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REVIEW

Single vision during ocular deviation in intermittent exotropia

Ignacio Serrano-Pedraza[1], Michael P Clarke[1,2] and Jenny CA Read[1]

[1]Institute of Neuroscience, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK and [2]Eye Department, Royal Victoria Infirmary, Newcastle upon Tyne, UK

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Correspondence: Ignacio Serrano-Pedraza
E-mail address: i.s.pedraza@ncl.ac.uk

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Abstract

Intermittent exotropia is a common oculomotor anomaly where one eye intermittently deviates outwards. Patients with this type of strabismus are often not aware of the exodeviation and do not usually experience diplopia. In this review, we discuss what is known about the cortical mechanisms which achieve single vision during exodeviation in this condition, and highlight some outstanding questions.

Introduction

Intermittent exotropia [X(T)] is a disorder of binocular eye movement control, in which one eye intermittently turns outwards, as in *Figure 1*. The exodeviation is most likely to occur at far viewing distances, when the oculomotor convergence drive is weakest, and occurs most often when the patient is tired, ill, under stress, or in particular test situations.[1] While X(T) can also occur at near fixation (e.g. convergence insufficiency) we will restrict this review to childhood-onset intermittent distance and basic exotropia. Intermittent exotropia is usually diagnosed in early childhood, and is the most common form of exotropia, with an incidence of 1% in children under 11 years old.[2,3] It is a common reason for strabismus surgery, particularly in Asia.[4] Growing up with this disorder affects how the two eyes work together to produce a single view of the world.

A constant strabismus usually leads to a loss of binocular vision, which often remains permanent even if the strabismus is subsequently corrected surgically. Patients may have severely reduced visual acuity in the deviating eye (amblyopia), and even if acuity is preserved in both eyes, they are likely to lack stereo '3D' vision.

In contrast, in intermittent exotropia, the periods of correct binocular alignment serve to prevent much of this loss. While their eyes are correctly aligned, patients with intermittent exotropia generally show near-normal binocular visual function, especially for near viewing. Indeed, their stereoacuity at near distances appears to be completely normal.[5,6]

At far distance (6 m) stereoacuity in some patients is worse than that of controls.[6] However, this does not appear to reflect a problem with combining the two eyes' images in visual cortex. Rather, it appears to be a side-effect of poorer eye control at large viewing distances,

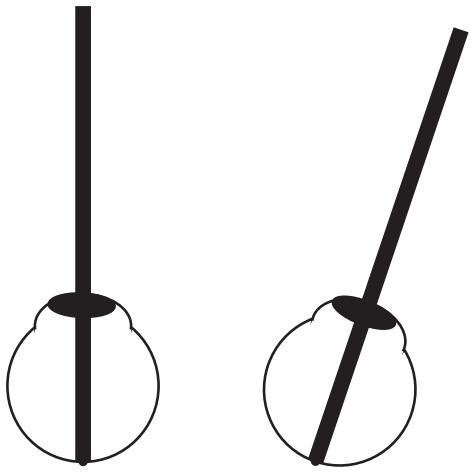

Figure 1. Exodeviation. The eyes are attempting to view a distant object, so the optic axes (thick black lines) should be parallel, but the right eye is deviating outwards.

resulting in less accurate binocular fixation. Standard measures of stereoacuity require the subject to compare the disparity of two adjacent surfaces (*Figure 2*). Such comparisons are much more accurate if one of the surfaces is at the fixation point; any 'pedestal disparity' between the fixation point and the reference surface has a devastating effect on performance, with 1° of pedestal disparity reducing stereoacuity by an order of magnitude.[7] Any fluctuations in vergence would introduce a constantly-changing pedestal disparity, which would lower the stereoacuity. Presumably for this reason, vergence is normally tightly controlled, with a standard deviation about the desired fixation plane of just 0.05° in control humans and monkeys.[8–13] In patients with intermittent exotropia, the weaker convergence drive at far viewing distances leads to an increased tendency to exodeviation, but may also lead to increased fluctuations in vergence even without frank exodeviation. A standard deviation of 0.5° in vergence, for example, would be very difficult to detect either by inspection or with eye-tracking devices, and yet would introduce substantial average absolute pedestal disparities which would reduce stereoacuity. For this reason, distance stereoacuity in these patients has been used as an indirect measure of their control of strabismus or misalignment, and thus as an indication for surgery.[6]

Despite their apparently normal binocular function during alignment, during periods of exodeviation, patients with intermittent exotropia show an important difference from controls. In control observers, if one eye moves outwards for some reason, this results in double vision (diplopia), because images of the same object now fall in non-corresponding points of the two retinas (*Figure 3b*). Accordingly, an acute exodeviation due to an acquired paralysis of an extraocular muscle always results in diplopia (in a visually mature individual). Some patients with intermittent exotropia close one eye during periods of exodeviation, especially in bright light conditions.[14] However, even those who keep both eyes open generally report no diplopia, nor other troubling visual phenomena such as confusion (seeing images of different objects apparently superimposed), even while their eyes are deviated. Indeed, often they are not even aware of the exodeviation.[1,15,16] Evidently, their unusual visual experience as a result of their eye movement disorder has led them to develop specific mechanisms to prevent diplopia during exodeviation. In this paper, we discuss what is known about these mechanisms.

Mechanisms which maintain single vision during exodeviation

During correct binocular alignment (orthotropia, *Figure 3a*), the fixated object projects to each fovea by definition. Other objects in the visual field project to the

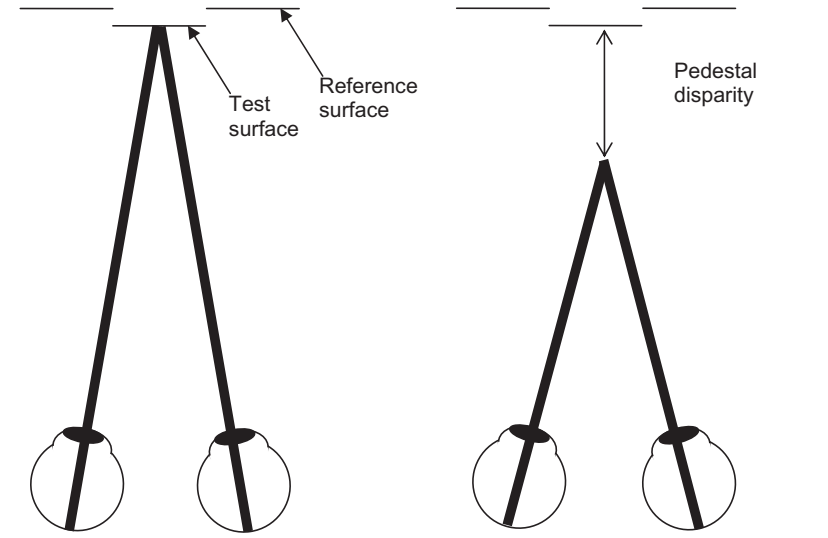

Figure 2. How poor vergence control can result in lower estimates of stereoacuity. Classic tests of stereo vision, e.g. the Frisby or randot tests, involve discriminating whether the test surface is in front of or behind a reference surface. Optimal performance is achieved when the subject is accurately fixating on one of the surfaces (a). Inaccurate vergence introduces a 'pedestal disparity' (b) between the fixation point and the surfaces whose disparity is to be compared.

right of the fovea if they are in the left visual hemifield, or to the left if they are in the right hemifield. This geometry is reflected in how retinal location is converted into a sense of direction, and in how the two retinal images are matched up. The two foveal images are perceived as lying in the same direction, while a point with a given nasal eccentricity in one eye is perceived as lying in the same direction as a point with the same temporal eccentricity in the other. This *normal retinal correspondence* is sketched in *Figure 4a*.

When one eye deviates outwards, *Figure 3b*, the fixated object (here the sunflower) projects to the temporal

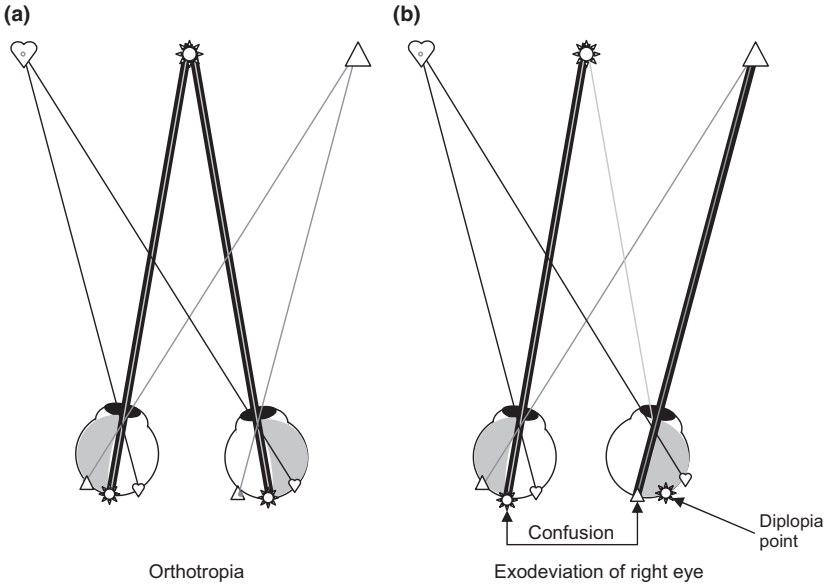

Figure 3. How objects project to the two retinas (a) during correct binocular alignment or orthotropia, (b) during exodeviation. The heavy black lines indicate the optic axis of each eye, i.e. a line passing through the fovea and the nodal point. The temporal half of each eye is shaded. During deviation, objects project to different physical positions in the two eyes. E.g., the sunflower projects to the fovea of the fixating eye, and to the temporal hemiretina of the deviating eye. The separation between these positions is much greater than the fusible range of disparities, and so control observers will experience double vision. The term 'diplopia point' (also called zero point or Deckstelle) refers to the point in the deviating eye which views the object foveated by the fixating eye.

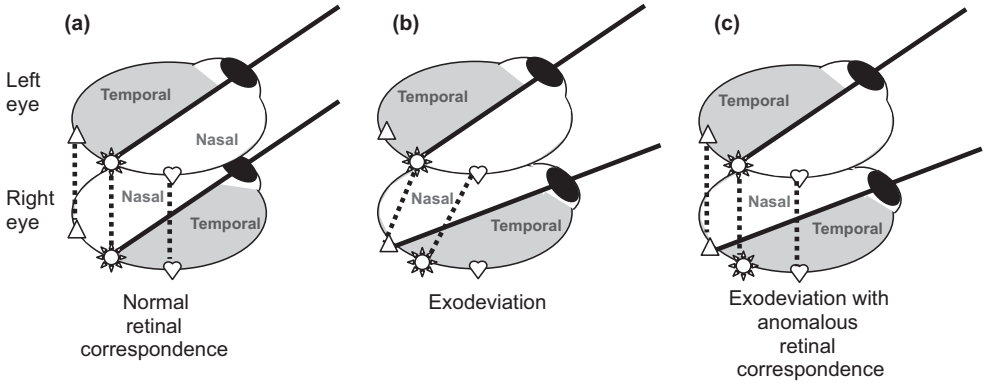

Figure 4. Circular sections along the horizontal retinal meridian, showing how the two retinas relate in normal and anomalous retinal correspondence. (a) In normal retinal correspondence, images which fall at roughly the same position in both eyes relative to the fovea are perceived lying in the same visual direction. These correspondences are marked by the dashed vertical lines. (b) When exodeviation occurs, these correspondences are inappropriate: 'corresponding' retinal locations are stimulated by different objects, resulting in confusion and/or diplopia. (c) In anomalous retinal correspondence, the corresponding points are remapped to account for the deviation. Now images falling at very different retinal locations, much further apart than the normal range of fusible disparities, are perceived as lying in the same direction.

hemiretina of the deviated eye, while a different object (here the triangle) projects to the fovea of this eye. The point in the deviating eye which receives the image of the fixated object is called by various authors the *diplopia point*, *Deckstelle, zero point* or *zero measure point*.[17] If the deviating eye looks outwards, the diplopia point lies in temporal hemiretina (shaded in *Figures 3 and 4*), whereas if it looks inwards (esodeviation), the diplopia point lies in nasal hemiretina.

Adults with an acute deviation experience two distinct forms of visual disruption. The first is diplopia, in which the same object is perceived in two different visual directions. For example, in *Figure 3b*, the sunflower would be seen both straight ahead, corresponding to its foveal location in the left eye, and on the left, corresponding to its temporal location in the right eye. The second is confusion, in which two objects are perceived at the same visual direction. For example, in *Figure 3b*, both the sunflower and triangle might be perceived, impossibly, at the same location. Patients with an acute exodeviation often complain initially of diplopia, but on closer examination are even more troubled by the confusion.[1]

The causes of such acquired exodeviations include internuclear ophthalmoplegias, paresis or myopathy affecting the medial rectus muscle, and surgical overcorrection of esotropic deviations. If the exodeviation occurs after the end of the sensitive period for this particular visual function (estimated at anything from 6 to 9 years old,[1,17]) the diplopia and confusion may persist as long the deviation persists,[18] although some sensory adaptation remains possible at older ages.[19,20]

In contrast, children who grow up with a congenital or early onset deviation do not experience either diplopia or confusion. Their unusual visual experience is reflected in special cortical mechanisms which achieve single vision despite the deviation. Two different basic forms of these *anti-diplopic mechanisms* have been recognized in the literature: *anomalous retinal correspondence* (*Figure 4*)[21,22]; and *suppression.*[17,23] Although both these proposed mechanisms avoid double vision, they do so in quite different ways. In patients where suppression is the only diplopia-avoiding mechanism, the binocular field of the strabismic eye must be suppressed from consciousness so that vision is essentially monocular while the suppression is active. In anomalous retinal correspondence, the normal relationship between the two retinas is remapped to account for the deviation, so that vision continues to be binocular despite the deviation. The two mechanisms are by no means mutually exclusive; indeed, anomalous correspondence is almost always associated with suppression in certain regions of the visual field.[1,22,24,25]

Suppression

Suppression is probably conceptually the simpler mechanism. In order to avoid conflict between the different retinal images experienced during deviation, one eye's image is simply suppressed, so that it is never perceived consciously. Effectively, the eye becomes blind to stimuli falling within the suppression scotoma. However, the neuronal changes underlying this process occur in the brain rather than in the eye. For example, stimuli which were never perceived, due to suppression, can still produce aftereffects, demonstrating that they were registered in the early stages of vision.[26]

For exodeviation, the diplopia point lies in the temporal hemiretina (shaded in *Figure 3*). Accordingly, suppression in exodeviation mainly affects the temporal hemiretina. As discussed below, the shape and size of the suppression scotomata is highly variable between studies and individual patients. However, suppression is usually reported to be most reliable and most profound around the fovea and the diplopia point of the deviating eye.[17,27,28] It is easy to appreciate the significance of these two retinal locations. In most circumstances, the fixated object will be the object to which the observer is attending and which is most significant to them. During forced exodeviation in control observers, we have the highly undesirable situation that this significant object is perceived twice: straight ahead, due to its foveal image in the fixating eye, and to one side, due to its temporal image at the diplopia point of the deviating eye (sunflower in *Figure 3b*). Suppressing the vicinity of the diplopia point ensures that the fixated object is perceived in only one visual direction. Similarly, control observers during exodeviation may experience confusion, in which the fixated sunflower at the fovea of the fixating eye and the triangle at the fovea of the deviated eye are both perceived at the same location in the visual field. Suppressing the fovea of the deviated eye avoids this, though at the cost of losing stereo vision during the deviation. Because our visual experience is largely driven by what is at the fovea, these two locations – the fovea, and the point corresponding to it – are the most critical to suppress in order to achieve single vision. The nasal retina of the deviating eye is apparently generally not suppressed, presumably because it sees objects which are either not visible, or are visible but very eccentric, in the fixating eye. Even when we are fixating correctly, such large disparities between objects in peripheral retina are common, and we are not usually aware of this physiological diplopia.

Anomalous retinal correspondence

In anomalous retinal correspondence, the normal relationship between the two retinas (*Figure 4a*) is remapped

to account for the deviation (*Figure 4b,c*), so that vision continues to be binocular despite the deviation. In normal binocular vision, objects in the plane of fixation fall at nearly the same retinal locations in the two eyes, where 'same' is defined by superimposing the two eyes and aligning landmarks such as the fovea and nodal point. Accordingly, in normal retinal correspondence, images which fall on the same or very similar retinal locations in the two eyes can be fused and are perceived as lying in the same visual direction. If one eye deviates outwards by an angle ξ, then the images in the deviated eye are all displaced through ξ (*Figure 3b*). If this deviation occurs often enough early in development, this can lead to an anomalous retinal correspondence. The region of temporal retina between the angle of deviation and the fovea in the deviating eye will now act like nasal retina, and correspond to temporal retina in the fixating eye. It has also been suggested that, at least in some cases, anomalous retinal correspondence may be the cause of the ocular misalignment, rather than vice versa.[29,30]

In harmonious anomalous retinal correspondence, the offset from normal correspondence matches the deviation, i.e. images which are offset by ξ in the two retinas are perceived as lying in the same visual direction. More rarely, inharmonious anomalous retinal correspondence has been reported, but it is not clear whether this is due to difficulties in measurement, or to recent changes in the angle of deviation.[24] Anomalous retinal correspondence is more common for small angles of deviation.[31]

Advantages of anomalous retinal correspondence

Anomalous retinal correspondence enables some form of binocular vision to be maintained during deviation, in contrast to suppression which renders vision locally monocular. Accordingly, it has been reported that anomalous correspondence enhances binocular performance on visuomotor tasks, compared to a patients with pure suppression.[24,32] Furthermore, anomalous correspondence may enable panoramic vision,[24,33] however some authorities dispute that panoramic vision and anomalous correspondence can coexist.[1] If the normal correspondence between the foveas can be broken, then the fovea of the deviating eye does not need to be suppressed in order to avoid confusion, but can be ascribed the correct visual direction. This means that the field of view is expanded compared to that of a normal observer (*Figure 5*). There has, however, been no quantitative work demonstrating that this produces a measurable benefit in practice.

A second advantage may be that anomalous retinal correspondence remains functional even in bright lighting conditions. Wang and Chryssanthou[34] report that 90% of intermittent exotropia patients with normal retinal correspondence close one eye in bright sunlight, presumably because suppression cannot function under these conditions. In contrast, only 35% of patients with anomalous retinal correspondence show monocular eye closure in sunlight.

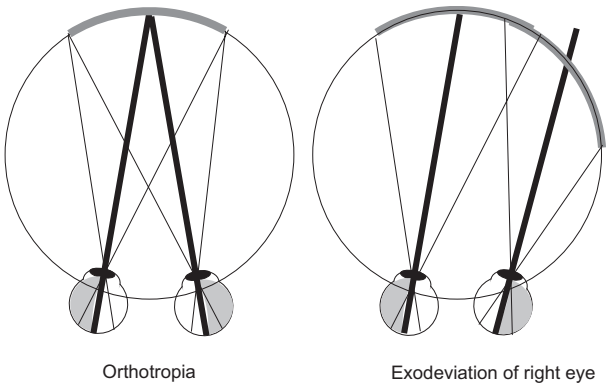

Figure 5. Anomalous retinal correspondence can expand the field of view. The gray arc shows the central 20° or so for each eye. Exodeviation expands the region viewed by at least one eye. Anomalous retinal correspondence avoids the need to suppress the deviating eye, and means that visual information is potentially available throughout this expanded region.

What triggers these mechanisms?

Even in patients with a constant strabismus, the specialized anti-diplopic mechanisms can be dynamic, not static. For example, patients with an alternating strabismus may suppress whichever eye is currently not fixating. Thus neither eye has a permanent scotoma, but can be turned on or off as necessary.[28] In patients with intermittent exotropia, the anti-diplopic mechanisms are necessarily dynamic, since they are needed only during the periods of exodeviation. Some patients with intermittent exotropia have normal retinal correspondence while their eyes are aligned, shifting to anomalous during deviation.[35,36] Apparently, when the deviating eye turns outward, the egocentric localization of the visual directions displaces with the eye so that no diplopia occurs.[23] Some patients with constant exotropia shift from normal to anomalous retinal correspondence when the input to the strabismic eye is dimmed with a neutral density filter.[37]

During correct binocular alignment (orthotropia), patients with intermittent exotropia are often said to have normal binocular function.[17] Accordingly, many studies have induced exodeviation before examining anti-diplopic mechanisms in intermittent exotropia. Some patients can exodeviate at will,[36] but more often, exodeviation has to be induced by a long period of patching.[38] This makes experiments more time-consuming and difficult for both

researchers and patients. However, anti-diplopic mechanisms in intermittent exotropia can be demonstrated even while the eyes are correctly aligned. For example, Pritchard and Flynn[39] found that patients with intermittent exotropia did not experience the usual physiological diplopia for physical objects with large crossed disparities, such that both eyes' images projected to temporal retina. However, it is not clear from their data whether the diplopia was avoided by suppression, or because these patients had an extended range of fusible disparities. Interestingly, it has been suggested that physiological diplopia acts as the stimulus for convergence[40] so this could explain why intermittent exotropes have weaker convergence.

The visual stimulus is critical in determining whether patients with intermittent exotropia display suppression during periods of orthotropia. When intermittent exotropia patients view a complex visual scene with correct binocular alignment, they do not show suppression in either eye.[27] However, if they view a sparse stimulus consisting of a single object, presented to the fovea of one eye and to temporal retina of the other, they perceive only a single image, whereas controls perceive two. This offset image simulates the retinal effects of exodeviation (*Figure 3*), and thus triggers anti-diplopic mechanisms in the patients. If non-identical images are presented in the same positions, the anti-diplopic mechanisms are not triggered, and intermittent exotropia patients now also perceive both images. This demonstrates that the anti-diplopic mechanisms which ensure single vision during exodeviation can be triggered by purely retinal information, and do not require a physical exodeviation to occur.

This indicates that the visual system of these patients has developed a 'similarity detector' which compares the retinal images, assesses whether deviation has occurred and triggers anti-diplopic mechanisms if it has.[41] This similarity detector can be observed also in constant strabismus.[17,25,41,42] For example, dichoptic grating stimuli are more likely to trigger suppression if they have similar orientations.[42] It is not currently known whether the anti-diplopic mechanisms which can be triggered by purely retinal information differ from those triggered by a physical exodeviation.

The shape, size and location of suppression scotomas are strongly dependent on the stimuli, background, and experimental method used, making it difficult to draw general conclusions. Studies of suppression have generally used a small fixation image in one eye and a small test image at various locations in the other. These have often revealed relatively small suppression scotomas, usually around the fovea and diplopia point in the deviating eye.[17,22,27] Yet in natural viewing, single vision is experienced across the whole visual field. Schor[25] has suggested that this may be because stimuli suppress the corresponding retinal location in the other eye; thus a peripheral stimulus in the fixating eye may produce a suppression scotoma about the corresponding peripheral location in the deviating eye. In agreement with this suggestion, Pratt-Johnson & Wee[28] found that when the two eyes view different regions of a large, complex scene, a larger area of temporal hemi-retina is suppressed than when only points are visible (*Figure 6*). Similarly, Cooper *et al.*[43] found most suppression when the test stimuli were presented on complex backgrounds. Cooper and Record[35] suggest that suppression is more likely to occur with white backgrounds and less likely with black backgrounds.

Temporal factors are also important. For example, flashed stimuli may not be suppressed, while Joosse *et al.*[44] reported that 400 ms is the optimal stimulus duration to elicit suppression.

Finally, it is not yet known what brings episodes of exodeviation to an end, although to some extent this is under voluntary control. Normally, binocular disparity is a powerful cue to vergence. Changes in stimulus disparity trigger reflex vergence movements which cancel out the disparity introduced and keep the disparity at the fovea zero (*Figure 7*). Suppression in particular presumably removes or greatly weakens this cue. Accordingly, many visual therapies for intermittent exotropia are aimed at overcoming the suppression, attempting to make the patient experience diplopia, which can then be used as a vergence stimulus to return the eyes to correct alignment.[45] However, this form of treatment is rarely

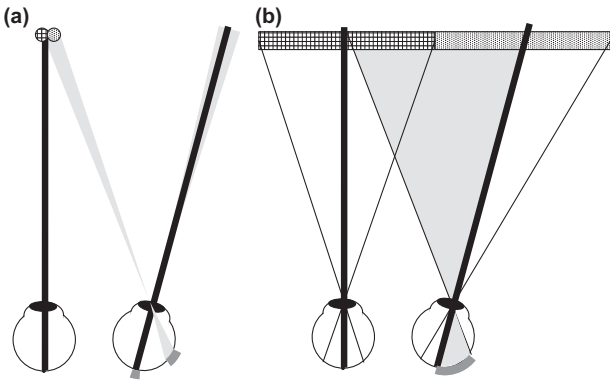

Figure 6. Suppression scotomas in the deviating eye are more limited when probed with point stimuli (a) than with a complex dichoptic visual scene (b) Pratt-Johnson and Wee.[28] These authors found that, with point test stimuli, the deviating eye was suppressed around the fovea and the diplopia point, (a, suppressed regions shaded gray). When the two eyes viewed different parts of a complex scene (texture in b), the suppression scotoma extended across the temporal hemiretina. In this figure, cross-hatching represents stimuli presented to the right eye and dots represent stimuli presented to the left.

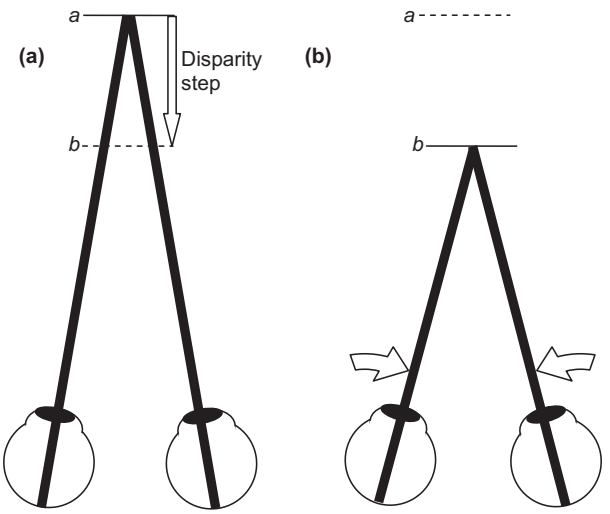

Figure 7. Disparity changes trigger short-latency reflex vergence changes. (a) The subject is fixating the surface at distance *a*, when the surface suddenly jumps in disparity to distance *b*. This triggers a reflexive vergence change (b), which ensures the eyes remain fixated on the surface.

successful, and carries the risk of inducing permanent diplopia, if the suppression is overcome but the deviation remains.

Experimentally distinguishing suppression from anomalous retinal correspondence

Both suppression and anomalous retinal correspondence have been invoked to explain single vision during exodeviation in intermittent extropia, the latter more often in patients with small-angle deviation.[15,23,24,35,46] Distinguishing these two candidate mechanisms is not always easy, and different studies have produced very different estimates for the prevalence of anomalous correspondence in patients with intermittent exotropia. If identical images are presented at different retinal locations in the two eyes but only one is perceived, there is no way of telling whether this is because the two images have been fused or because one image has been suppressed, nor in the latter case which of the two images has been suppressed. Using the reported direction of the single perceived image is also unwise, given that the relationship between retinal location and perceived direction may be non-standard. To avoid this ambiguity, most studies have used different stimuli in the two eyes, either of different shape or of different colour. But as noted in the previous section, anti-diplopic mechanisms change depending on the particular stimulus presented. Thus if different images are presented to the two eyes, both may be perceived, resulting in smaller estimates of the suppression area.[28]

Bagolini striated glasses are sometimes used to distinguish suppression and anomalous retinal correspondence.[15,47] For patients with alternating deviations two lenses are used.[48,49] The lenses of these glasses are striated in orthogonal directions in the two eyes (45° and 135°), causing the point light source to be perceived as a streak. If during exodeviation only one diagonal streak is perceived, the other eye must be suppressed. If both streaks are perceived but offset from one another, retinal correspondence may be normal. Conversely if both are perceived superimposed to form a cross shape, retinal correspondence must be anomalous. A single Bagolini lens with horizontal striations may also be used in front of the deviated eye in a patient with unilateral strabismus, in which case the patient is asked if the perceived vertical line seen through the single Bagolini lens passes though the spotlight seen with the uncovered eye.[19,48,49] The modified fixation disparity test (MFDT, or modified large OXO test) gives similar results to the Bagolini lens.[49]

Anomalous retinal correspondence is also demonstrated by the use of retinal after-images.[1,15,50] using vernier stimuli or, more commonly, horizontal and vertical lines presented to each eye.[49] In normal retinal correspondence, the vernier after-images from each eye are perceived to be aligned, or a cross is seen, depending on the test used. In contrast, in anomalous retinal correspondence, the after-images are perceived to be displaced, in accordance with the type and size of strabismus. In intermittent exotropia, after-image tests may indicate normal correspondence when the eyes are aligned and anomalous correspondence during deviation.[1,36]

Relationship to anti-diplopic mechanisms in other conditions

Constant strabismus vs intermittent exotropia

Both suppression and anomalous retinal correspondence are also found in constant strabismus, and indeed most studies of these phenomena have used patients with constant strabismus (esotropes and exotropes).[1,44] This may be because it appears easier to study anti-diplopic mechanisms in patients with a constant deviation. To study vision during deviation in intermittent exotropia, the deviation first has to be provoked, using dissociating methods such as patching. These may take a long time,[38] and once the patient becomes aware of the deviation, they may immediately correct the eye position.[28]

At the moment, there is little evidence against the conservative hypothesis that the same neuronal mechanisms underlie suppression in both convergent and divergent strabismus,[51] and in both constant and intermittent strabismus. The extent and location of the suppression varies depending on the nature of the misalignment. Broadly

speaking, the region of suppression in esotropia is confined to the nasal retina and the region of suppression in exotropia is confined to temporal retina.[1,17] However, the properties of the suppression appear similar in both cases.[18] Schor[25] suggested that different neuronal mechanisms may underlie small-angle (< 15°) and large-angle strabismus.

Binocular rivalry

Binocular rivalry is an intriguing phenomenon which occurs in observers with normal binocular vision when dissimilar images (e.g. vertical vs horizontal gratings, or a face vs a house) are presented in corresponding retinal locations of the two eyes. These images cannot be fused, so normal stereo vision cannot operate. Instead, the two images compete for perceptual dominance, with each image being alternately perceived and suppressed from consciousness. There is currently no consensus regarding whether strabismic suppression and normal binocular rivalry suppression are mediated by the same underlying neural mechanisms[21,51–55] or not.[42,56–58] For example, Leonards and Sireteanu[59] showed that the time courses of suppression for amblyopes and normal observers were similar when balancing the two eyes in amblyopes. However, they used orthogonal stimuli which favour binocular rivalry suppression and stimuli with low luminance that reduce suppression. They concede that constant suppression might include additional, and probably different, neural mechanisms.

Ramachandran *et al.*[36] studied rivalry in one patient with intermittent exotropia. They generated foveal after-images of circular grating patches in each eye, with the lines vertical in one eye and horizontal in the other. With correct binocular alignment, the patient reported that the grating after-images rivalled, being perceived alternately in the same visual location. When one eye deviated outwards, the two grating after-images drifted apart, indicating anomalous retinal correspondence triggered by the eye movement. But surprisingly, the gratings continued to rival: that is, they continued to be perceived in alternation, not simultaneously, despite the fact that they were now perceived in different visual locations. This interesting experiment has, as far as we are aware, not been attempted in other patients.

Binocular rivalry has been much studied in fMRI experiments. One difficulty is that the competing rivalrous images are in the same visual location, and thus also the same cortical location. In patients with intermittent exotropia, an image in one eye can suppress an identical image many degrees away in the other eye.[60–62] Thus, it may be easier to track activation due to these competing images through different cortical areas, and thus observe when and where suppression occurs in the brain. For this reason, patients with intermittent exotropia may prove a useful model for studying the cortical locus of suppression.

Underlying cortical mechanisms

Currently, rather little is known about the cortical mechanisms which may underlie these anti-diplopic mechanisms. One problem is that there is no animal model of intermittent exotropia, so all the physiological studies relate to constant strabismus. This produces a dramatic reduction in the number[63,64] or in the metabolic activity[65] of binocular neurons in primary visual cortex, which presumably does not occur in intermittent exotropia, given the spared stereo depth perception.

There are no studies examining the cortical mechanisms responsible for suppression specifically in intermittent exotropia. Many studies of suppression in binocular rivalry have not yet produced a consensus regarding where in the visual pathway images are suppressed, or which cortical areas are involved in this process.

It has been proposed that anomalous retinal correspondence in constant strabismus reflects a remapping of the deviated eye onto primary visual cortex.[1] It has also been suggested that sensory shifts in retinal correspondence can occur in normal human subjects.[66–68]

In animals with normal visual experience, binocular neurons in primary visual cortex receive inputs from similar regions in the two retinas, with only relatively small (< 1° visual angle) differences in the position and structure of the left- and right-eye receptive fields. This retinotopic mapping is presumably the cortical substrate for normal retinal correspondence, while the small differences allow encoding of binocular disparities within Panum's fusional range.[69] One might imagine, therefore, that anomalous retinal correspondence is wired analogously, with receptive fields in the two eyes offset by the extent of the anomaly. There is some evidence for this in cats,[70,71] at least in those which have been raised from birth with a surgically induced strabismus. Wong *et al.*[31] suggest that a similar mechanism accounts for abnormal retinal correspondence in strabismic humans, and that this explains why abnormal retinal correspondence is more common for smaller angles of deviation, for which the retinotopic distance necessary to achieve harmonious anomalous correspondence can be spanned by the axonal arbours of two V1 neurons. However, McCormack,[72] using visual evoked potential topographic mapping in six strabismic patients, found no evidence for this remapping. In intermittent exotropia, retinal correspondence can shift dynamically from normal to anomalous as the eyes exodeviate. There is no evidence for such plasticity

in the binocular inputs of neurons in early visual cortex, so it is not clear whether altered V1 receptive fields can underlie anomalous retinal correspondence in intermittent exotropia. An intriguing possibility is that this form of dynamic retinal correspondence may be mediated by head-centric, not retino-centric disparity mechanisms.[73] This is a form of stereo vision which has been proposed on theoretical grounds[74] and recently demonstrated in control observers.[75] In this form of stereo vision, retinal images are first converted to a headcentric visual direction based on the current direction of the eye's optic axis, and then the intersection of these headcentric directions are used to compute the object's position in space. In observers with normal vision, head-centric disparity may be used mainly to produce depth estimates when disparities exceed the range encoded retinotopically in primary visual cortex, for instance underlying 'qualitative' stereo judgments which can still be made in diplopic images.[76] Head-centric disparity may enable some form of stereo vision in observers with strabismus,[73] and would account automatically for anomalous retinal correspondence.

Individual variation

The published literature shows considerable variation between patients with intermittent exotropia. For example, in our recent study[60,61] we found that almost all patients reliably showed suppression when identical images were presented to the fovea of one eye and temporal hemiretina of the other. However, when we asked where the single image was perceived, we found different patterns of results in different patients. At the moment, little is known about what controls this variation. Factors such as age at onset of the deviation, angle of deviation, which eye deviates and how often, visual acuity in each eye, refractive error, probably all contribute to determining outcomes such as whether the patient develops anomalous retinal correspondence and/or suppression, the depth of any suppression, which retinal areas are suppressed, etc. For example, if it is always the right eye which exodeviates, we might predict that it would always be this eye which is suppressed in order to avoid diplopia, whereas if both eyes deviate alternately, one would expect both to be suppressed in turn. Intermittent exotropia has been subdivided into classes by Burian,[21] but we are not aware of any studies examining how these relate to different forms of suppression. It has been suggested that anomalous retinal correspondence may be more likely to arise when the angle of deviation is small, but this also has not been rigorously tested, nor is it known what may cause a small constant strabismus with anomalous retinal correspondence gradually to decompensate into a larger strabismus with suppression. Understanding how all these factors contribute to vision in these patients may help us develop better vision therapies,[77,78] and may also reveal how the underlying cortical mechanisms are influenced by visual experience during development.

Conclusions

Intermittent exotropia is an intriguing condition which demonstrates the flexibility of visual processing and their ability to adapt to disruption early in development. Patients with this condition develop sophisticated mechanisms to maintain single vision during periods of deviation. Many questions remain regarding these mechanisms. Where and how do these anti-diplopic mechanisms develop in the brain? What determines whether a particular patient develops suppression or anomalous retinal correspondence, or both? What can be done to improve binocular control in these patients and restore normal visual function? How are these anti-diplopic mechanisms in intermittent exotropia related to visual suppression in observers with normal binocular alignment? Answering these questions will enable better treatment for binocular eye movement disorders, improve our understanding of binocular visual processing in general, and shed new light on how photic stimulation at the retina produces the conscious experience of sight.

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