intermediate area in microtropia. A deficit of magnocellular neurons in areas 17 and 18 has also been proposed as the primary deficit in ARC supported by one recent study of microstrabiic cats, although the majority of animal experimental studies have failed to confirm a change in cortical connections. The perceived change in retinal correspondence from ARC pretreatment to NRC post-treatment in these nine patients carries considerable implications for our understanding of the neurophysiology of ARC in microtropia. There is mounting evidence to support the concept of flexibility in the retinocortical interconnections within the “normal” visual system, with multiple connections between foveal receptive fields of one (dominant) eye and those of the retina of the other eye. The restoration of NRC, and therefore maximal precision of pairing of receptive fields in areas 17 and 18 of the visual cortex in these patients, strongly supports this concept of flexibility, and opposes the concept of a permanent deficit of neurons within these cortical areas.

We postulate that the transition occurred in response to occlusion therapy. As the fovea regained maximum visual acuity and the central scotoma was eliminated, the area in the microtropic eye “corresponding” to the fovea of the non-microtropic eye approached a more central area with smaller receptive fields (ultimately the fovea), allowing greater precision of binocular interaction and cortical representation at area 17, the “seat” of normal BSV. This flexibility can presumably only be possible if the foundations for BSV with precise foveo-foveal correspondence and projections to area 17 and 18 of the striate cortex have developed before any disruption.

Such flexibility is likely to explain the retention of BSV in some cases of manifest strabismus, via pairing of receptive fields over a large cortical area. Von Noorden’s observed recovery in three patients following intensive treatment but no details were given. Therefore, ARC may be considered a normal manifestation of the malleability of
Recovery in microtropia

The maintenance of BSV in all nine patients throughout the period of change in the angle, and in some cases the direction of deviation, from heterotropia to heterophoria, further supports adaptability of the retinocortical connections to a changing motor status.

Stereopsis was measured with the Frisby stereo test, a real depth test which is easily understood and has good compliance in young children. It has been shown to be a reliable means of assessing high level stereopsis in both adults and normal infants and to be comparable with TNO, despite previous criticisms of monocular cues and lack of standardisation between plates. The invariable stereopsis deficit in microtropia was evident in these patients, although the positive response with Frisby manifested in five patients before treatment is not atypical. An initial recordable level of stereopsis may be a good prognostic sign for recovery of microtropia, as it implies some prior development of normal retinocortical architecture. The restoration of high grade stereopsis following occlusion treatment is however atypical, with achievement of a minimum of 60 seconds of arc confirming bifoveal BSV. This achievement implies the onset of microtropia occurred after the critical period of stereopsis development in infancy—that is, beyond 6–8 months of age as disruption before this period severely retards maturation of bifoveal binocular single vision and high grade stereopsis, and limits the best achievable outcome to poorer than 60 seconds of arc. The period from 11 weeks to 6 months is a window of particular vulnerability of cortical architecture development, with the vulnerability diminishing with age, concurrent with the rate of synaptogenesis activity. The age at presentation had no demonstrable effect on the initial or final stereoscopic level.

The remarkable recovery of precise foveal fixation, following an initial small degree of uniocular eccentric fixation (parafoveal fixation), suggests that eccentric fixation was secondary to the central scotoma, with sensorimotor adaptation of fixation at the edge of the scotoma. The change in fixation pattern was gradual, with increasing periods of foveation noted concurrent with improvement in visual acuity level. This resulted in restoration of normal position sense and subjective localisation. It could be argued that some of our patients were merely anisometropic amblyopes with eccentric fixation. However, we subscribe to the view that any degree of eccentric fixation constitutes a form of strabismus. The consistent eccentric fixation pattern and change in egocentric localisation and fixation reflex locus (ZRP) before treatment strongly supports the diagnosis of microtropia in our patients, as opposed to purely anisometropic amblyopia.

The previous literature on achievable visual outcomes in microtropia is sparse. Visual acuity is thought to be responsive to occlusion therapy, but outcome is limited by the presence of eccentric fixation and high grade stereopsis, as cases of alternating strabismus may also demonstrate 6/5 Snellen acuity in each eye. Conventionally, 6/9 Snellen visual acuity is considered to be a minor degree of amblyopia for which occlusion may not be considered. However, as any degree of visual inequality may act as a barrier to normal binocular single vision, our aim was to achieve equal acuity, while carefully monitoring the risk of decompensation and insuperable diplopia by repeated measurement of fusional reserves. The importance of achieving a high level of visual acuity is emphasised by our findings that recovery in microtropia only occurred when the visual acuity improved to 6/9 Snellen in seven patients and 6/6 Snellen in the remaining two patients. Three patients with an initial Snellen visual acuity of 6/9 regained normal binocular single vision, when their visual acuities improved to 6/5 following occlusion. Persistence with occlusion in microtropia until the maximal Snellen visual acuity is obtained, therefore, offers the prospect of restoration of bifoveal binocular single vision and high grade stereopsis. It is noteworthy that decompensation and diplopia did not develop in any instance.

Anisometropia, a common association of microtropia, was present in four patients. There was no significant correlation between the pretreatment interocular acuity difference and the SER difference, as has been found in previous studies of pure (non-strabismic) anisometropic amblyopes. This implies a difference in the pathogenesis of anisometropic amblyopia and microtropia, highlighted by the fixational discrepancies described. Persistent anisometropia, particularly hypermetropic anisometropia, is acknowledged as a critical factor in the development of amblyopia and strabismus, but as the refractive history of our patients is unknown, the true influence of anisometropia on the aetiology remains undetermined.

The time period for recovery was relatively short in two patients (2 months in A and F). Such a short recovery period is difficult to reconcile with the concept of major restructuring of retinocortical mapping, but suggests a flexibility in the normal retinocortical relations, responsive to occlusion therapy.

Although the aetiology of microtropia is difficult to identify in individual patients, previous hypotheses may be considered in relation to our clinical findings. The contribution of anisometropia has already been discussed, but other possible influences include an inherent inability for bifoveal fusion, a genetic/hereditary disposition to ARC, and an anomaly of the fixation reflex. The development of bifoveal BSV in all patients excludes an
inherent inability for bifoveal fusion, although clearly there was temporary suspension of NRC due to suppression and amblyopia. A positive family history of strabismus, amblyopia, or hypermetropia or parents or siblings in four patients suggests a multifactorial mode of inheritance as in other forms of strabismus. Precision in the development of the fixation reflex is essential for the evolution of normal BSV, and an anomaly of this reflex has been postulated as an aetiological factor in microtropia and eccentric fixation.\textsuperscript{2,5} The change in ZRP from an eccentric fixation locus to the fovea strongly supports the concept of plasticity in the development of this reflex.

Malleability of the visual system within the sensitive period of development is well documented. The attainment of NRC and high grade stereopsis in these patients may be explained in two ways. Firstly, there may have been a transition from anomalous to normal correspondence on the basis of pre-existing retinocortical connections (via a flexible pairing of foveal receptive fields of one eye with a range of loci in the other retina at cortical level). The second possible explanation is the development of new retinocortical pathways and connections. The age of the patients at presentation, all of whom were well outside the sensitive period of development, favours the former explanation.

The limited size of this series makes it impossible to draw definitive conclusions from statistical analysis. However, no specific pre-treatment patient characteristic or clinical feature predicted recovery. All microtropes do not appear to possess the same potential for restoration of normal bifoveal binocular single vision and, indeed, 21 of 30 patients studied previously\textsuperscript{41} did not recover despite the application of the same management strategy, and many achieving improvement in visual acuity. The reason for this discrepancy is unclear. It can be postulated that those patients who did not achieve recovery of NRC suffered an earlier disruption of their developing binocularity before the formation of normal retinocortical connections. This concept implies disruption before the onset of high grade stereocuity—that is, before 6–8 months of age.

Further studies of codeveloping visual functions, such as motion processing, hyperacuities, and fixation stability within their critical periods of neural development may help to improve our understanding of the aetiology of microtropia. During development a detrimental effect on one function may have an adverse effect on the others, while preservation of these functions in the presence of ARC and microtropia suggests a later onset in the breakdown of retinal correspondence and may constitute a favourable prognostic sign for the recovery of NRC. Assessment of the sum binocular visual evoked potential response before and after treatment may also prove a valuable area of future study, as an objective assessment of binocularity for comparison with subjective clinical measures.\textsuperscript{55}

The recovery of microtropia and the perceived change from ARC to NRC support a plasticity in the retinocortical relation and the existence of ARC on the basis of normally existing retinocortical connections, facilitated by flexibility of pairing of receptive fields over a relatively wide cortical area. As the normal precise foveo-foveal relation was restored in the nine patients documented, accompanied by high grade stereo acuity, it is likely that a period of normal retinocortical architecture development preceded the onset of the microtropia. Appropriate refractive correction and occlusion therapy alleviated amblyopia, suppression, and eccentric fixation, thus removing the factors contributing to the suspension of NRC. In order to re-establish NRC and high grade stereopsis, occlusion therapy must be aimed at the achievement of equal visual acuity. The view that 6/9 Snellen visual acuity is an acceptable outcome in microtropia should be abandoned, as in our patients recovery was only achieved when visual acuity improved to 6/6 Snellen or better. Therefore, occlusion therapy should be continued as long as any improvement in visual acuity and stereopsis is taking place.

Recovery in microtropia


34 Bishop PO. Control of eye vergence and anomalous retinal correspondence. Binoc Vis 1991:675–82.


