VISUAL FIELDS IN STRABISMIC SUPPRESSION AND AMBLYOPIA

Book design & production: BOOST-R, Den Haag
Cover illustration painted by Paul Dijkman, Amsterdam

ISBN 90-9012949-9

Subject heading: human, monkey, strabismus, esotropia, amblyopia, visual fields, perimetry, suppresion

Copies of this publication can be ordered from the author by telephone (070 3302930) or by email mvjoosse@euronet.nl

The research presented in this thesis was supported by:
Allergan Nederland; BOOST-R; Ciba Vision Nederland; ERGRA Opticiens; Het Leids Universiteits Fonds; Medical Workshop; Rockmed B.V.; Tramedico B.V.; Het Westeinde Ziekenhuis

VISUAL FIELDS

in strabismic suppression and amblyopia

Gezichtsvelden bij amblyopie en suppressie
ten gevolge van scheelzien

Proefschrift

Ter verkrijging van de graad van doctor
aan de Erasmus Universiteit Rotterdam
op gezag van de rector magnificus
Prof. Dr. P.W.C. Akkermans M.A.
en volgens het besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 15 september 1999 om 13.45 uur

door

Maurits Victor Joosse

Geboren 15 november 1962
te 's-Gravenhage

Promotor:	Prof. Dr. P.T.V.M. de Jong
Co-promotor:	Priv. Doz. Dr. H.J. Simonsz
Overige leden:	Prof. Dr. H. Collewijn
	Prof. Dr. G. van Rij
	Prof. Dr. Ir. H. Spekreijse

Ter herinnering aan mijn moeder,

Voor mijn vader,

Voor Arjan, Martijn, Marjet, Lucas en Daniël.

Content

CONTENT

Publications and manuscripts on which this thesis is based

Chapter 2

Joosse, M.V., Simonsz, H.J., Jong, P.T.V.M. de, Visual fields in strabismic suppression and amblyopia. Historical overview (to be submitted).

Chapter 3

Wilson, J.R., Lavallee, K.A., Joosse, M.V., Hendrickson, A.E., Boothe, R.G., Harwerth, R.S. (1989). Visual fields of monocularly deprived macaque monkeys. *Behav. Brain Res.* 33: 13-22.

Chapter 4

Joosse, M.V., Wilson, J.R., Boothe, R.G. (1990). Monocular visual fields of macaque monkeys with naturally occurring strabismus. *Clin. Vision Sci.* 5, 2: 101-111.

Chapter 5

Joosse, M.V., Simonsz, H.J., Minderhout, H.M. van, Jong, P.T.V.M. de, Noordzij, B., Mulder, P.G.H. (1997). Quantitative perimetry under binocular viewing conditions in microstrabismus. *Vision. Res.*, 37,19: 2801-2812.

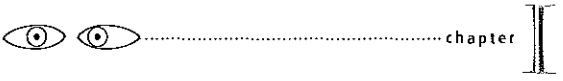
Chapter 6

Joosse, M.V., Simonsz, H.J., Minderhout, H.M. van, Mulder, P.G.M., Jong, P.T.V.M. de. Quantitative visual fields under binocular viewing conditions in primary and consecutive divergent strabismus. *Graefe's Arch Clin Exp Ophthalmol.*, 237: 535-545.

Chapter 7

Joosse, M.V., Simonsz, H.J., Spekreijse, H., Mulder, P.G.M., Minderhout, H.M. van, Jong, P.T.V.M. de. Optimal stimulus to elicit suppression in small angle convergent strabismus (submitted).

General introduction



1.1 Double vision, suppression and amblyopia

Double vision (diplopia) is a very unpleasant sensation. In some cases, people with diplopia even get a sense of nausea or dizziness. Most adults with double vision usually avoid it by closing one eye. Double vision can occur when being extremely tired or intoxicated e.g. with alcohol. Readers with sufficient visual acuity, who normally do not squint, can easily get a sense of double vision, if they fixate at one finger at 50 cm distance from the eyes while holding another one at 25 cm. The nearest finger will be seen double and vice versa. Thus the eyes are not at the appropriate angle with each other, needed for single vision in both situations.

As a matter of fact under everyday viewing conditions, we all partly consciously, partly unconsciously, deal with double vision. Under normal binocular viewing conditions we direct the central part of the retina (the fovea) of both eyes at the object of interest, leading to a sensation of single perception. Within certain limits, an image falling on retinal points outside the fovea of the two eyes can also be seen single.

For each given viewing distance, objects projected onto points outside the fovea can be seen single on the basis of some form of correspondence in the visual cortex of the brain. In general, it can be stated that each point on the retina of one eye corresponds with a retinal point in the other.

Centuries ago it was found out by Aguilonius, that a frontoparallel plane can be drawn through each object point that is fixated, on which objects are seen single.

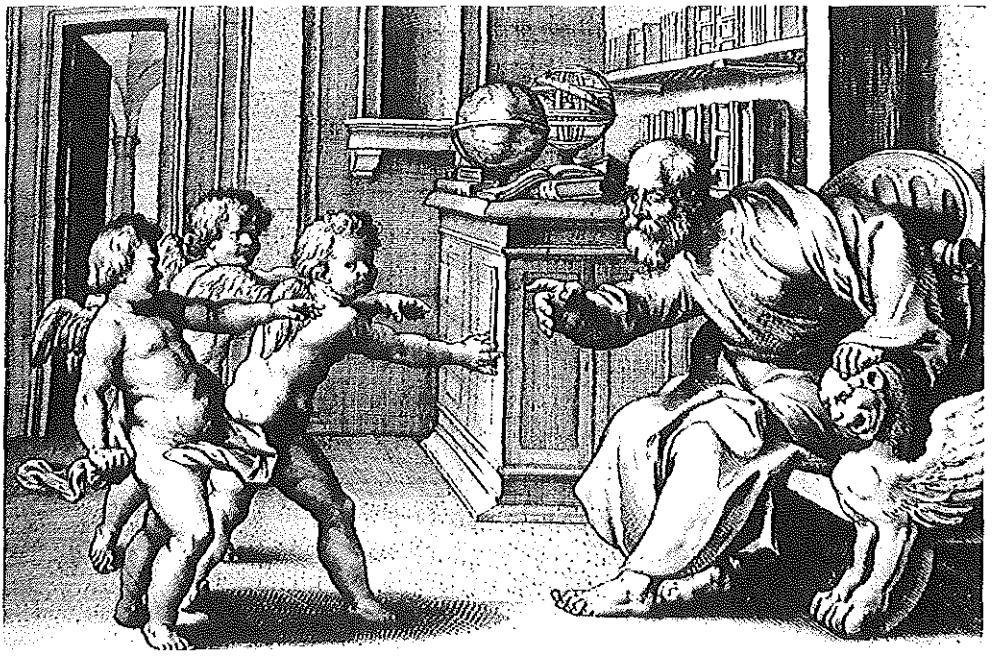


Figure 1 — Reproduction taken from Franciscus Aguilonius' book *Opticorum* (1613). Original print by Rubens. Courtesy of Museum Plantin-Moretus.

Aguilonius named this plane the *horopter.*[1] An illustration taken from the book on optics by Aguilonius is shown in figure 1. Duke-Elder defined the horopter as the locus of those points in space of which the images, for a given position of the eye, fall on corresponding retinal points.[4] Two centuries after Aguilonius, it was theorized that the horopter had to be a somewhat toric plane. This plane is built up from the collection of intersections of the lines which can be drawn through all pairs of corresponding retinal points for a given viewing distance, rather than the flat frontoparallel plane of Aguilonius.[6, 7, 11, 13] Panum described that there is an area around the toric horopter in which not exactly corresponding points can be seen single by means of fusion.[13] This area (Panum's area) is broader in the periphery and narrower in the center. Every object that is nearer or further than Panum's area is likely to be seen double (figure 2). Under normal viewing conditions objects positioned at various distances from the horopter are seen simultaneously. But as I have tried to demonstrate with our simple test with two fingers, we can only fixate one object and will have double vision of objects positioned nearer or further. This could be called *physiological double vision.*

Strictly speaking, physiological double vision consists of two components: physiological diplopia and physiological confusion. *Physiological diplopia* is the

phenomenon that occurs when under normal viewing conditions an object is projected onto the fovea of one eye and on an eccentric point of the retina of the other eye, like with the aforementioned test with our fingers. *Physiological confusion* occurs when under normal viewing conditions an object is projected onto the fovea of one eye and another object onto the fovea of the other eye. These two phenomena occur continuously under binocular viewing conditions, when objects other than the fixated object fall onto the retina of both eyes. Why don't we continuously suffer from diplopia and confusion? There must be a mechanism that takes care of this tendency to see double. This mechanism is called *physiological suppression.*

Suppression is the cortical mechanism that protects against diplopia and confusion. It erases one of the two images that might cause diplopia (and confusion) from conscious regard. Which aspect of diplopia is the trigger for suppression? Clearly, there is a difference in contour, brightness and color between the images of the eyes, causing a phenomenon called *rivalry.* There is still a lot of discussion in the literature on the correlation between rivalry and suppression.[2, 17, 20] We don't know exactly where the mechanisms for suppression (and rivalry) are located. Do they occur in the retina, in the neural pathways, or in the visual cortex?

Thus, under normal circumstances, people never suffer from double vision because of physiological suppression. However, persons who suddenly become cross-eyed above the age of six often have double vision. Their double vision is based on the aforementioned phenomena of diplopia and confusion together with a lack of suppression. It is a clinical fact that suppression is a phenomenon that can occur up to the age of six, or according to our own observations even up to the age of twelve.[8] If one becomes cross-eyed later in life, one usually will suffer from persistent diplopia and confusion.

When children squint before the age of six, they usually do not suffer from diplopia. Even if they do, it is usually only for a few weeks. We still do not exactly know why people with early onset squint do not suffer from double vision. Do they use the same suppressive mechanism that is commonly used to get rid of physiological double vision? Whichever mechanism they use, it must be rather potent. We commonly call this mechanism 'strabismic suppression'. *Strabismic suppression* can be defined as a neuronal process leading to the reduction in sensitivity of a part of the retina of the deviating eye while the other eye is fixating. Suppression is the defense mechanism of persons with strabismus against diplopia and confusion. Suppression usually consists of an area of reduced sensitivity in the visual field of the squinting eye under binocular viewing conditions, the so-called suppression scotoma.

On a theoretical basis it can be postulated that there are two suppression scotomas in strabismus: a fixation point scotoma and a central scotoma. A fixation

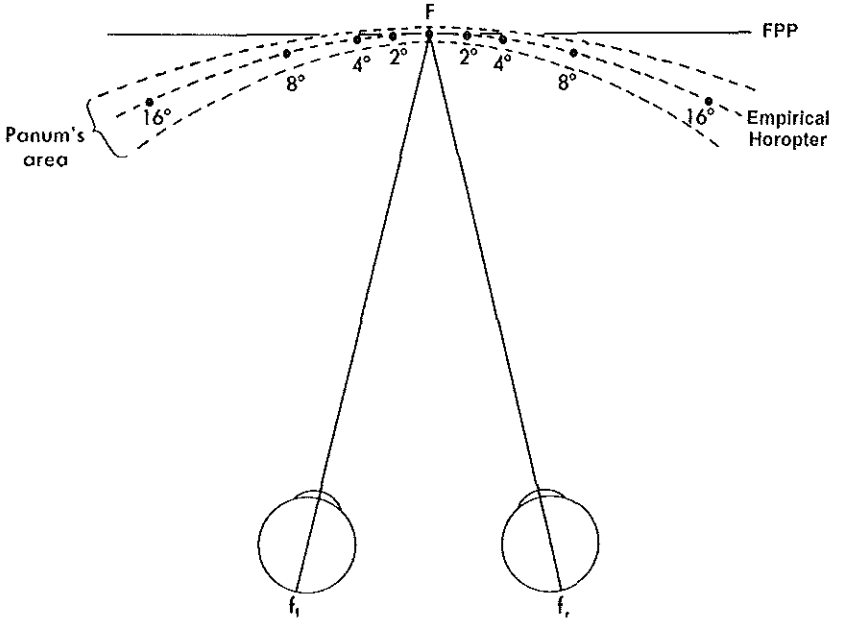


Figure 2 — Schematic drawing of the horopter as originally defined by Aguilonius (FPP= fronto-parallel plane) in relation to the empirical horopter and Panum's area. Note: F = fixation point. Fr= fovea of right eye, Fl= fovea of left eye.

point scotoma is a scotoma centered around the point on the retina of the deviating eye, onto which the image of the fixating eye projects (the diplopic point). A central scotoma is a scotoma centered around the fovea of the deviating eye (the point of confusion).

Many aspects of suppression are still enigmatic. The exact site in the visual system, where suppression originates, is not yet known. We also do not know exactly which amount of suppression is needed to get rid of double vision.

Suppression is strongly associated with *anomalous retinal correspondence* (ARC). Parks defines ARC as 'the cortical adjustment in directional values supplied by the retinal elements in strabismic eyes'.[14] He also stated that 'ARC permits fusion of similar images projected onto non-corresponding retinal areas by object points peripheral to the area of conscious regard'. Briefly, ARC is an internal compensa-

tion mechanism for external squint. It can only compensate for small angles of convergent squint (maximum 6°). Although ARC may lead to strong distortions in the periphery of the perceived image of the deviating eye[5,19] it hardly ever poses a serious problem to the subject. Sireteanu and Fronius have shown in comitant strabismus that ARC is present in the peripheral visual field and that the central visual field is more likely to show suppression.[18] In the part of the visual field with suppression, no binocular functions can occur. This will cause a loss of stereopsis, a cortical deficit that leads to lack of depth perception that can sometimes have consequences for the choice of profession. For example: with this defect it can be a problem to be a tennis-player or an ophthalmic surgeon.

Amblyopia is a Greek term introduced by Hippocrates, but he used it as a general term to describe loss of vision due to organic defects in the eye, such as cataract. In 1777, Plenk already gave a more specific definition of the term.[16] He stated that amblyopia is weakness of vision without an organic defect. This is very much in line with the modern definition as given by Levi and Harwerth.[10] They state that amblyopia is a unilateral reduction in visual acuity (and contrast sensitivity) due to a developmental disturbance in the visual system following ocular misalignment, asymmetrical refractive error or other stimulus deprivation to one eye. It is known that strabismic amblyopia in some cases may be associated with a relative visual field defect in the affected eye.[5] It is commonly agreed that prolonged suppression of one eye in children leads to amblyopia. Eccentric fixation can only be found in subjects with strabismic amblyopia, and is characterized by the fixation of the deviating eye with a point outside the foveola.

1.2 Classification of Strabismus

Strabismus can be divided in two forms: (con)comitant strabismus and incomitant (paralytic) strabismus. *Comitant strabismus* is a misalignment of the eyes occurring in childhood, in which the angle of deviation remains unchanged, regardless of the direction of gaze.[15] *Incomitant strabismus* is an ocular misalignment, that is caused by a malfunction of an extraocular muscle or its innervation with a varying angle of deviation, that is greatest when looking in the direction of the paralyzed muscle. This form of strabismus occurs mainly later in life.

Strabismus can also be divided in: manifest strabismus (heterotropia) and latent strabismus (heterophoria). *Manifest strabismus* is an evident ocular misalignment, which can be detected under everyday circumstances. *Latent strabismus* is an ocular misalignment that only occurs under circumstances of dissociation between the eyes, such as fatigue, debilitating disease or use of sedatives or alcohol. The prevalence of manifest strabismus ranges from approximately 1.5% [12] to 6.5%.[3] Nearly every person has some degree of latent strabismus.

Another way to classify strabismus is according to the direction of the ocular misalignment. Horizontally, there are manifest and latent convergent strabismus (esotropia or esophoria) and divergent strabismus (exotropia or exophoria). Convergent strabismus occurs in 75 to 80% of all forms of manifest strabismus, whereas divergent strabismus occurs in only 20%.[3, 12] Vertically, there is manifest and latent sursumvergent (upward) strabismus (hypertropia or hyperphoria) and deorsumvergent (downward) strabismus (hypotropia or hypophoria). Vertical strabismus is much rarer than horizontal strabismus and is present only in the remaining 1 to 5 percent of the strabismic cases.

Strabismus can also be divided in a primary, consecutive and secondary form. This division sometimes shows some overlap. Primary strabismus is cross-eyedness that occurred naturally, i.e. after exclusion of other causes, and could also be called congenital strabismus. Consecutive strabismus is cross-eyedness following operative under- or overcorrection of primary strabismus. Secondary strabismus is a squint due to (neuro)ophthalmologic disease.

Since convergent and divergent strabismus make up for the main types of strabismus it seems important to inform the reader about some specific forms of these two types of squint. The most common form of comitant convergent strabismus can be found as a part of the congenital squint syndrome. Children with this condition have an esotropia, diagnosed typically under the age of 6 months, associated with latent nystagmus (nystagmus, occurring only when one eye is occluded and beating in the direction of the open eye), dissociated vertical deviation or DVD (upward drift of an eye, when occluded) and asymmetry of the horizontal optokinetic nystagmus (a stronger beating of the eyes following stimulation with a line grating moving in the nasal direction, than with one moving in the temporal direction). Although the congenital squint syndrome mostly applies to esotropia, it can sometimes also occur with exotropia.

Another important category of persons with convergent squint is the group with accommodative esotropia. Subjects with this form of strabismus have a convergent squint, with an angle of deviation greater at near viewing than at far. These subjects have hypermetropia as an underlying cause of their convergent squint. A pair of spectacles will improve the ocular deviation. This type of esotropia is often diagnosed in children older than 6 months of age.

A third distinct category of persons with convergent squint is the group with microstrabismus. Lang defines microstrabismus as small angle esotropia (angle < 5 deg.) and some form of stereopsis on the basis of a cortical adjustment to the angle of deviation, called anomalous retinal correspondence (ARC).[9] In many cases microstrabismus might be concurrent with the congenital squint syndrome or with accommodative esotropia. Comitant convergent strabismus, especially when associated with the congenital squint syndrome or microstrabis-

mus has many sensorial implications. Some are monocular, such as amblyopia and eccentric fixation, and some binocular, such as ARC, suppression and loss of stereopsis.

Three important types of divergent strabismus have to be mentioned. The most common type is that of intermittent exotropia. It is stated that up to 80% of exotropes are of the intermittent type, and thus have good ocular alignment under some circumstances.[3] Constant exotropia, which has a constant angle under all viewing directions and distances, is much rarer. A common third variety of divergent squints is that of convergence insufficiency, where the subject cannot converge the eyes enough at reading distance. This disorder can be the cause of eyestrain and headache. Subjects with divergent squint very rarely have amblyopia.

1.3 Questions addressed in this thesis

This thesis focuses on perimetric research into amblyopia and suppression. These two sensory phenomena are most likely the result of binocular interaction. We have studied them with different perimetric methods. In this thesis we want to answer the following questions:

1 What is the extent of the visual field under monocular viewing conditions in primates with early onset strabismus and amblyopia?
2 What is the extent of the visual field under binocular viewing conditions in human subjects with convergent and divergent strabismus? What are the sizes and depths of suppression scotomas in strabismus?
3 What is the optimal stimulus for the detection of strabismic suppression?

With our monocular as well as with our binocular visual field studies in human and non-human primates we focussed on the effects of binocular interaction or competition on the visual field. In other words, with the studies performed under monocular viewing conditions we determined the extent of the visual field in amblyopia. With the studies under binocular viewing conditions we gained more insight into the full extent of suppression.

1.4 Outline of the present thesis

Following the current chapter, the general introduction to this thesis (Chapter 1), a review is given of the literature on both the visual field under monocular as well as under binocular viewing conditions in animals and humans with amblyopia and strabismus (Chapter 2). In the following chapters (Chapters 3 and 4) we will try to answer the first question on the basis of data from three studies on the extent of the visual field under monocular viewing conditions in amblyopic pri-

mates. Chapter 3 deals with the extent of the monocular visual field in monkeys with monocular deprivation. Chapter 4 deals with the extent of the monocular visual field in monkeys, as well as with a study of the monocular visual field in human subjects with convergent strabismus with amblyopia.

Question number 2 is answered in Chapters 5 and 6. In chapter 5, we measured the extent and depth of suppression scotomas in microstrabismus and small angle convergent strabismus in humans with a method of quantitative binocular perimetry. In Chapter 6 we present the results of testing the extent and depth of suppression in humans with divergent strabismus.

In the next chapter (Chapter 7) the third question is answered on the basis of our work on the characteristics of the optimal stimulus to measure strabismic suppression in humans. With a method of central binocular perimetry we determined which stimulus length and luminance profile are best to measure suppression. In conclusion, a general discussion of the main findings of the research described in this thesis is formulated (Chapter 8), followed by a summary.

References

1 Aguilonius, F. (1613) Francisci Aguilonius e Societate Jesu opticorum libri sex. Philosophis iuxta ac mathematicis utiles, Antwerpiae, ex Officina Plantiniana, Apud Viduam et Filios Moreti.
2 Belsunce, S. de & Sireteanu, R. (1991). The time course of interocular suppression in normal and amblyopic subjects. Invest. Ophthalmol. Vis. Sci. 32, 2645-2652.
3 Decker, W. de (1995). Strabismus (Kaufmann, H. ed.). Enke Verlag, Stuttgart, Vol. 2, Chapt. 4, pp. 209-282.
4 Duke-Elder, S. (1973). Abnormal ocular motility. Henry Kimpton, London, Volume 6, Chapter 6, pp. 223-317.
5 Fronius, M. & Sireteanu, R. (1989). Monocular geometry is selectively distorted in the central visual field of strabismic amblyopes. Invest. Ophthal. Vis. Sci. 30, 9: 2034-2044.
6 Helmholtz, H. (1864). Ueber den Horopter. Arch. f. Ophthal. 10: 1-60.
7 Hering, E. (1863). Beiträge zur Physiologie. 3. Heft: Vom Horopter. Wilhelm Engelmann, Leipzig.
8 Joosse, M.V., Simonsz, H.J., Minderhout, H.M. van, Mulder, P.G.M., Jong, P.T.V.M. de (1999). Quantitative visual fields under binocular viewing conditions in primary and consecutive divergent strabismus. Graefe's Arch Clin Exp Ophthalmol, 7, 237: 535-545.
9 Lang, J. (1968) Evaluation in small angle strabismus or microtropia. Strabismus Symposium, Giessen, Karger, Basle, 219-222.
10 Levi, D.M. and Harwerth, R.S. (1977). Spatio-temporal interactions in anisometropic and strabismic amblyopia. Invest. Ophthalmol. Vis. Sci. 16: 90.
11 Müller, J. (1826) Zur vergleichenden Physiologie des Gesichtssinnes des Menschen und der Thiere nebst einem Versuch über die Bewegungen der Augene und über den menschlichen Blick. C. Cnobloch, Leipzig.
12 Noorden, G.K. von (1990) Binocular vision and ocular motility, Fourth Edition, The Mosby Company.
13 Panum, P.L. (1858). Physiologische Untersuchungen über das Sehen mit zwei Augen. Schwerssche Buchhandlung, Kiel.
14 Parks, M.M. (1990) Binocular Vision Adaptations in Strabismus, In Tasman, W. & Jaeger, E.A. (Eds.), Duanes Clinical Ophthalmology, Vol. 1, Chapt. 8, pp. 1-7. Philadelphia: J.B. Lippincott.

15 Parks, M.M. and Wheeler, M.B. (1990). Concomitant esodeviations, In Tasman, W. & Jaeger, E.A. (Eds.), Duanes Clinical Ophthalmology, Vol. 1, Chapt. 12, pp. 1-14. Philadelphia: J.B. Lippincott.
16 Plenk, J.J. (1777). Doctrina de morbis oculorum. Vienna.
17 Sengpiel, F., Blakemore, C., Harrad, R. (1995). Interocular suppression in the primary visual cortex: a possible neural basis of binocular rivalry. Vision Res. 35, 2: 179-195.
18 Sireteanu, R. and Fronius, M. (1981). Different patterns of retinal correspondence in the central and peripheral visual field of strabismics. Invest. Ophthalmol. Vis. Sci., 30, 2023-2033.
19 Sireteanu, R., Lagreze, W.D., Costantinescu, D.H. (1993) Distortions in two dimensional visual space perception in strabismic observers. Vision res., 33, 5/6: 677-690.
20 Wolfe, J.M. (1983). Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion on briefly presented dichoptic stimuli. Perception. 12, 447-456.

Review of the literature

2.1 History of research on binocular perception in normal and strabismic subjects

It is still not exactly known how people with comitant strabismus perceive the world. How much do subjects with strabismus actually see of their surroundings? One of the biggest problems in the study of perception in strabismus is that the person with strabismus is not completely aware of what he sees and what he misses of the outside world. Perception in strabismic persons is even harder to grasp than perception in normals.

In the year 1613, the Jesuit priest Franciscus Aguilonius already wrote a lengthy treatise on the physiology of binocular vision in normal persons.[1] In this Latin text containing beautiful illustrations by Peter Paul Rubens (Figure 1), Aguilonius introduced the term 'horopter', as mentioned in Chapter 1. He postulated that the horopter is an unlimited frontoparallel plane through each object point that is fixated, on which all objects are seen single. Objects positioned closer or further than this plane are seen double. More than two centuries later, Muller was the first to criticize the work of Aguilonius, stating that the horopter had to be a perfect circle, rather than a frontoparallel plane.[72] Helmholtz, Hering and Panum postulated that the horopter had to be a slightly toric plane through the nodal point of both eyes as well as through the object of fixation.[42, 43, 77]

In 1760, Du Tour performed a very important experiment in order to explain why subjects with normal visual functions see things single, whereas in actual fact they see slightly different images with their separate eyes.[101] He observed that looking through a yellow glass with one eye and a blue one with the other, did not result in seeing green, but parts of the image were blue and others were yellow. In fact this was a very early description of interocular rivalry.

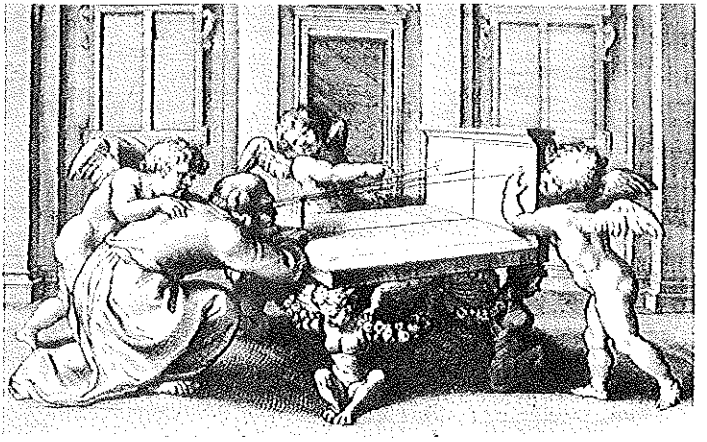


Figure 1 — Picture by Rubens taken from 'Opticorum' by Aguilonius, courtesy of Museum Plantin-Moretus.

In the eighteenth century also an interest in abnormal binocular function started to develop, leading to the earliest insight in strabismic amblyopia and its treatment. In 1748 De Buffon accurately described that a strabismic eye has a lower visual acuity.[13] He believed that this reduction in visual acuity was the cause of strabismus. He was the first to indicate that occlusion of the fixating eye is beneficial. However he believed that occlusion therapy would cure the strabismus rather than the low visual acuity of the strabismic eye. In 1777 in the book 'Doctrina de morbis oculorum' Plenk gave a definition of amblyopia in Latin which still is commonly used: 'Amblyopia est visus debilitas sine admodum visibile oculo vitio' (amblyopia is weakness of vision without a visible defect in the affected eye).[81] With this definition he updated the broad meaning Hippocrates gave to amblyopia: weakness of vision due to organic defects.

In the second half of the nineteenth century many studies on binocular vision were performed. Good examples of these can be found in the works of the following authors:

- Meyer (1855), who stressed the importance of contour on the maintenance of fusion.[71]
- Panum (1858), who performed the famous rivalry experiment with line gratings at right angles in front of each eye, and found a mosaical pattern of the two images.[77]
- Helmholtz (1864) and Hering (1868 and 1869), who were arguing on the fact whether binocular impression is built up from simple addition (Helmholtz) or integration (Hering) of monocularly perceived points.[42-44]

– Donders (1867), who stressed the importance of convergence and the associated change in bilateral retinal position on our sense of depth.[24, 25]

The interest in strabismus and its sensorial aspects was triggered by the introduction of the strabismus operation by the German general surgeon Johann Dieffenbach in the year 1839.[22] After he started performing complete myotomy of the medial rectus muscle in patients with convergent strabismus, there were many followers across the western world. This operation that was always performed without any form of anesthesia led in the majority of cases to an overcorrection. In many adult cases this overcorrection led to an almost intractable diplopia. It was this diplopia or the lack thereof in children that was the actual stimulus for German clinicians and researchers to study perception in strabismus.

In 1854, Albrecht von Graefe wrote a clear description of suppression, anomalous retinal correspondence (ARC) and other aspects of perception in his strabismic subjects, even though much of the modern specialistic terminology, such as suppression, diplopia, confusion and ARC, was not yet available to him.[34]In this article entitled: 'Über das Doppelsehen nach Schieloperationen und Incongruenz der Netzhäute', Von Graefe described why some of his patients who had an operation for squint did not suffer from diplopia, and others did. In this impressive study, he used very simple means, such as a candle, prisms and a red glass. One of his most important conclusions in this article was: 'Das schielende Auge is nicht unbedingt untätig, sondern es trägt durch Über den ganzen Umfang der Netzhaut ausgedehnte quantitative Lichtempfindung und durch seitliche qualitative Wahrnehmung zur Vergrösserung des Gesichtsfeldes bei'. 'Es handelt sich hier um physiologische Unterdrückung, die qualitative Eindrücke annuliert' (The squinting eye is not totally incapacitated, but it contributes to an expansion of the visual field by a quantitatively reduced sensitivity across the retina and by qualitative perception of the periphery. This is a physiological suppression, that annihilates qualitative impressions). It can be concluded from Von Graefe's work in patients with strabismus, that the sensitivity for light stimuli in the deviating eye was reduced when tested under binocular viewing conditions. However the subjects could perceive stimuli in the periphery of the visual field of the deviating eye. Instead of the term 'suppression', he used the term 'Unterdrückung' for this phenomenon. A few years later Von Graefe referred to the phenomenon of suppression with the empirical term 'Spielraum' (playing space) as an area of freedom, within which he could reposition a muscle in a patient with strabismus, without causing diplopia.[36]

In 1860, Donders described the observation that there is an association of convergent strabismus and hypermetropia.[24] This association is nowadays known as accommodative convergent strabismus. In 1863, Donders postulated that con-

vergent strabismus almost always is based on an underlying hypermetropia and that divergent strabismus is albeit to a lesser extent, associated with an underlying myopia.[25] Even though he somewhat overestimated the value of accommodative factors as the basis of strabismus, we have to be grateful for his contribution to the way of thinking about strabismus.

2.2 The visual field in amblyopia

In the following I will give a review of the literature on the visual field in strabismus and other forms of early visual deprivation. Firstly, I will discuss the studies on the monocular visual field (i.e. the visual field under monocular viewing conditions) in animals and humans with amblyopia and strabismus. Also the animal studies on the neuro-anatomical basis of potential field defects will be discussed. Secondly, the results of studies on the binocular visual field (i.e. the visual field under binocular viewing conditions) in humans with convergent as well as divergent strabismus will be discussed. These studies deal with the extent of suppression in strabismus. Here I will also include studies on the neuro-anatomical and electrophysiological basis of the presence or absence of suppression scotomas.

2.2.1 The monocular visual field in strabismus and visual deprivation

In normal humans the monocular visual field (i.e. the visual field under monocular viewing conditions) of each eye can be subdivided into three segments: a binocularly perceived nasal segment, a binocularly perceived temporal segment and a strictly monocularly perceived temporal segment (the temporal crescent).

The first report of monocular visual field studies in normal persons and in subjects with various ophthalmic diseases was by Von Graefe in 1855.[35] Unfortunately, he did not examine the visual field in amblyopia. He performed kinetic perimetry with a Bjerrum-like screen (grating of black crossed lines) with objects of different size and brightness. In normal subjects he found a monocular visual field of up to 174° horizontally by 105° vertically. Heine found an extent of the monocular visual field of 60° nasally to 100° temporally.[41] Much later, Goldmann confirmed this finding in static as well as kinetic perimetry. [33] He also found, like Fisher that the visual field shrinks somewhat with age.[29] This shrinkage is located mainly temporally and starts at the age of 20 years. By the age of 60 years 5° in the temporal periphery are lost. Glaser found that there were no racial differences in the nasal extent of the visual field due to different shapes of the nose.[325] In all subjects the nasal visual field did not exceed 64°, thus there seems to be more a retino-cortical than a facio-structural limitation

of the nasal visual field. In short it could be stated that the outermost temporal retina is blind. On the other hand Schmidt et al. found a nasally enlarged visual field in a 75-year-old subject with fixed divergent strabismus of 110°.[85] The nasal as well as the temporal edge of the field was at an eccentricity of 80°. Thus under special circumstances there could be some plasticity in the outer nasal retina.

Since amblyopia is more likely to occur in convergent than in divergent strabismus, the vast majority of studies on the monocular visual field in strabismus and amblyopia were performed in subjects with convergent squint. The first study of the monocular visual field in convergent strabismus and deep amblyopia was by Guillery in 1896.[37] He found a strong variance in perimetry results; in some cases there was a central scotoma, in some mostly nasally located shrinkage, in others a temporally located restriction of the field. In some, however, he found a total shrinkage of the field, whereas in others there were no field abnormalities. In convergent strabismus, Heine did not find any peripheral field defects; he only found a central scotoma with a diameter of 10'.[41] Tron described a form of 'localized amblyopia' associated with the blockage of the peripheral retina due to the large angle deviation (temporally by the orbit or nasally by the bridge of the nose).[104] For example, in convergent strabismus the outer temporal retina receives less visual input, and this will lead to nasal shrinkage of the visual field. In small angle strabismus however, he found a limitation on the exact opposite side of the visual field, due to eccentric fixation and some form of abnormal correspondence. He did not find a correlation between the angle of deviation and the size of the field defect. In his description of strabismic amblyopia, like Heine,[41] Bielschowsky described a central scotoma, but did not study the peripheral visual field.[10]

Braun did not observe any abnormalities in the monocular visual field of esotropes.[12] Mackensen only found slightly steeper drop-off of the peripheral sensitivities in monocular perimetry of esotropes.[67] Duke Elder stated that there are no peripheral visual field defects in strabismic amblyopes.[27] These three authors indicated that there is a loss in the central sensitivity in the monocular visual field (relative central scotoma). Mehdorn detected large nasal field defects or in some cases even nasal hemianopia in humans with deep strabismic amblyopia.[68] In subjects with amblyopia with a visual acuity > 0.2 he found normal monocular visual fields. Sireteanu and Fronius did not find nasal field losses in esotropes with deep amblyopia (VA < 0.1).[95] They mentioned however, a reduction in sensitivity across the whole visual field.[95] Very recently, Donahue et al. performed automated perimetry of the central 30° of the visual field of humans with amblyopia due to strabismus or other causes.[23] They found only a slight reduction in sensitivity (2 to 3 dB) across the visual field of the amblyopic eye in strabismic and anisometropic subjects. In the subjects with strabismic amblyopia they found a statistically significant selective reduction of the overall sensitivity of the temporal hemifield of

the amblyopic eye compared to that of the non-amblyopic eye.

In order to find the underlying neuro-anatomical and neuro-physiological basis of amblyopia and associated visual field defects, animal studies have been performed on cats, dogs and monkeys. In the fair number of reports on monocular visual field studies in strabismic and amblyopic animals, there were significant differences in outcome, but there was also a different outcome in many of these studies from those undertaken in humans.

Normal cats, dogs and monkeys have a similar extent of the monocular visual field as humans, ranging from 50° nasally to 100° temporally.[89, 90, 113] In humans, the nasal edge extends slightly further, up to 60°.[32] The reason for this can be a difference in nasal or retinal anatomy but differences in stimulus size and method of stimulus presentation might also play a role.

Perimetry studies in cats or monkeys with monocular deprivation with lid-suture, occluder-contact lens or esotropia (induced or naturally occurring) have shown various outcomes. From studies of the monocular visual field in animals with monocular visual deprivation, the general conclusion can be drawn: the deeper the deprivation, the more extensive the field loss.

No visual field defects can be detected in cats with mild deprivation, such as alternating convergent strabismus.[7] In moderate deprivation with temporary early monocular occlusion or experimentally induced strabismus in cats, visual field defects were found involving only the far temporal periphery and/or the binocularly perceived nasal half of the monocular field.[8, 28, 51, 105, 106]

In cases of more severe early monocular deprivation with early monocular occlusion (black contact lens or lid-suture) or early surgically induced strabismus in cats, field loss in both the nasal as well as the temporal part of the binocularly perceived segment was found.[89, 90, 93] These defects were in some cases combined with a loss of the far temporal side of monocularly perceived segment of the field.[11] In the most extreme cases of monocular deprivation, in animals with monocular lid-suture or occlusion, no responses could be found across the entire monocular visual field.[92]

In conclusion, it can be stated that in primates with esotropia and moderate amblyopia, no or if any, only a small field defect in the far temporal periphery of the monocular visual field can be found. The rare large nasal or naso-temporal field defects might only occur in primates with esotropia and deep amblyopia or in primates with deep amblyopia due to early monocular occlusion.

2.2.2 *The neural basis of amblyopic field defects*

There has been a small number of elaborate studies on the neuro-anatomical and neuro-physiological basis for visual field loss in humans and animals with deep amblyopia. The most commonly used explanation for the sometimes extensive visual field defects in amblyopia is based on the model of 'binocular competition'. This model is largely based on the Nobel Prize winning work of Wiesel and Hubel published in 1963.[111] They performed single cell recordings in the lateral geniculate body of kittens with monocular occlusion and found a significant reduction in size of the cells in those layers of the geniculate body that were driven by the deprived eye. In the same year they also published work on single cell responses in the visual cortex of monocularly deprived cats.[112] They showed that there was an almost total unresponsiveness of the binocularly driven cells in the striate cortex to stimulation of the deprived eye. In this model, the non-deprived eye had a strong dominance in the use of the geniculocortical pathways.

Von Noorden[73] and Von Noorden and Middleditch[74] found in monkeys with experimental deprivation or strabismic amblyopia, in agreement with the monocularly deprived cats of Wiesel and Hubel,[111] that the layers in the geniculate driven by the deviating eye were atrophic. These studies gave an explanation for those deprivation studies in which only a loss of the binocularly perceived segment of the monocular visual field was found. Ikeda et al. showed that there was a marked reduction in function and size of the cells in the geniculate body that corresponded to the nasal visual field in cats reared with induced convergent strabismus; thus in cats it can be stated that the cells corresponding to the nasal visual field are more susceptible to deprivation than those corresponding to the temporal side of the binocular segment of the monocular visual field.[52] In monkeys, Horton and Stryker found shrinkage of the cortical ocular dominance columns corresponding to an eye rendered amblyopic by early lid-suture.[48] However, Horton et al. showed in a human postmortem study, that amblyopia (visual acuity 20/800) due to accommodative esotropia does not cause shrinkage of the ocular dominance columns corresponding to the amblyopic eye.[50] In this study they also found that there is no reduction in cell volume of the ocular dominance columns of the amblyopic eye in monkeys. Thus it can be stated that amblyopia due to anisometropia or esotropia is more likely to have its basis in the lateral geniculate body than in the cortex. But it remains a fact that there can be found at least functional defects in the cortex of amblyopes. Sireteanu et al. have recently reported on such defects in the higher cortical levels using functional MRI (fMRI).[97]

Visual field defects in the binocular segment of the monocular visual field can be satisfactorily explained by the above-mentioned model of interocular interaction. The defects in the far temporal periphery of the visual field (temporal crescent) in eyes with visual deprivation, as described by Tron[98] and Berman and Murphy[8] are more difficult to explain, because supposedly there is no interocular interaction in this segment of the visual field. We can only speculate about the basis of this field loss.

Another model for the explanation of the field defects in amblyopia is based on a defect in the visuomotor system i.e. a malfunction in the cortico-tectal pathways (the connections between the superior colliculus and the visual cortex). Lesions in the superior colliculus supposedly cause disturbances in visually guided behaviour leading to contralateral visual neglect.[2,99] Some authors discussed the possible higher susceptibility of the temporal retina in the cat to monocular deprivation and correlated this with the fact that in this animal only the uncrossed retinotectal pathways are affected following monocular deprivation.[89,108] The monkey has more crossed fibers in its retinotectal pathways and thus could be less susceptible to visual deprivation. It is conceivable that in monkeys with visual deprivation the only defect found is in the far temporal periphery because of the visuomotor defect, caused by a lesion in the contralateral superior colliculus. Thus the temporal field loss might be more a sensory motor than a strictly sensory field defect.

Tron raised a hypothesis of localized peripheral nasal retinal hyposensitivity in esotropes. He stated that there is a lack of stimuli to this part of the retina caused by the ocular deviation and thus that there is anatomical limitation of visual input causing some kind of peripheral 'amblyopia'.[104] Fisher found that due to aging there is a shrinkage of the temporal side of the visual field. It might be possible that strabismus or strabismic amblyopia might cause a quicker 'aging' or less maturation of the visual field and thus might cause temporal shrinkage of the field.[30] Tychsen and Lisberger showed a maldevelopment of the cortical visual motion processing system in esotropes.[107] They found a defect in naso-temporal smooth pursuit; objects moving in a nasal direction evoked a more vigorous response than objects moving in the opposite direction. This might also be a causative factor for loss of the far temporal periphery in monocular visual deprivation.

2.3 The binocular visual field in strabismus: studies on suppression

As stated in chapter 1, suppression is the defense mechanism of people with strabismus against diplopia and confusion. Generally it is stated that there are two suppression scotomas in strabismus: a fixation point scotoma and a central scotoma. As mentioned in the former chapter a fixation point scotoma is a scotoma

centered around the point on the retina of the deviating eye, onto which the image of the fixating eye projects (the diplopic- or fixation-point). A central scotoma is a scotoma centered around the fovea of the deviating eye (the point of confusion).

Suppression occurs only under conditions of unhampered binocular viewing and is lifted when there is any form of dissociation between the eyes. Dissociation can be introduced easily under test circumstances, but without some form of dissociation between the eyes suppression cannot be measured. In the past, various methods of dissociation have been used such as: colored or polarizing filters,[34, 67, 91] mirrors,[103] phase difference haploscopy[3] or striated glasses by Bagolini.[5] Campos, Herzau and Mehdorn all compared the earlier mentioned methods of binocular perimetry.[14, 42, 63] They agreed that the more dissociating the method of binocular perimetry, the smaller the detectable amount of suppression would be. They concluded that there is a gradient in dissociating effect across the various perimetric methods of determining suppression-scotomas, ranging from Bagolini's striated glasses as the least dissociating, via phase difference haploscopy, polarizing filters, and synoptophore to red-filters as the most dissociating method.

The value of the suppression measurement also depends strongly on the cooperation and analytic capacity of the test subject. This aspect makes it very difficult to perform suppression measurements in animals. This is probably the reason why there have not been reports on measurements of suppression in animals. On the other hand animals will, at least when they are in a cooperative mood, be perfect unbiased observers, whereas humans might make their own interpretations of the test procedure and might thus be more susceptible to dissociation.

In the following I will give a review of the literature on the subject of strabismic suppression, in which a lot of contradicting results can be found. Since there are clinical indications for the existence of a structural difference in the sensory status of subjects with convergent and divergent strabismus, I will discuss these two categories of strabismus separately.[20, 54, 70]

2.3.1 Suppression in convergent strabismus

The first report of interocular suppression and correspondence in convergent strabismus was in 1854 by von Graefe.[34] He described an area of regional exclusion or 'Unterdrückung' (later called suppression) centered around the fovea of the deviating eye. Many aspects of suppression are still enigmatic. The exact site of suppression is not yet known. We also do not know exactly which amount of suppression is needed to avoid suffering from double vision. Von Graefe found the same type of regional exclusion in divergent strabismus. This probably is the

first report of the central scotoma. In this experiment he used a Bjerrum-like screen, with a candle light as fixation stimulus and a red glass in front of one eye. Sachs showed in 1897 that alternating esotropes with binocular perimetry by mirror dissociation have rapidly alternating perception.[84] He did not find evidence for the existence of localized suppression scotomas. In 1900, Bielschowsky showed with mirror dissociation that the central part of the field of the deviating eye was not perceived during binocular viewing (central scotoma).[9] Braun found kidney-shaped suppression scotomas in esotropes with a red glass in front of the fixating eye.[12]

Travers described with the mirror-screen test (dissociation by mirrors and a Bjerrum-like screen) an absolute, circularly shaped fixation-point scotoma in the squinting eye.[103] In 1938 Harms was the first to find two scotomas in esotropes.[39] He used a method of dissociation with red and green glasses. He found a large fixation-point scotoma and a smaller central scotoma in a group of esotropes with an angle of deviation > 6°. In subjects with small angle esotropia (< 6°), he did not find any suppression.

Swan described a theoretical condition in persons with an esotropia of 12 to 18°, where the blind spot exactly overlapped the fixation point.[100] Under test circumstances, with the help of an haploscopic device he could substantiate this theory. Under clinical circumstances this condition is very unlikely to occur, because it can only happen if the fixated object has a smaller projection than the blind spot. For example, this exact locking on the blind spot can never be maintained while the angle of deviation is changing with a change in viewing distance.

Mackensen detected with static binocular perimetry with polarizing filters only a fixation-point scotoma in an overall slightly reduced sensitivity level across the field of the deviating eye.[67] In microstrabismus Lang found a large fixation point scotoma with a method using binocular Amsler charts in the synoptophore.[58] In 1978 Lang performed binocular perimetry with a phase difference haploscope introduced by Aulhorn;[59, 3] again only a fixation-point scotoma (zero-point scotoma) was seen in microstrabismus. In large angle esotropia he found in a small number of cases a central scotoma (fovea-scotoma). Where present, these scotomas were often overlapping.[6]

Pratt-Johnson and MacDonald observed in binocular perimetry with polarising filters and a complex visual background large round scotomas encompassing both the fovea as well as the fixation point.[83] They found the same scotomas in convergent as in divergent strabismus. Sireteanu and Fronius (1981) showed with red-green perimetry in esotropes, that there was suppression of the area that extended from the central to the nasal retina.[91] Schuy found a fixation-point scotoma in microstrabismus in a method of profile perimetry with phase difference haploscopy.[87]

2.3.2 *Suppression in divergent strabismus*

As mentioned before in the year 1854 Von Graefe was the first to mention central scotoma-like suppression in divergent as well as convergent strabismus in a famous study on diplopia and ARC in patients who underwent strabismus surgery in his clinic.[34] In 1897 Tschermak published a lengthy description of his own condition of intermittent exotropia and anisomyopia.[102] He found an overall reduction of sensitivity with relative sparing of the fovea of the deviating eye with a method of color-filter dissociation. This is probably the first report on the fixation point scotoma. Bielschowsky[9] found in an exotrope, like von Graefe in 1854,[34] a central scotoma with dissociation with colored filters. Since the beginning of the twentieth century the majority of studies showed suppression of the nasal half of the visual field, corresponding with the temporal half of the retina, including the fixation point, but in most cases sparing the fovea of the deviating eye.

We will first mention the advocates of the nasal hemisuppression theory. With mirror-field perimetry Travers (1938) found a large nasal fixation-point scotoma excluding the fovea of the deviating eye.[103] Harms (1938) demonstrated with red-green perimetry nasal hemisuppression including the fixation point as well as the fovea of the deviating eye.[39] Herzau (1980) found in binocular perimetry with striated glasses nasal hemisuppression excluding the macula of the deviating eye in divergent strabismus with ARC. In divergent strabismus with normal retinal correspondence (NRC), he observed nasal hemisuppression including the macula of the deviating eye.[46] Knapp, Jampolsky and Parks (1990) found support for the hemisuppression theory in their clinical observations.[54, 56, 79]

There are, however, exceptions to the theory of nasal hemisuppression by Bagolini.[6] He found with his striated glass test suppression of the whole binocular segment of the visual field of the deviating eye in persons with large angle divergent strabismus, without ARC. Awaya et al. and Pratt-Johnson and MacDonald showed that a complex background is a much more realistic stimulus for the measurement of suppression in strabismus.[4, 83] With their tests they found large suppression areas encompassing both the fixation point as well as the fovea of the deviating eye. Cass as well as Cooper and Feldmann demonstrated that many subjects with intermittent exotropia have an absence of suppression, an enlarged peripheral field of view and a form of facultative ARC.[3, 17] They called this triad of symptoms: 'panoramic viewing'.

2.3.3 The neural basis of suppression

Only since two decades there has been a small number of publications on the neuro-anatomical and neurophysiological basis of suppression. In humans these studies have been confined to electrophysiological, visual evoked pattern (VEP) studies. Since it is commonly agreed that prolonged monocular suppression in early life leads to amblyopia it can be expected that there is some overlap in the findings of the studies that try to find the neural basis of amblyopia and suppression. Franceschetti and Burian found in a haploscopic VEP study of alternating esotropes that there is an alternate reduction in the VEP upon stimulation of the non fixating eye, whereas there is no reduction in the VEP when the fixating eye is stimulated.[30] They based this on a form of instable amblyopia, or suppression, as we would be more inclined to call this. This finding resembles the VEP findings in binocular rivalry in normal subjects as found by Lawill and Biersdorf.[51] Campos and Chiesi found reduced summation in the pattern binocular VEP responses in esotropes that had clinical suppression as found with Bagolini's striated glasses.[15] However, this finding might also be an electrophysiological proof of ARC as well as of suppression. These results might indicate that suppression as well as anomalous (retinal) correspondence are most likely to be located in the visual cortex.

Leguire et al. found in a study of binocular summation in early onset esotropia that neuronal processes involved in the flash VEP are different from those in the pattern VEP.[62] They did not give an indication where these different processes are located in the brain. We will indicate that a flash is much more dissociating and suppression breaking than a light that goes on and off in a gradual fashion. Maybe flash stimulation interferes more with the cortical system responsible for attention, whereas pattern stimulation is more an indicator of the cortical region where binocular fusion is located.

What the role is of the LGN in suppression and rivalry is still not clear. Varela and Singer have found inhibitory processes in the LGN of cats with rivalrous square wave gratings shown to the eyes.[109] Sengpiel et al. did not find inhibition in the LGN using rivalrous sinusoidal gratings, they only found intracortical inhibition.[88] Perhaps the difference in luminance profile of the stimuli that were used in these studies explains these different results.

It is still not clear if rivalry in normal subjects and suppression in strabismic subjects are based on the same neural process. Studies on the time course of the processes can be helpful in this question. De Belsunce and Sireteanu, Kauffman and Wolfe investigated the time course of rivalry and suppression.[7, 55, 114, 115] They found evidence that suppression of rivalrous images needs some time to build up. De Belsunce and Sireteanu found that patterns of lines directed at right angles shown to the eyes for a period shorter than 0.1 s, led to superimposition of the two

images, whereas presenting the images for 0.1 to 0.5 s. led to suppression. If the competing images were shown for periods longer than 0.5 s. rivalry occurred.[7]

It can be stated that rivalry suppression and strabismic suppression are separate processes, having a different time course with different cortical localisations. Perhaps alternating esotropia and exotropia are more like rivalry suppression, as has also been described in normals. Non-alternating esotropes might have the more constant strabismic type of suppression. However, this is contradicted by Leonards and Sireteanu in a behavioural study in humans and by a recent electrophysiological study by Sengpiel et al. in cats.[63, 88] They have found an indication that strabismic suppression might build up in the same time frame as rivalry suppression. With single cell recordings Sengpiel et al. localized these processes in the ocular dominance columns in the primary visual cortex for normal as well as strabismic cats.[88] In this same area Wiesel and Hubel have also found structural anomalies in cats rendered deeply amblyopic with lid-suture.[112] However, in humans and monkeys with deep amblyopia due to esotropia and anisometropia no shrinkage of the cortically localized ocular dominance columns could be found.[45, 46] This might indicate that suppression in persons with strabismus or anisometropia could be only a physiological cortical defect, localized in the ocular dominance columns. However there is also strong evidence that rivalry and suppression involve more cortical areas than the primary visual cortex (area 17) such as the prestriate cortex, the parietal visual fields and even frontal cortical areas both on an electrophysical basis as well on the basis of PET scan studies in humans. [38, 64] The question remains: are there more visual areas involved in suppression than in amblyopia, or the other way round? Or could it be that these phenomena involve exactly the same areas.

References

1 Aguilonius, F. (1613) Francisci Aguilonius e Societate Jesu opticorum libri sex. Philosophis iuxta ac mathematicis utiles, Antwerpiae, ex Officina Plantiniana, Apud Viduam et Filios Moreti.

2 Albano, J.E., Mishkin, M., L.E. Westbrook, Wurtz, R.H. (1982). Visuomotor deficits following ablation of Monkey superior colliculus. J. Neurophysiol., 48, 2: 338-351.

3 Aulhorn, E. (1966). Phasendiffferenz-Haploskopie. Klin. Mbl. Augenheilk. 148: 540.

4 Awaya, S., Nozaki, H., Itoh, T., Harada, K. (1976). in Moore, Mein & Stockbridge (eds) Orthoptics, Past, Present & Future. Miami, Symposia Specialists, pp. 531-546.

5 Bagolini, B. (1958). Tecnica per l'esame della visione binoculare senza introduzione di elementi dissocianti (test del vetro striato) Boll. d'Oc. 37, 195.

6 Bagolini, B. (1976). Sensorial anomalies in strabismus, Part 1. Doc. Ophthal. 41, 22 amblyopic subjects.

7 Belsunce, S. de & Sireteanu, R. (1991). The time cours of interocular suppression in normal and amblyopic subjects.Invest. Ophthalmol. Vis. Sci. 32, 2645-2652.

8 Berman, N and Murphy, E. (1981) The critical period for alteration in cortical binocularity resulting from divergent and convergent strabismus. Dev. Brain Res. 2, 181-202.

9 Bielschowsky, A. (1900). Untersuchungen ueber das Sehen Schielenden. Albr. v. Graefe's Arch. f. Ophthalmol. 50:406-509.
10 Bielschowsky, A. (1926). Zur Frage der Amblyopie. Klin. Mbl. Augenheilk. 77: 302-314.
11 Bisti, S. & Carmignoto, G. (1986). Monocular deprivation in kittens differently affects crossed and uncrossed visual pathways. Vision Res. 26, 6: 875-884.
12 Braun, G. (1934). Gesichtsfelduntersuchungen bei Schielenden. Klin. Mbl. Augenheilk. 92, 600-613.
13 Buffon, G.L. de (1748) Sur la cause du strabisme ou des yeux louches. Mem. Acad. Roy. Sci. 321-345.
14. Campos, E.C. (1982) Binocularity in comitant strabismus: binocular visual field studies. Doc. Ophthal. 53, 249-281.
15 Campos, E.C. & Chiesi, C. (1982). Binocularity in comitant strabismus: II. Objective evaluation with visual evoked responses. Doc. Ophthal. 53, 277-293.
16 Cass (1937). Divergent strabismus. Br. J. Ophthalmol. 21, 11: 538-559.
17 Cooper, J. & Feldmannn, J. (1979). Panoramic viewing, visual acuity deviating eye, and anomalous retinal correspondence in the intermittent exotrope of the divergence excess type. Am. J. Optometry Phys. Optics. 56(7), 422-429.
18 Crewther, D.P. and Crewther, S.G. (1990). Neural site of strabismic amblyopia in cats: spatial frequency deficit in primary cortical neurons. Exp. Brain Res. 79: 616-622.
19 Crewther, S.G. and Crewther, D.P. (1993). Amblyopia and suppression in binocular cortical neurones of strabismic cat. Neuroport 4, 1083-1086.
20 Decker, W. de (1995). Strabismus (Kaufmann, H. ed.). Enke Verlag, Stuttgart, Vol. 2, Chapt. 4, pp. 209-282.
21 Demer, J.L., Noorden, G.K. von Volkow, N.D., Gould, K.L. (1988). Imaging of cerebral blood flow and metabolism in amblyopia by positron emission tomography. Am J. Opthalmol., 105, 4: 337-347.
22 Dieffenbach, J.F. (1839). Ueber die Heilung des angeborenen Schielens mittelst Durchschneidung des inneren geraden Augenmuskels. Medicinische Zeitung 8,1.
23 Donahue, s.P, Wall, M, Kutzko, K.E., Kardon, R.H. (1999) Automated perimetry in amblyopia: a generalized depression. Am. J. Ophthalmol. 127, 3, 312-321.
24 Donders, F.C. (1860) Beiträge zur Kenntniss der Refractions- und Accommodationsanomalien. Archiv f. Ophthal. 6: 62-105.
25 Donders, F.C. (1863). Zur Pathologie des Schielens. 9: 99-155.
26 Donders, F.C. (1867). Das binoculare Sehen und die Vorstellung von der dritten Dimension. Archiv f. Ophthal. 13: 1-48.
27 Duke-Elder, S. (1973). Abnormal ocular motility. Henry Kimpton, London, Volume 6, Chapter 6, pp. 223-317.
28 Elberger, A.J., Smith, E.L., White, J.M. (1983). Optically induced strabismus results in visual field losses in cats. Brain Res. 268: 147-153.
29 Fisher, R.F. (1968) The variations of the peripheral visual field with age. Docum. Ophthal. 24, 41-67.
30 Franceschetti, A.T. and Burian, H.M. (1971). Visually evoked responses in alternating strabismus. Am. J. Ophthalmol., 71, 6:1292-1297.
31 Fronius, M. & Sireteanu, R. (1989) MOnocular geometry is selectively distorted in the central visual field of strabismic amblyopes. Invest. Ophthal. Vis. Sci. 30, 9: 2034-2044.
32 Glaser, J.S. (1967). The nasal visual field. Arch. Ophthal. 77: 358-360.
33 Goldmann, H. (1969). Lichtsinn mit besonderer Berueeksichtigung der Perimetrie. Schweiz. Ophthal. Ges., 2. Fortbildungskurs, Bern 1968 Ophthalmologica 158: 362-386.
34 Graefe, A. von (1854). Ueber das Doppelsehen nach Schiel-Operationen und Incongruenz der Netzhaute. Arch. f. Ophthalmol. 1: 82-120.
35 Graefe, A. von (1855). Ueber die Untersuchung des Gesichtsfeldes bei amblyopischen Affectionen. Arch. f. Ophthalmol. 2: 258-298.
36 Graefe, A. von (1857). Beiträge zur Lehre vom Schielen und von der Schiel-Operationen. Arch. f. Ophthalmol. 3: 177-386.
37 Guillery (1896). Arch.f. Ophthalmol. 33: 45.

38 Gulyas, B. an Roland, P.E. (1994). Binoculair disparity discrimination in human cerebral cortex: functional anatomy by positron emission tomography. Proc. Nat. Acad. Sci. U.S.A., 91, 1239-1234.
39 Harms, H. (1938). Ort und Wesen der Bildhemmung bei Schielenden, Albr. v. Graefe's Arch. f. Ophthalmol.138, 149-210.
40 Harting, J.K. and Guillery, R.W. (1976). Organization of retino-collicular pathways in the cat. J. Comp Neurol., 166, 133-144.
41 Heine, L. (1905). Uber das zentrale Skotom. Klin. Mbl. Augenheilk. 43, 1: 10-40.
42 Helmholtz, H. (1864). Ueber den Horopter. Arch. f. Ophthal. 10: 1-60.
43 Hering, E. (1863). Beiträge zur Physiologie. 3. Heft: Vom Horopter. Wilhelm Engelmann, Leipzig.
44 Hering, E. (1868). Bemerkungen zu der Abhandlung von Donders über das binoculare Sehen. Arch. f. Ophthal. 14: 1-12.
45 Hering, E. (1869). Ueber die Rollung des Auges um die Gesichtslinie. Arch. f. Ophthal. 15: 1-16.
46 Herzau, V. (1980). Untersuchungen über das binokulare Gesichtsfeld Schielender. Doc. Ophthal. 49, 221-284.
47 Hess, R.F., Campbell, F.W. and Zimmern, R.C. (1980). Differences in the neural basis of human amblyopias: the effect of mean luminance. Vision Res, 20, 295-306.
48 Horton, J. and Stryker, M.P. (1993) Amblyopia induced by anisometropia without shrinkage of ocular dominance columns in human striate cortex. Proc. Natl. Acad. Sci. U.S.A., Vol. 90, 5494-5498.
49 Horton J. and Hocking, D.R. (1996) Pattern of ocular dominance columns in human striate cortex in strabismic amblyopia. Vis. Neurosci. 13, 787-795.
50 Horton, J., Hocking, D.R. and Kiorpes, L. (1997) Pattern of ocular dominance columns and cytochrome oxidase activity in a macaque monkey with naturally occurring anisometropic amblyopia. Vis. Neurosci., 14, 681-689.
51 Ikeda, H. and Jacobson, S.G. (1977). Nasal field loss in cats reared with convergent squint: behavioral studies. J. Physiol. (Lond.) 270: 367-381.
52 Ikeda, H., Plant, G.T., Tremain, K.E. (1977). Nasal field loss in kittens reared with convergent squint: neurophysiological and morphological studies of the lateral geniculate nucleus. J. Physiol. 270: 345-366.
53 Imamaura, K., Richter, H., Fisher, H., Lennerstrand, G., Franzen, O., Rydberg, A., Andersson, J., Schneider, H., Onoe, H., Watanabe, Y., Längström, B. (1997).
54 Jampolski, A. (1955). Characteristics of suppression in strabismus. Arch. Ophthalmol., 154, 683-696.
55 Kaufman, L. (1963). On the spread of suppression and binocular rivalry. Vision Res. 3, 401-415.
56 Knapp, P. (1953). Intermittent exotropia: Evaluation and therapy, Am. Orthoptic J., 3: 27-33.
57 Lang, J. (1968). Evaluation of small angle strabismus or microtropia. Strabismus Symposium, Giessen, Karger, Basle, pp. 219-222
58 Lang, J. (1971). Binocular Amsler's charts. Brit. J. Ophthal. 55: 284-285.
59 Lang, J. (1978). Die Scotome im binokularen Gesichtsfeld bei hochgrädiger Amblyopie und bei Microstrabismus. Klin. Mbl. Augenheilk. 173: 470-476.
60 Lang, J. (1982). Mikrostrabismus. Bücherei des Augenarztes. Heft 62. Enke Verlag Stuttgart.
61 Lawill, T. and Biersdorf, W.R. (1968). Binocular rivalry and visual evoked responses. Invest. Ophthalmol. Vis. Sci. 7: 378.
62 Leguire, L.E., Rogers, G.L., Bremer, D.L. (1995). Flash visual evoked response binocular summation in normal subjects and patients with early-onset esotropia before and after surgery. Doc. Opthal. 89: 277-286.
63 Leonards, U., Sireteanu, R.. (1993) Interocular suppression in normal and amblyopic subjects: The effect of unilateral attenuation with neutral density filters. Perception and Psychophysics 54, 1: 65-74.
64 Leopold, D.A. and Logothetis, N.K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. Nature 397, 6565: 549-533.
65 Levi, D.M. and Harwerth, R.S. (1977). Spatio-temporal interactions in anisometropic and strabismic amblyopia. Invest. Ophthalmol. Vis. Sci. 16: 90.
66 Lin, C.S. and Kaas, J.H. (1980). Effects of monocular deprivation on geniculocortical pathways in

the owl monkey, Actus trivirgatus, Neurosci. Lett., 18: 267-273
67 Mackensen, G. (1959). Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgaenge beim Schielen. v. Graefes Arch. f. Ophthalmol. 160: 573-587.
68 Mehdorn, E. (1986). Nasal field defects in strabismic amblyopia. Docum. Ophthal. Proc. Ser. 45: 318-328.
69 Mehdorn, E. (1989). Suppression scotomas in microstrabismus – perimetric artefact. Doc. Ophthalmol. 71, 1-18. 64.
70 Mein, J. & Trimble, R. (1994). Diagnosis and management of ocular motility disorders, Second Edition, Section 1, Chapt. 7 (pp. 116-146). Blackwell Science.
71 Meyer, H. (1855). Ueber den Einfluss der Aufmerksamkeit auf die Bildung des Gesichtsfeldes überhaupt und des gemeinschaftlichen Gesichtsfeldes beider Augen im Besonderen. Arch. f. Ophthal. 2: 77-92.
72 Müller, J. (1826). Zur vergleichenden Physiologie des Gesichtssinnes des Menschen und der Thiere nebst einem Versuch über die Bewegungen der Augen und über den menschlichen Blick. C. Cnobloch, Leipzig.
73 Noorden, G.K. von. (1973) Histological studies of the visual system in monkeys with experimental amblyopia. Invest. Ophthal. Vis. Sci. 12, 10: 727-738.
74 Noorden, G.K. von and Middleditch, P.R. (1975). Histology of the monkey lateral geniculate nucleus after unilateral lid closure and experimental strabismus: further observations. Invest. Ophthal. Vis. Sci. 14, 9: 674-683.
75 Noorden, G.K. von (1990) Binocular vision and ocular motility, Fourth Edition, The Mosby Company.
76 Olivier, P. and Noorden, G.K. von (1981). The blind spot syndrome: does it exist? J. Pediatr. Ophthalmol. Strab. 18: 20-22.
77 Panum, P.L. (1858). Physiologische Untersuchungen über das Sehen mit zwei Augen. Schwerssche Buchhandlung, Kiel.
78 Parks, M.M. (1990) Binocular Vision Adaptations in Strabismus, In Tasman, W., Jaeger, E.A. (Eds.), Duanes Clinical Ophthalmology, Vol. 1, Chapt. 8, pp.1-7. Philadelphia: J.B. Lippincott.
79 Parks, M.M. and Wheeler, M.B. (1990). Concomitant esodeviations, In Tasman, W. & Jaeger, E.A. (Eds.), Duanes Clinical Ophthalmology, Vol. 1, Chapt. 12, pp. 1-14. Philadelphia: J.B. Lippincott.
80 Parks, M.M. and Wheeler, M.B. (1990). Concomitant exodeviations, In Tasman, W. & Jaeger, E.A. (Eds.), Duanes Clinical Ophthalmology, Vol. 1, Chapt. 12, pp. 1-13. Philadelphia: J.B. Lippincott.
81 Plenk, J.J. (1777). Doctrina de morbis oculorum. Vienna
82 Pollack, J.G. and Hickey, T.L. (1979). The distribution of retino-collicular axon terminals in Rhesus monkey, J. Comp. Neurol., 185, 587-602.
83 Pratt-Johnson, J.A. & MacDonald, A.L. (1976). Binocular visual field in strabismus. Canad. J. Ophthal. 11: 37-41.
84 Sachs, M. (1897). Ueber das Sehen der Schielenden. Alb. v. Graefe's Arch. f. Ophthalmol. 43: 597-612.
85 Schmidt, D., Reuscher, A., Kommerell, G. (1971). Ueber das nasale Gesichtsfeld bei Strabismus fixus divergens. Alb. v. Graefes Arch. Klin. Expp. Ophthal. 183: 97-104.
86 Schor, C. (1977). Visual stimuli for strabismic suppression. Perception, 6, 583-593.
87 Schuy, K. (1987). Binoculare statische Perimetrie und raumliches Sehen bei Patienten mit Microstrabismus und Normalpersonen mit kunsticher einseitiger Visusherabsetzung. Inaugural-Dissertation, Giessen.
88 Sengpiel, F., Blakemore, C., Harrad, R. (1995). Interocular suppression in the primary visual cortex: a possible neural basis of binocular rivalry. Vision Res. 35, 2: 179-195.
89 Sherman, S.M. (1973). Visual field defects in monocularly and binocularly deprived cats. Brain Res. 49, 25-45.
90 Sherman, S.M. and Wilson, J.R. (1975) Behavioural and morphological evidence for binocular competition in the postnatal development of the dog's visual system. J. Comp. Neurol. 161, 183-196.
91 Sireteanu, R. & Fronius, M. (1981). Naso-temporal asymmetries in human amblyopia: consequence of long-term interocular suppression. Vision Res., 21, 1055-1063.

92 Sireteanu, R., Fronius, M., Singer, W. (1981). Binocular interaction in the peripheral visual field of humans with strabismic and anisometropic amblyopia. Vision Res., 21: 1065-1074.
93 Sireteanu R.and Singer, W. (1984) Impaired visual responsiveness in both eyes of kittens with unilateral surgically induced strabismus. Invest. Ophthal. Vis Sci. (Suppl.) 26, 216.
94 Sireteanu, R. & Fronius, M. (1989). Different patterns of retinal correspondence in the central and peripheral visual field of strabismics. Invest. Ophthal. Vis. Sci., 30: 2023-2033.
95 Sireteanu R. & Fronius, M. (1990). Human amblyopia: structure of the visual field. Exp. Brain Res. 79: 603-614.
96 Sireteanu, R., Lagreze, W.D., Costantinescu, D.H. (1993) Distortions in two dimensional visual space perception in strabismic observers. Vision res., 33, 5/6: 677-690.
97 Sireteanu, R., Tonhausen, N.,Muckli, L., Lanfermann, H., Zanella, F.E., Singer, W.,Goebel, R. (1999). Cortical site of amblyopic deficit in strabismic and anisometropic subjects investigated with fMRI. Invest. Ophthalmol. Vis. Sci. (Suppl.) 39, 4: 909.
98 Sparks, D.L., Mays, L.E., Gurski, M.R., Hickey, T.L. (1986). Long- and short-term monocular deprivation in the rhesus monkey: effects on visual fields and optokinetic nystagmus. J. Neurosci. 6, 6: 1771-1780.
99 Sprague, J.M., Meikle, T.H. (1965). The role of the superior colliculus in visually guided behavior. Exp. Neurol. 11: 115-146.
100 Swan, K.C. (1948). The blind-spot syndrome. Arch. Ophthalmol. 40: 371.
101 Tour, M. du. (1760). Discussion d'une question d'optique. Memoires présentés a l'Academie Royale Science (Paris) 3, 514-530.
102 Tschermak, A. (1899). Ueber die anomale Sehrichtungsgemeinschaft der Netzhaute bei einem Schielenden. Alb. v. Graefes Arch. f. Ophthal. 47: 508-550.
103 Travers, T. aB. (1938). Suppression of vision in squint and its association with retinal correspondence and amblyopia. Brit. J. Ophthal. 22: 577-604.
104 Tron (1925). Ueber einige Eigentuemlichkeiten des Sehens der Schielenden. Klin. Mbl. Augenheilk.75: 109-118.
105 Tumosa, N., Tieman, S.B., Hirsch, H.V.B. (1982). Visual field defects in cats reared with unequal alternating monocular exposure. Exp. Brain Res. 47: 119-129.
106 Tumosa, N., Tieman, S.B. and Hirsch, H.V.B. (1982). Visual field measurements in monocularly deprived and normal cats. Exp. Brain Res. 30: 353-368.
107 Tychsen, L & Lisberger, S.G. (1986). Maldevelopment of motion processing in humans who had strabismus with onset in infancy. J. Neurosci., 6, 9: 2495-2508.
108 Van Hof-van Duin, J (1977). Visual field measurements in monocularly deprived and normal cats. Exp. Brain Res. 30, 353-368.
109 Varela, F.J. & Singer, W. (1987). Neural dynamics in the visual corticothalamic pathway revealed through binocular rivalry. Exp. Brain Res., 66: 10-20.
110 Vital-Durand, F., Garey, L.J. and Blakemore, C. (1978) Monocular deprivation in the monkey: morphological effects and reversibility. Brain Res. 158: 45-64.
111 Wiesel, T.N. & Hubel, D.H. (1963a) Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. J. Neurophysiol. 26: 978-993.
112 Wiesel, T.N. & Hubel, D.H. (1963b). Single-cell responses in striate cortex of kittens deprived of vision in one eye. J. Neurphysiol. 26: 1002-1017.
113 Wilson, J.R., Lavallee, K.A., Joosse, M.V., Hendrickson, A.E., Boothe , R.G., Harwerth, R.S. (1989). Visual fields of monocularly deprived macaque monkeys. Behav. Brain Res., 33: 13-22.
114 Wolfe, J.M. (1983). Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion on briefly presented dichoptic stimuli. Perception. 12, 447-456.
115 Wolfe, J.M. (1986). Briefly presented stimuli can disrupt constant suppression and binocular rivalry suppression. Perception. 15, 413-417.

Visual fields in monocularly deprived macaque monkeys

James R. Wilson,[1,2,3] Karen A. Lavallee,[1] Maurits V. Joosse,[1] Anita E. Hendrickson,[5]
Ronald G. Boothe,[1,3,4] and Ronald S. Harwerth[6]

Behav. Brain. Res (1989) 33:13-22

The effects of postnatal monocular deprivation have been studied in macaque monkeys using behavioral perimetry field testing. The types of deprivation were: (1) early eyelid suture at 22-26 days after birth and then reverse suture at 10-13 months postnatally, (2) late eyelid suture beginning at 3 or 5 months postnatally and continued for 18 months, and (3) long-term occlusion by contact lenses. Response levels were normal for group 1 monkeys with some reduction in visual field extent. A reduced response level but no change in visual field extent was observed for the deprived eyes of group 2 monkeys. One monkey from group 3 that wore an occluder lens from birth to 19 months postnatally had no responses in any part of the visual field. Two other monkeys of group 3, whose occlusion started at 9 or 12 days of age and lasted for 2 years, had no responses to stimuli presented to the previously occluded eyes in their nasal visual fields and had reduced levels of response to stimuli presented in their temporal fields. These results indicate that the effects of monocular deprivation on macaque monkeys are affected by the start, length and type of deprivation. Some of these results are also consistent with a model of binocular competition in which the magnitude of the competition declines along a nasal-to-temporal gradient of

1 Yerkes Regional Primate Research Center, 2 Departments of Anatomy and Cell Biology, 3 Ophthalmology and 4 Psychology, Emory University, Atlanta, GA 30322 (U.S.A.); 5 Departments of Biological Structure and Ophthalmology, University of Washington, Seattle, WA 98195 (U.S.A.) and 6 College of Optometry, University of Houston, TX 77004 (U.S.A.).

visual field eccentricity. However, a mechanism that is independent of binocular competition is needed to account for the loss of responses to stimuli presented in the monocular visual segment.

Introduction

Cats and dogs which have been monocularly deprived by lid-suture during the early postnatal period retain functional visual pathways for the monocular part of the visual field, which is that portion of the visual field extending from about 45° to 90° temporally.[1, 10, 23, 25-27, 31-33] In many of these studies, there were no responses to visual stimuli elicited in the binocular part of the deprived eye's visual field which extends to about 45° on either side of the midline.[23, 26, 27, 31, 32] Other studies of monocularly deprived cats obtained similar results in the deprived eye's monocular segment, but also observed responses in the binocular portion of the temporal visual field.[1, 10, 33]

A model based on 'binocular competition' has been proposed to explain some of these results. This model argues that the functional loss following neonatal monocular deprivation is due to postnatal competition between the two eyes for the commonly shared or binocular parts of the geniculocortical pathways.[6, 24, 25, 39] In this model, the non-deprived eye has a competitive advantage over the deprived eye so that unequal binocular interactions occurring during the postnatal sensitive period cause the non-deprived eye to capture almost complete control of the binocular portion of the geniculocortical pathways. On the other hand, the deprived eye might develop full functional capabilities in the monocular portion of these geniculocortical pathways because here the eyes have no direct interactions so that the non-deprived eye cannot exert its influence. In support of this hypothesis, monocularly deprived animals have obvious changes in the soma sizes of neurons in the binocular portions of the lateral geniculate nucleus (LGN), while such changes are small or unnoticeable in the monocular portions,[6, 12, 13, 17, 24, 27] and nearly all neurons in the binocular part of the visual cortex are driven only by the non-deprived eye (e.g. refs. 38,39).

An alternative to the model of binocular competition through the geniculocortical pathways is that retinotectal pathways may function for behavioral responses after monocular deprivation. Several studies in cats have discussed the possibilities of retinotectal pathways subserving behavioral responses in the temporal visual fields following various deprivation conditions.[14, 23, 27, 33] With mostly crossed pathways from the retinas to the colliculi in cats,[7] the nasal fields may be the most susceptible to deprivation effects. However, the monkey has a relatively large (40%) uncrossed pathway to the superior colliculi and might be more resistant to nasal field loss.[22]

Anatomical and physiological data obtained from primates also indicate that binocular competitive mechanisms operate in their visual pathways during postnatal development.[2, 3, 16, 20, 29, 34-37] Behavioral studies with the prosimian primate Galago or bushbaby show a functional sparing of only the monocular part of the visual field of an eye deprived by neonatal lid-suture.[16] Changes of cell size are observed only in the binocular segment of the LGN and not in the monocular segment of prosimians.[3] However, the relative importance of binocular competition appears to be less pronounced in the macaque monkey because there are clear cell size changes in both the binocular and monocular regions of the LGN in monocularly deprived[19, 34-37] and binocularly deprived macaques.[9, 29]

In contrast to the studies carried out with cats, behavioral observations of monocularly lid-sutured macaque monkeys which have been deprived from 8-14 days postnatally to 18-26 months of age indicate that the deprived eye displayed no visual function in either the binocular or monocular visual fields.[30] This unresponsiveness was still present even after the lids had been opened for 12 months (Sparks, personal communication). In another study, monkeys that underwent forced usage of the deprived eye by reverse-suture 10-14 months after birth did not show a central field deficit.[11] Thus, neither of these studies with monkeys produced a pattern of results that is the same as those obtained from cats, dogs or prosimian primates.

The mixed behavioral results cited above for macaques, coupled with the importance of primate data for comparison to those of humans, prompted the present investigation which reexamined the effects of monocular deprivation on visual function in monocular and binocular portions of the visual fieds of macaque monkeys. Sparks et al.[30] have already reported that longterm monocular deprivation by early lid-suture leads to unresponsiveness throughout the visual field for the deprived eye, and for this reason no further animals of this type were studied here. In this report, we tested the visual perimetry of monkeys reared under other deprivation conditions: reverse lid-suture, late-suture, and continuous occlusion.

Materials and methods

The visual fields of 4 Macaca nemestrina and six Macaca mulatta monkeys were tested. Rearing conditions for each animal are summarized in Table I. The specific details of rearing for these monkeys were guided by designs of other experiments in which these monkeys also participated. Six of the monkeys received an asceptic lid-suture of one eye while under general anesthesia. Three other monkeys wore extended-wear contact lenses.[5, 40] These lenses were opaque for one eye of each monkey and clear with a high positive power to correct for aphakia in the other eye. All procedures conformed with NIH guidelines for the use of primates.

The tested eyes can be divided into 4 rearing groups. The first group contains those eyes which have had no manipulation – those of one normal monkey (PVH) – and the non-deprived eyes of two of the monocularly deprived monkeys (8021, 8024). The second group contains those eyes which had been lid-sutured during early postnatal development and then reverse-sutured to force usage of the originally deprived eye (G6, N6, K1, AF). Monocular deprivation started at 22-26 days postnatally and reverse suture was carried out at 10 months. Note from Table 1 that 3 of these monkeys had a central retinal lesion placed in the initially non-deprived eye. K 1's lesion was at the time of the first lid-suture while N6 and G6 were at the time of the reverse suture. The third category contains the deprived eyes of two monkeys (8021, 8024) who had a late monocular lid-suture (92 or 153 days postnatally) followed by lid opening at 2 years of age and a long period of binocular vision before testing. The last category contains the eyes of 3 monkeys (N896, QK, PK) that wore an occluder lens on one eye from 1 to 12 days postnatally until 19-27 months of age (see Table 1 for details).

The behavioral testing apparatus is illustrated in the photograph of Fig. 1. It consisted of two semicircular white strips of metal (28 cm in height) which were arranged so that they were separated horizontally by 10 cm. and overlapped vertically by 3-4 cm. Older monkeys were positioned in a primate chair at the center of the apparatus as shown in Fig. 1. Monkeys less than 3 years old were hand-held by a second, non-testing person at the center of a similar apparatus. For monkeys which were not reversed-sutured, single eyes were tested by placing an occluding,

Table I — Animals and ages of experimental treatment

Monkey	Macaque species (Nemestrina or Mulatta)	First lid-suture or occlusion (days)	Reverse suture (months)	lid-suture or occluder removal (months)	Test age (months)
PVH	M	—	—	—	60
AF	N	26	10	—	12
KI	N	22*	10	—	21
G6	N	24	10**	—	24
N6	N	26	13**	—	20
8024	M	92		21	72
8021	M	153		23	72
N896	M	1***		19	28
QK	M	9.3***		24	29
PK	M	12***		27	29

*/** A lesion was made in the central retina of the open eye at the time of first lid-suture (*) or at the time of reverse suture (**) for a separate study.[11]

*** Occluder lens worn on left eye for indicated months: right eye had a tensectomy and a corrective contact lens worn on this aphakic eye for a similar period for a separate study.[49]

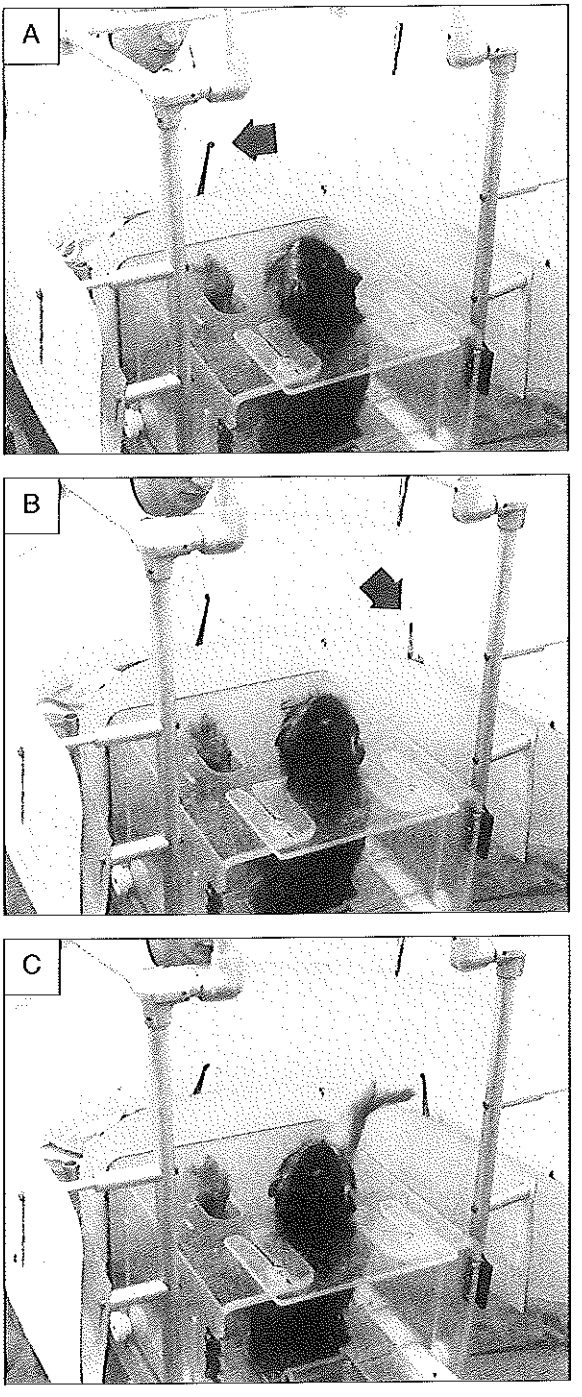


Figure 1 — Photographs of the apparatus used for perimetry testing of the older monkeys. The monkey is sitting in a primate chair facing the circular white boards.
A: the initial fixation stimulus is introduced between the metal arcs to obtain the monkey's attention and fixation at the 0° position (arrow).
With no further test stimulus introduced, the monkey is given a food reward at the 0° position if fixation is maintained for 1–2 s.
B: the monkey turns its eye and head to look at the second test stimulus (arrow) which is presented in the periphery shortly after the 0° position fixations stimulus.
C: the monkey receives a food reward from the peripheral stimulus position.

soft contact lens in the other eye. Testing was carried out using a strategy similar to that previously used for cats, dogs, and prosimians.[16, 23, 27] Each monkey was trained to fixate on a piece of food (apple, banana, raisin, etc.) introduced at the 0° position [straight ahead at 40 cm.] between the circular boards (Fig. 1A) and to retain fixation for 1-2 s in order to obtain a food reward. A novel visual stimulus was then introduced within the fixation time at various positions across the horizontal visual field with 11° of separation between each position (Fig. 1B).

The novel stimulus was food held in a forceps or a black cardboard circle (5° visual angle) on the end of a stick. A positive response was recorded if the monkey attended to the new stimulus by eye movement (and also usually head movement; Fig. 1B). A negative response was recorded if the monkey retained fixation on the initial 0 degree position stimulus. Each position was tested a total, across all sessions, of 10-40 times with more tests given near the edges of the visual field. The final response level for each field location was the percentage of positive responses. Despite training, the monkeys, like cats and dogs, sometimes moved their eyes away from the fixation stimulus even when no novel stimulus was presented. To measure the level of these false responses, control trials were given which consisted of simply presenting the fixation stimulus without introducing the novel, second stimulus. If the monkey's eye moved from the fixation stimulus, it was scored as a positive blank trial; if no eye movement occurred, it was scored as a negative blank trial. We considered that the monkey could see any position which had a response level above the positive blank trial rate. Larger black circles were sometimes used to compensate for refractive error or amblyopia and to eliminate any possible olfactory cues, but no differences in response levels from the smaller food stimuli were observed. Response levels dropped to less than the blank response rate peripherally because a positive response was only given when the monkey turned its eyes to the position associated with the novel stimulus, whereas blank trials were scored positive any time the eyes moved away from the fixation stimulus.

Ten to thirty test sessions of about one hour each were given to each monkey. To insure that the primary experimenter was not providing any visual or auditory cues to the animal, at least one final test session was run for the older monkeys using both a randomly-determined sequence of novel stimulus positions and an introduction of the novel stimulus by a second, naive tester. All testing regimes gave essentially identical results.

Results

Normal eyes

Perimetry test response levels are shown in Figs. 2-5. Tests for each eye individually are shown in Fig. 2 for a normally reared monkey (PVH). The overall percentages of positive blank responses (shown as horizontal dashed lines) averaged about 12% for this monkey. The temporal visual fields extend to about 100° laterally and the nasal visual fields extend to about 45° across the midline.

Reverse-sutured eyes

The results from the initially deprived eyes of 4 early monocularly lid-sutured monkeys (G6, N6, K1, AF) are depicted in Fig. 3. The response levels for these deprived eyes were essentially the same as those of the normal eyes shown in Fig. 2. The visual field of the deprived eye extended from about 90° laterally to between 33-56° across the midline. These fields were slightly reduced in range compared to those of the normal eyes shown in Fig. 2. The opposite eyes were not tested because they were sutured at the time of the testing.

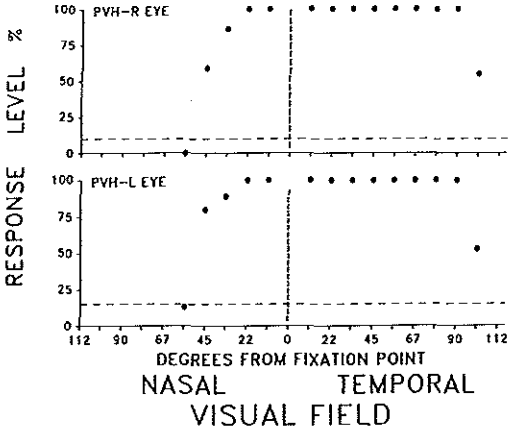


Figure 2 — Plots of perimetry testing results showing response levels across the visual field for a normally reared monkey (PVH). Response levels are shown by the percent of the trials to which the monkey looked at the test stimulus at each perimetry position. The horizontal dashed line represents the percent positive response (eye movements away from the fixation stimulus) when no test stimulus was presented. The vertical dashed line represents the fixation axis (0°). The visual field of each eye of this monkey represents control ranges against which those of deprived and non-deprived eyes can be compared in the other figures. The visual field for the left eye has been plotted as its mirror image for easier comparisons in this and the other figures.

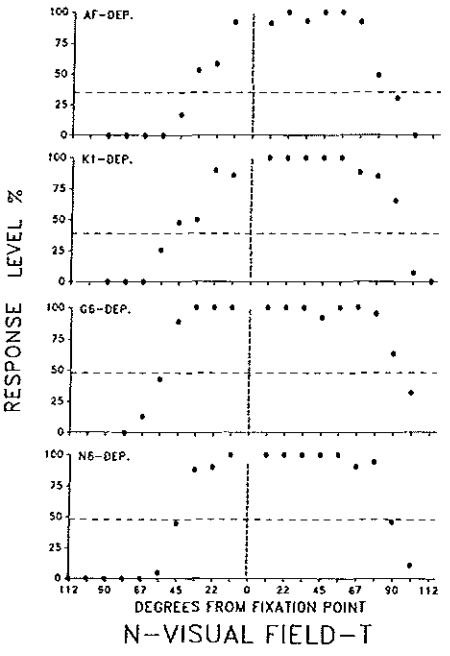


Figure 3 — Plots of response levels for previously lid-sutured eyes of 4 monocularly deprived monkeys (AF, K1, G6, N6). The opposite eyes were not tested. The times of deprivation and reverse-suture for each monkey are given in Table 1.
Note that the visual fields are all relatively normal exept for some reduction at the edges. T, temporal visual field: N, nasal visual field. Other figure symbols as in Fig. 2.

The other eye was aphakic and wore a corrective lens. The acuity of these eyes was: N896 = 8.9 cycles/degree; PK = 20.5 cycles/degree; QK = 26.2 cycles/degree. Because of the low or unmeasurable acuities for the occluded eyes, large visual stimuli usually were used to test them (black cardboard circles about 5° across). Monkey N896 displayed no responses to any visual target at any position across the visual field, including the monocular segment, regardless of the size or proximity of the stimulus to the eye. No data are shown in the figures for this monkey because all response points were zero. Monkeys PK and QK responded to stimuli presented in the temporal visual field for the previously occluded eye, but not in the nasal field. The response levels were also clearly lower for this eye compared to the fellow eye's response levels. Whereas PK's response levels were above the blank trial level in the entire ipsilateral hemifield, those of QK rose above the blank trial level only beyond 45° laterally, i.e. in the monocular segment. However, the blank trial response level is quite high (48 %) for this monkey, leaving some doubt as to its actual visual field range.

For monkeys QK and PK, a separate set of trials were made using signal detection theory methods. For these trials, one experimenter presented the stimuli and a separate observer scored the responses, but could not see the stimuli.

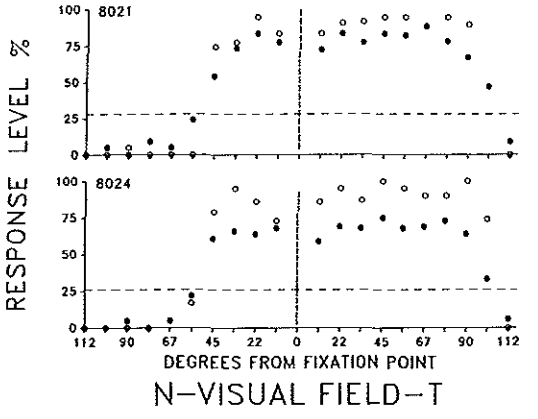


Figure 4 — Plots of response levels for two monkeys (8021, 8024) which had late monocular lid-sutures. Monkey 8021 was lid-sutured at 3 months of age and monkey 8024 was lid-sutured at 5 months of age. The responses of the deprived eyes (solid circles) can be directly compared with those of the non-deprived eyes (open circles). Note that the deprived eye of 8021 had slightly lower response levels compared with those of its non-deprived eye while 8024 had considerably lower response levels through its deprived eye. However, the extent of the visual fields for deprived eyes are basically the same as the non-deprived eyes. Other figure symbols as in Fig. 2 and 3.

Fig. 4 shows us the results of testing both the deprived and non-deprived eyes of two late-sutured monkeys (8021, 8024). For both monkeys, the response level through the deprived eye was lower for every position tested compared to the non-deprived eye. Animal 8024, which was lid-sutured at 3 months of age, showed an average response difference between the eyes of 23%, while animal 8021, which was lid-sutured at 5 months of age, had a smaller average response difference of 11%. The response level of monkey 8024's deprived eye improved somewhat during the several weeks of perimetry testing during which it was forced to use this eye, but it never reached the response levels obtained through the non-deprived eye. The extent of the fields was the same for the two eyes. The visual acuities of the deprived eyes were about 0.3 cycles/degree and over 20 cycles/degree for the non-deprived eyes 8

Occluded eyes

The last 3 monkeys to be tested (N896, QK, PK) were reared with an extended-wear soft contact occluder lens in one eye from near birth (1-12 days postnatally) to 19-27 months of age (Fig. 5). Behaviorally tested acuities for the occluded eyes of these monkeys were: N896 and PK = light/dark only; QK = 1.2 cycles/degree.

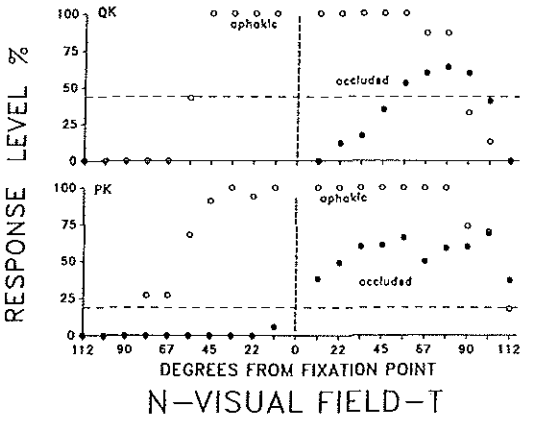


Figure 5 — Plots of response levels for two monkeys (QK, PK) which wore occluder lenses on one eye (solid circles) and corrective lenses on the aphakic eye (open circles), over the time period given in Table 1. A third monkey (N896) had similar lenses worn from the day of birth, but showed no reponses to visual stimuli using the occluded eye (i.e. the data points were all zero). The aphakic eyes had essentially normal visual fields. Note that the previously occluded eyes of the two monkeys had responses only in the temporal visual fields with better responses in the far periphery (monocular segment) for monkey QK. Other figure symbols as in Figs. 2 and 3.

These data were collected at only two of the stimulus positions: 33° (temporal binocular field) or 78° (temporal monocular field). On about one-half of the trials, the experimenter did not present the test stimulus after the fixation stimuli. The obsever judged whether a stimulus was or was not presented for each trial. The actual presence or absence of a stimulus was then scored along with the observer's judgement. As shown in Table II, the two monkeys (PK and QK) responded to stimuli presented in both the binocular (33°) and in the monocular (78°) temporal visual fields. Both monkeys had better response levels in the monocular segment compared to the binocular segment.

Discussion

The following main points can be made from the results: (1) Response levels and visual field extent are normal if the deprivation is initiated at approximately 3 weeks postnatally and lasts for about one year: (2) responses elicited through the deprived eye are slightly reduced, but the size of the visual fields is unaffected in late lid-suture cases deprived for 18 months; and (3) monkeys having continuous monocular occlusion from near birth to 19 months of age show either no responses

Table II — Results of objective perimetry test at 33° and 78° in the temporal field of the previously occluded eye of monkeys QK and PK

Visual field position		Hit rate	False alarm rate	n	Dprime
	33°	0.8	0.08	60	2.25
QK	78°	1.0	0.03	60	5.60
	33°	0.97	0.14	80	3.01
PK	78°	1.0	0.13	80	4.85

Evaluations were made using Receiver Operating Characteristic (ROC) curves. The hit rate is the proportion of correct choices by the observer when a stimulus was presented to the monkey at a position. The false alarm rate is the proportion of incorrect choices by the observer when a stimulus was not presented to the monkey (i.e. the observer guessed there was a stimulus presented when, in fact, no stimulus was presented to the monkey). A Dprime value of 1.96 is significant at the 0.05 level and becomes more significant at higher values.

or responses restricted to the temporal visual field. In the latter case, the response levels in the monocular segment are better than those in the binocular segment.

In the study of Sparks et al.,[30] monkeys with short periods of lid-suture (1-2 weeks) revealed no deficits in their visual fields. Our monkeys with deprivation periods of about one year also had no changes in their fields. Because these latter monkeys had the deprived eye opened while still in the late part of the sensitive period,[8] they were apparently able to recover from some of the effects of this long period of lid-suture, and this recovery may also have been facilitated by the reverse suture. Although 3 of these monkeys (K1, G6, N6) had a foveal lesion in the initially non-deprived eye, this factor did not appear to have any effect on the perimetry results because an unlesioned monkey (AF) had similar fields.

Our two lid-sutured monkeys with no reverse-suture (8021, 8024) started their deprivation rather late at 3 and 5 postnatal months, but the length of deprivation lasted for 18 months. This long period of late onset deprivation caused a reduction in response level throughout the visual field of the deprivated eye. The low acuities for both monkeys through the deprived eyes may have contributed to the lower response rates, but even larger targets (5° black circles) did not improve the response levels. Monkey 8021, sutured at a younger age, showed a larger defect, suggesting that both age of onset and length of deprivation are important factors in altering visual field responses.

Two of our occluded monkeys responded reasonably well in the monocular segments of their occluded eyes, poorly in the temporal part of the binocular segments, and not at all in the nasal visual fields. The aphakic eyes which had been corrected by a contact lens had essentially normal visual fields. The response in the monocular part of the occluded eye's visual field are explicable using a binocular competition model.[6, 24, 25, 39] Because the monocular segment does not receive competitive interactions from the other eye, visual function is preserved there.

The responses observed in the binocular part of the visual field for these monkeys can also be explained by an extension of this model. The extension takes into account the relative density of ganglion cells in the monkey's nasal and temporal retina. Beyond 20° eccentricity, there are about 3 times as many ganglion cells in the nasal part of the retina compared with the temporal part.[4, 21] Assuming that binocular competition results from the summed interactions of the pathways from each eye onto binocular neurons, then the amount of synaptic input from each eye will determine functional eye dominance. Because there are fewer connections being driven by the temporal retina at greater visual field eccentricities in the visual cortex,[18] there is less competition from the non-deprived eye in the visual cortex ipsilateral to it (contralateral to the deprived eye) as stimuli are presented at more peripheral temporal positions. The result is a nasal-to-temporal gradient for the deprived eye with the greatest competition to this eye's pathways occuring in its nasal visual field (temporal retina), less competition in its binocular, temporal field (nasal retina) decreasing with eccentricity, and no competition in the monocular segment. Such a gradient has previously been proposed by Tieman et al..[31]

As described in the Introduction, some previous studies in cats have also observed responses in both the monocular and binocular parts of the temporal field and attributed the results to retinotectal pathways. That is, if the deprived eye's geniculocortical pathways were nonfunctional, then the retinotectal pathways might provide an alternate system for the responses in the perimetry test. Because both the monkey and the cat have an ipsilateral projection of the nasal field to the colliculus,[7, 22] some form of competition could occur between the two eyes at this level as well as through the geniculocortical pathways. Although the presence of a crossed nasal field in the retinotectal pathways of the cat[7] complicates this possibility, it does not eliminate these pathways as possible routes for subserving the responses. The data from our two monkeys also cannot differentiate whether the geniculocortical or retinotectal pathways were used for their responses, but still demonstrate a nasal-to-temporal gradient in response levels in either case.

A further factor that might be relevant to the results for these two monkeys involves a developmental sequence. There is evidence for a slower development of ipsilateral compared with contrateral projections and peripheral compared to central projections (see ref. 20 for a review). If deprivation affects the later-developing projections, then the nasal field and the monocular segment of the temporal field should be the most affected. In general, we found the monocular segments to be the least affected, which appears to be inconsistent with this possibility. However, careful examinination of the data from all our animals reveals that every one of our deprived eyes exhibits a lowered response at 90° in the temporal periphery compared to the eyes of our normal control (PVH) and the non-deprived eyes of 8021 and 8024. Similar findings have been noted for

cats following various kinds of deprivation.[15, 28, 32] Thus, some of our results might be due to the greater sensivity to deprivation effects of later developing pathways.

The results of the third occluded monkey and the 5 lid-sutured monkeys of Sparks et al.,[30] all of whom had no responses throughout the visual field, cannot be attributed strictly to a binocular competition model. In these cases, a direct or deprivation per se effect is more likely the cause of the deficits, at least in the monocular segment. This effect is not dependent on interactions between the two eyes, but is apparently the result of inoperative pathways caused by the abnormal visual environment during development. Such an effect may be occuring in the other occluded monkeys as well, because the overall response levels of the late sutured and occluded monkeys were poorer than normal even in the monocular segment.

In attempting to analyze why only one of the three occluded monkeys had no visual field responses, it was noted that the occlusion started on the day of birth for the unresponsive monkey as opposed to over a week's period of binocular vision for the other two monkeys. However, the monkeys of Sparks et al.[30] had 8-14 days of normal vision prior to lid-suture and still remained visually unresponsive even long after lid-opening at 18-24 months of age.[30] Perhaps a short period of postnatal binocular vision is sufficienct to maintain visual fields for one year, but not for 18 months of more. Clearly, more data from monkeys that are reared with systematically varied onsets and lengths of deprivation will be necessary before the relevant factors leading to changes in various parts of the visual field can be isolated. Our results lead us to conclude that macaques have a nasal-to-temporal gradient of binocular competition and at least one other important non-competitive mechanism that can eliminate visual responsiveness even in the monocular segment.

References

1 Bisti, S. and Carmignoto, G., Monocular deprivation in kittens differently affects crossed and uncrossed visual pathways, Vision Res. 26 (1986) 875-884.

2 Boothe, R.G., Dobson V. and Teller, D.Y., Postnatal development of vision in human and non-human primates, Ann. Rev. Neurosci. 8 (1985) 495-545.

3 Casagrande, V.A. and Joseph, R., Morphological effects of monocular deprivation and recovery on the dorsal lateral geniculate nucleus in Galago, J. Comp. Neurol. 194 (1980) 413-426.

4 Curcio, C.A., Sloan, K.R., Packer, O., Hendrickson, A.E. and Kalina, R.E., Distribution of cones in human and monkey retina: individual variability and radial asymmetry, *Science* 236 (1987) 579-582.

5 Gammon, J.A., Boothe, R.G., Chandler, C.V., Tigges, M. and Wilson, J.R., Extended wear soft contact lenses for vision studys in monkeys, Invest. Ophthal. Vis. Sci., 26 (1985) 1636-1639.

6 Guillery, R.W. and Stelzner, D.J., The differential effects of unilateral lid closure upon the monocular and binocular segments of the dorsal lateral geniculate nucleus in the rat. J. Comp. Neural., 139 (1970) 413-422.

7 Harting, J.K. and Guillery, R.W., Organization of retinocollicular pathways in the cat, J.Comp. Neurol., 166 (1976) 133-144.
8 Harwerth, R.S., Smith, E.L., Duncan, G.C., Crawford, M.L.J. and von Noorden, G. K., Multiple sensitive periods in the development of the primate visual system, Science, 232 (1986) 235-238.
9 Headon, M.P. and Powell, T.P.S., The effect of bilateral eye closure upon the lateral geniculate nucleus in infant monkeys, Brain Res., 143 (1978) 147-154.
10 Heitländer, H. and Hoffmann, K.-P., The visual field of monocularly deprived cats after late closure or enucleation of the non-deprived eye, Brain Res. 145 (1978) 153-160.
11 Hendrickson, A., Boles, J. and Mc Lean, E.B., Visual acuity and behavior of monocularly deprived monkeys after retinal lesions, Invest. Ophthalmol. Vis. Sci. 16 (1977) 469-473.
12 Hickey, T.L., Development of the dorsal lateral geniculate nuclueus in normal and visually deprived cats, J. Comp. Neurol., 189 (1980) 467-481.
13 Hickey, T. L., Spear, P.D. and Kratz, K.E., Quantitative studies of cell size in the cat's dorsal lateral geniculate nucleus following visual deprivation. J. Comp. Neurol., 172 (1977) 265-282.
14 Hoffmann, K.P., Influence of visuel experience on ontogeny of optokinetic reflex in mammals. In J.P. Rauschecker and P. Mauler (Eds.), Imprinting and Cortical Plasticity, Wiley, (1987) 267-286.
15 Ikeda, H. and Jacobson, S.G., Nasal field loss in cats reared with convergent squint: behavioral studies, J. Physiol. (Lond.) 270 (1982) 367-381.
16 Joseph, R. and Casagrande, V.A., Visual defects and recovery following monocular lid closure in a promisian primate, Behav. Brain Res. 1 (1980) 165-186.
17 Kalil, R.E., A quantitative study of the effects of monocular enucleation and deprivation on cell growth in the dorsal lateral geniculate nucleus of the cat. J. Comp. Neurol., 189 (1980) 483-524.
18 LeVay, S., Conally, M., Houde, J. and Van Essen, D.C., The complete pattern of ocular dominance stripes in the striate cortex and visual field of the macaque monkey, J. Neurosci., 5 (1985) 486-501.
19 Lin, C.S. and Kaas, J.H., Effects of monocular deprivation on geniculocortical pathways in the owl monkey, Actus trivargatus, Neurosci. Lett. 18 (1980) 267-273.
20 Maurer, D., Lewis, T. and Brent, H., The effects of deprivation on human visual development. In F.J. Morrison, C.E. Lord and D.P. Keating (Eds.), Applied Developmental Psychology, Vol. 3. in press.
21 Perry, V.H. and Cowey, A., The ganglion cell and cone distributions in the monkey's retina: implications for central magni fication factors, Vision Res., 25 (1986) 1795-1810.
22 Polack, J.G. and Hickey, T.L., The distribution of retinocollicular axon terminals in Rhesus monkey, J. Comp. Neurol., 185 (1979) 587-602.
23 Sherman, S.M., Visual field defects in monocularly and binocularly deprived cats, Brain Res, 49 (1973) 25-45.
24 Sherman, S. M., Guillery, R.W., Kaas, J.H. and Sanderson, K.J. Behavioral, electrophysiological and morphological studies of binocular competition in the development of the geniculocortical pathways in cats, J. Comp. Neurol., 158 (1974) 1-18.
25 Sherman, S.M. and Spraque, J.M., Effects of visual cortex lesions upon the visual fields of monocularly deprived cats, J. Comp. Neurol., 188 (1979) 291-312.
26 Sherman, S.M. and Spear, P.D., Organization of visual pathways in normal and visually deprived cats, Physiol. Rev., 62 (1982) 738-855.
27 Sherman, S.M. and Wilson, J.R., Behavioral and morphological evidence for binocular competition in the postnatal development of the dog's visual systeem, J. Comp. Neurol., 161 (1975) 183-196.
28 Sireteanu, R. and Singer, W., Impaired visual responsiveness in both eyes of kittens with unilateral surgically induced strabismus, Invest. Ophthal. Vis. Sci., Suppl. 26 (1984) 216.
29 Sloper, J.J., Headon, M.P. and Powell, T.P.S., Changes in the size of cells in the monocular segment of the primate lateral geniculate nucleus during normal development and following visual deprivation, Dev. Brain Res., (1987) 267-276.
30 Sparks, D.L., Mays, L.E., Gurski, M.R. and Hickey, T.L., Long and short-term monocular deprivation in the rhesus monkey: effects on visual fields and optokinetic nystgamus, J. Neurosci., 6 (1986) 1771-1780.
31 Tieman, D.G., Tumosa, N. and Tieman, S.B., Behavioural and physiological effects of monocular

deprivation: a comparison of rearing with diffusion and occlusion, Brain Res., 280 (1983) 41-50.
32 Tumosa, N., Tieman, S.B. and Hirsch, H.V.B., Visual field deficits in cats reared with unequal alternating monocular exposure, Exp. Brain Res., 47 (1982) 119-129.
33 Van Hof-Van Duin, J., Visual field measurements in monocularly deprived and normal cats, Exp. Brain Res., 30 (1977) 353-368.
34 Vital-Durand, F., Garey, L.J. and Blakemore, C., Monocular deprivation in the monkey: morphological effects and reversibility, Brain Res., 158 (1978) 45-64.
35 Von Noorden, G.K. and Crawford, M.L.J., Form deprivation without light deprivation produces the visual deprivation syndrome in Macaca mulatta, Brain Res., 129 (1977) 37-44.
36 Von Noorden, G.K., Crawford, M.L.J. and Middleditch, P.R., The effects of monocular deprivation: disuse or binocular interaction? Brain Res. 111 (1976) 277-285
37 Von Noorden, G.K. and Middleditch, P.R., Histology of the monkey lateral geniculate nucleus after unilateral lid closure and expperimental strabismus: further observations. Invest. Ophthalmol. Vis. Sci., 14 (1975) 674-683.
38 Wiesel, T.N. and Hubel, D.H., Single cell responses in striate cortex of kittens deprived of vision of one eye. J. Neurophysiol., 26 (1963) 1003-1017.
39 Wiesel, T. N. and Hubel, D.H., Comparison of the effects of unilateral and bilateral eye
40 Wilson, J.R., Fernandes, A., Chandler, C.V., Tigges, M., Boothe, R.G. and Gammon, J.A., Abnormal development of the axial length of aphakic monkey eyes,Invest.Ophthal.Vis. Sci. 28 (1987) 2096-2098.
41 Wilson, M.E. and Toyne, M.J., Retinotectal and corticotectal projections in Macaca mulatta, Brain Res., 24 (1970) 395-402.

Monocular visual fields in primates with naturally occurring convergent strabismus

chapter IV

In this chapter we present two studies on the extent of the monocular visual field (VF). The first study is on the VF in monkeys with early onset convergent strabismus and amblyopia (Joosse et al., 1990), and the second is on the VF in humans with convergent strabismus and amblyopia (unpublished follow-up study).

4.1 Monocular visual fields of macaque monkeys with naturally occurring strabismus

M.V. Joosse,[1] J.R. Wilson[1, 2, 3] and R.G.Boothe[1, 2, 4]

Clin. Vis. Sci. (1990) 5, 2: 101-111

Summary

1 Using a perimetry technique, the horizontal extent of the monocular visual fields was determined in 9 monkeys that have naturally occurring convergent strabismus and 2 normal control monkeys.

2 In normally reared monkeys, the monocular fields extend from approx. 45° nasally to at least 90° temporally.

3 No nasal field loss was found for either eye of any of our naturally strabismic monkeys. This result is in agreement with results obtained from human patients who have a mild strabismic amblyopia, but differs from the commonly reported nasal field losses in kittens raised with experimentally induced strabismus.

1 Yerkes Regional Primate Research Center, 2 Departments of Ophthalmology, 3 Anatomy and Cell Biology and 4 Psychology, Emory University, Atlanta, GA 30322, U.S.A.

4 In 3 of our strabismic monkeys that had an eye preference for fixation, we found small deficits in the far temporal visual field (monocular segment) of the non-preferred eye. These results are consistent with some previous findings from kittens raised with experimentally induced strabismus. There have been no studies reported regarding the peripheral extents of the far temporal fields in humans with strabismus. The animal studies predict that some of these patients may have a small deficit.

5 The results of our study, when combined with previous studies of visually deprived animals and humans with amblyopia, show that monocular field deficits can be of graded severity.

Introduction

Normally reared cats, monkeys and humans have similar monocular visual fields that extend from about 45° contralateral (nasal) to about 90-105° ipsilateral (temporal). Each eye's visual field can be subdivided into three separate segments: a monocular temporal segment, a binocular temporal segment, and a binocular nasal segment (see Fig. 1). The binocular segments are so named because they have the potential to form an image in both eyes, whereas the monocular segments cannot form an image in the opposite eye. Most ganglion cells that respond to the temporal segments (nasal retina) cross at the optic chiasm to the opposite side of the brain, whereas most ganglion cells that respond to the nasal segment (temporal retina) remain uncrossed. Previous perimetry studies with animals that had been raised under conditions of visual deprivation have found varying degrees of field loss in each of these three separate segments of the visual field.[3, 5, 8, 18, 23-26, 28] Visual fields have also been studied following experimentally induced strabismus in cats, but to date there have been no reports of visual fields in strabismic monkeys. In cases of surgically induced strabismus in kittens[10, 11, 21] or in kittens raised under optical conditions that simulate a convergent strabismus,[7] the most commonly reported field deficits are in the binocular nasal segment and reduced levels of responding sometimes also extend partially into the binocular temporal segment. An exception is a study by Berman and Murphy in which they did not find any evidence of field loss in the binocular segments in cats with surgically induced esotropia.[2] A field deficit or reduced level of responding is sometimes seen in the far temporal field of the deviated eye of strabismic cats,[10, 21] although it has been suggested that this finding may simply reflect a procedural artifact due to the fact that the eye has a tendency to turn in during testing.[10]

Results of these kinds of animal studies have been used extensively during the past decade to develop models that attempt to explain the underlying mechanisms of human amblyopia.[9, 14, 15, 27] However, the visual field deficits commonly found in

visually deprived animals do not usually occur in humans with mild to moderate amplyopia that is often associated with conditions such as strabismus. Sireteanu and Fronius made perimetry measurements of monocular fields in over 20 human patients suffering from moderate amblyopia and reported that their subjects did not show field losses that resemble those found in any of the deprived cats models.[22] They concluded that models derived from field losses in cats may be directly relevant only to cases of deep amplyopia and not to the more commonly occurring cases of mild strabismic amblyopia. Mehdorn reported the presence of nasal hemianopia in some amblyopic patients, but it only occurred in the relatively rare cases of deep amblyopia.[16]

We have been conducting studies for the past several years on monkeys that have a naturally occurring strabismus and, in some cases, moderate amblyopia.[4, 6, 12, 13] These monkeys provide a potential non human primate model for studying human strabismus. In this report, we present measurements of the horizontal extent of the monocular visual fields of these monkeys. Our purpose was to compare visual fields in these monkeys to results from humans with strabismus and amblyopia, and to results from studies of visually deprived animals.

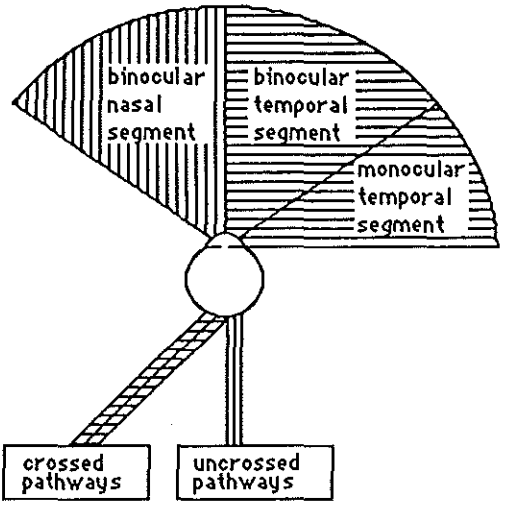


Figure 1 — Illustration of the three major segments of the visual field as represented for a right eye. The monocular temporal segment is from about 45 to 90-105° ipsilaterally and is the segment where the left eye has no respresentation. The binocular temporal segment lies from 0° (straight ahead) to about 45° ipsilateral. Both temporal segments send their axons mostly to the opposite side of the brain. The binocular nasal segment is from 0° to about 45° contralateral and sends its axons to the same or ipsilateral side of the brain, the right side for the right eye.

CHAPTER IV

Materials and methods

Subjects

Nine monkeys (Macaca nemestrina), all of which had a naturally occurring convergent strabismus, and two normal control monkeys (one Macaca nemestrina and one Macaca mulatta) were used as subjects in these experiments. The monkeys with strabismus have a syndrome in which most common features consist of hyperopia, anisometropia, onset of esotropia during infancy, and magnitude of the deviation greater at near than at distance.[6] These monkeys appear to simulate most closely human patients with early onset accommodative esotropia. Table I provides information about the characteristics of each individual test animal, including type and angle of strabismus, age of presentation, refractive errors and preferred eye for fixation.

Based on the clinical characteristics of the strabismus as judged by a cover test performed by an ophthalmologist, our subjects were divided into two groups: alternating esotropes that did not show a clear preference for fixation with either eye (monkeys T79139, T82265, and T82327); and esotropes that had a preferred eye for fixation (monkeys M75038, T81008, F82366, T83124, F84115, and T84151).

Procedures

All procedures were performed in compliance with the ARVO resolution on the Use of Animals in Research. We measured monocular visual fields along the horizontal meridian with a procedure adapted from that described by Sherman for cats and by Sherman and Wilson for dogs.[18, 19] This same procedure has also been used by Wilson et al. in our lab to measure visual fields in monkeys with stimulus deprivation amblyopia and a more complete description of our methods can be found there.[28] During each daily session, the monkey to be tested was placed in a primate restraining chair that a perimetry arc oriented in the horizontal plane attached to the front of it. The perimetry arc obscured the monkey's view of the experimenter's arms and hands. An opaque contact lens was inserted into the nontested eye for monocular testing. The monkey was trained to position its head and eyes in the straight ahead position where a fixation stimulus (a raisin or peanut in a forceps) was presented and then maintain this position for approx. 2 s. After the monkey learned this fixation task, a second visual stimulus (a raisin or a peanut in a forceps, or a black cardboard circle on the end of a stick) was sometimes introduced into the monkey's field of view during the fixation period. This second stimulus could be presented at various positions from behind the perimetry arc at intervals of 11°. Both the fixation stimulus and the second stimulus were presented at a distance of 40 cm in front of the monkey's eye. A positive

response was scored if the monkey moved its eye to the second (novel) stimulus with or without head movement. A miss was scored if the monkey, on presentation of the second stimulus, did not give any response and retained fixation on the fixation stimulus. The monkey was given a food reward following either of these conditions. A miss was also scored if the monkey looked anywhere but at the novel stimulus, but in this case no food reward was given to the monkey.

Blank trials were also included. On a blank trial, the second stimulus was positioned by the experimenter behind the perimetry arc, but was not introduced to the monkey's field of view. If the monkey maintained straight ahead fixation for the entire 2 s the trial was scored as a correct rejection and the monkey was given a food reward; otherwise the trial was scored as a false positive response and no food reward was given. A testing session consisted of a presentation of four or more trials at each test position along with presentation of a similar number of blank trials. At least three test sessions were conducted per eye and the results of these sessions accumulated. Therefore, each data point is based on a minimum of 12 trials.

The validity of this procedure depends upon the ability of the experimenter to make accurate judgements about whether or not the monkey was fixating in the straight ahead position at the time the second stimulus was presented. The ability to make this judgement accurately is especially important when testing strabismic animals in which eccentric fixation might be present. This judgement can be made by placing a penlight on axis with the fixation stimulus and observing the corneal reflections. We illustrate the fact that this judgement can be made with enough accuracy to satisfy the resolution requirements of our procedure (our data were grouped into bins of 11°) by the photographs in Fig. 2. These photos were taken of one of our monkeys while wearing an occluder in one eye and presented with fixation targets straight ahead (a), 10° off center (b), and 20° off center (c).

The majority of the results was obtained by a single experimenter who presented both the fixation target and the eccentric visual stimulus. In some cases this entire procedure was video-taped. In order to rule out cueing on the part of the experimenter, all major findings were confirmed for each monkey in a final session during which the experimenter presented only the fixation stimulus and a second person presented the second stimulus at various positions around the arc. The stimulus trials and blank trials were done in randomized order during this session. In all cases, this final session confirmed the results obtained by the single experimenter.

Table I

Monkey ID[1]	Age of presentation	Type of strabismus at the time of most recent examination[2]	Refractive error in diopters Near age of presentation OD	OS	Recent OD	OS
M75038	5 yr[3]	Accomm. ET up to 35PD OD Preferred	+6.5	+6.0	+1.75	-1.5
T81008	12 weeks	Accomm. LET up to 25PD	+4.0	+4.5	+4.5	+5.5
F82366	5 weeks	30D ET, OS preferred	+4.0	+1.0	+6.75	-2.0
T83124	4 weeks	Accomm. ET up to 20PD OD preferred	+7.5	+6.75	+9.5	+8.0
F84115	6 weeks	Accomm. ET up to 30PD OS preferred	+3.5	+3.5	+8.0	+6.0
T84151	6 weeks	Accomm. RET up to 20PD at near	+4.5	+4.5	+5.0	+4.0
T79139	15 weeks	Orthophoric[4]	+4.0	+2.5	+3.5	+7.0
T82265	5 weeks	14PD alternating ET	+5.0	+3.0	+3.0	+1.0
T82327	12 weeks	Accomm. ET up to 30PD at near	+5.0	+6.5	+2.0	+5.0

1 The first two digits of the monkey ID indicate the year of birth. For example, M75038 was born in 1975.

2 The angle of strabismus is expressed in prism diopters(PD). ET indicates esotropia. If one eye is consistently used for fixation we designate the deviating eye as L or R. For example, LET indicates that the monkey consistently used the right eye for fixation. If the monkey alternates fixation but shows a preference for one of the two eyes, we indicate an OS or OD preference. All of these examinations were performed by a pediatric ophthalmologist at the Ophthalmic Research Building Examination Suite of the Yerkes Regional Primate Center, and were carried out in 1986 or 1987.

3 Monkey M75038 was 5-yr-old when discovered and the age of onset is unknown. In all other monkeys the age of presentation was less than 16 weeks so that the age of onset is known to be within the first 4 months.

4 This monkey now appears orthophoric. We have included her because she had a well documented intermittent alternating ET during early infancy (Kiorpes, unpublished doctoral dissertation, University of Washington, Seattle, 1982).

Results

The results of our perimetry experiments are shown in Fig. 3-5. The abscissa of each figure shows the positions along the perimetry arc (in° of visual angle) at which the novel stimulus was presented. The ordinate in each figure indicates the percentage of positive responses. Thus, each data point indicates the percentage of positive responses for a particular position in the visual field. The overall false positive level is indicated by the horizontal dashed line in each plot. It can be noted from the figures that our monkeys often show a zero response level at several of the more eccentric locations even though they have overall false positive levels in the range 7-16 %. The reason for this is that when animals moved their head and eyes to a non-stimulus location, this was counted as a negative response during a stimulus presentation, but was counted as a false positive for the blank trials. The monkeys rarely ever turned towards the most eccentric positions when responding with a false positive, so the response level to targets presented at eccentric positions dropped towards zero.

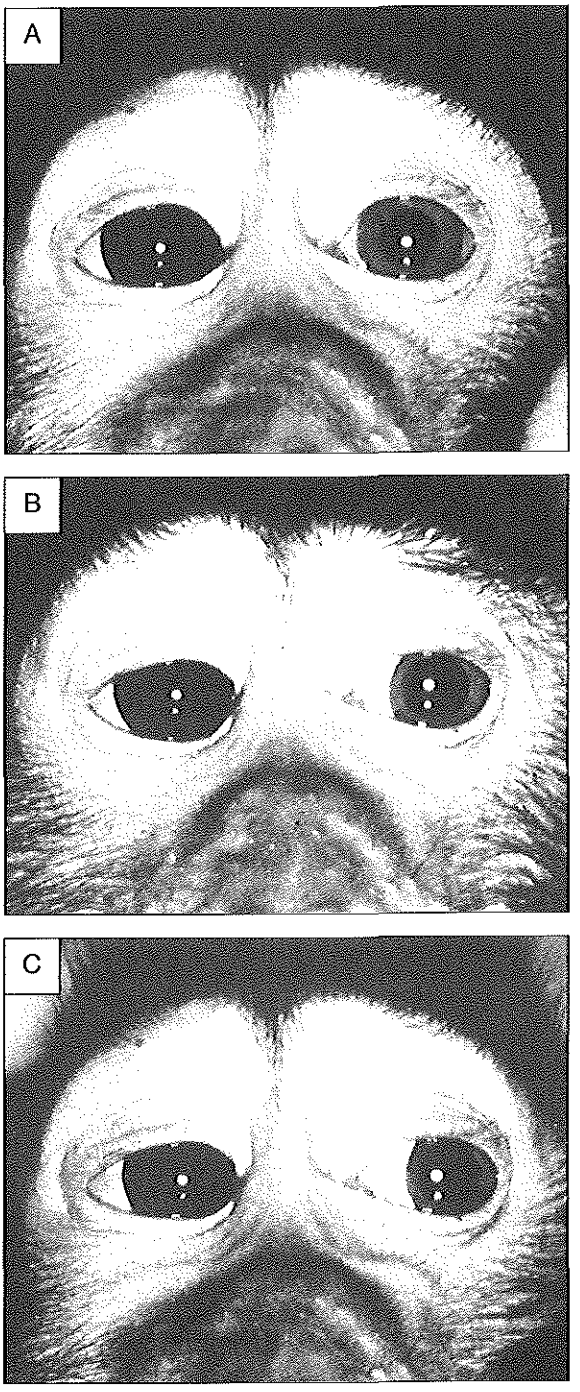


Figure 2 — Photographs of the eyes of one of our monkeys. Right eye is wearing an occluder lens. (a) monkey looking straight ahead. (b) monkey looking at a target 10° off center. (c) monkey looking at a target 20° off center.

Figure 3 shows the results of two normal control monkeys: RKR1 was 1-yr-old and monkey PVH was 5-yr-old. The response levels were usually 100% within the central region of each eye's visual field. The response levels started dropping off as the novel stimulus presentations approached the limits of the visual field on both the nasal and temporal sides. Response levels in our control monkeys remained above the overall false positive level to at least 45° nasally and to at least 90° temporally. In addition, no obvious asymmetries were seen in the rates of fall-off in the nasal segments of the two eyes or in the rates of falloff in the temporal segments from the two eyes. These overall results for our normal controls were similar to those reported by other investigators using comparable techniques[23] and served as a standard of comparison for the results in the strabismic animals.

All three monkeys that exhibited an alternating strabismus with no clear eye preference showed visual fields and response levels in both eyes that were not discernibly different from those of our normal controls (Fig. 4, monkeys T79139, T82265, and T82327). Thus, we conclude that the alternating esotropia in these monkeys had no measurable effect on their visual fields.

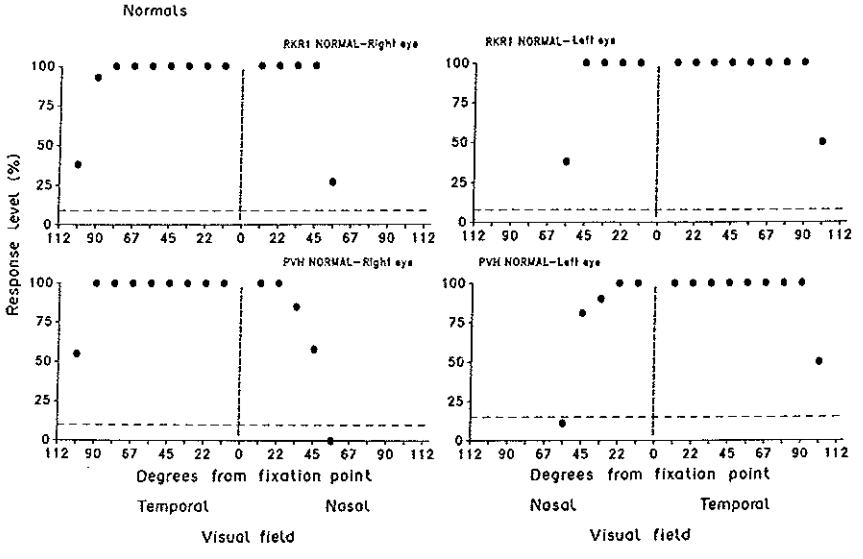


Figure 3 — Plots of the response levels of the eyes of two normally reared monkeys. Each point plotted represents the percentage of positive responses to novel stimuli presented at that position in the visual field. Visual field locations are indicated on the X-axis in° from the fixation point (0°-dashed vertical line) in the temporal or nasal visual fields. Each eye was tested with the fellow eye occluded. The dashed horizontal line gives the overall false-positive response level.

Three of our strabismic monkeys that exhibited a clearly preferred eye for fixation also showed normal visual fields and response levels in both eyes (Fig.5, monkeys T81008,T83124 and F84115). However, three other monkeys from this group (Fig.5, monkeys M75038, F82366, and T84151) showed lower response levels and some field loss near the peripheral extent of the monocular temporal segment of the non-preferred eye. The field loss in these monkeys is small but robust, with the field in the preferred eye consistently extending one or two sectors further than the field in the non-preferred eye. As asymmetry in the response levels from the two eyes can clearly be seen for all three monkeys at all locations in the temporal field beyond about 45°.

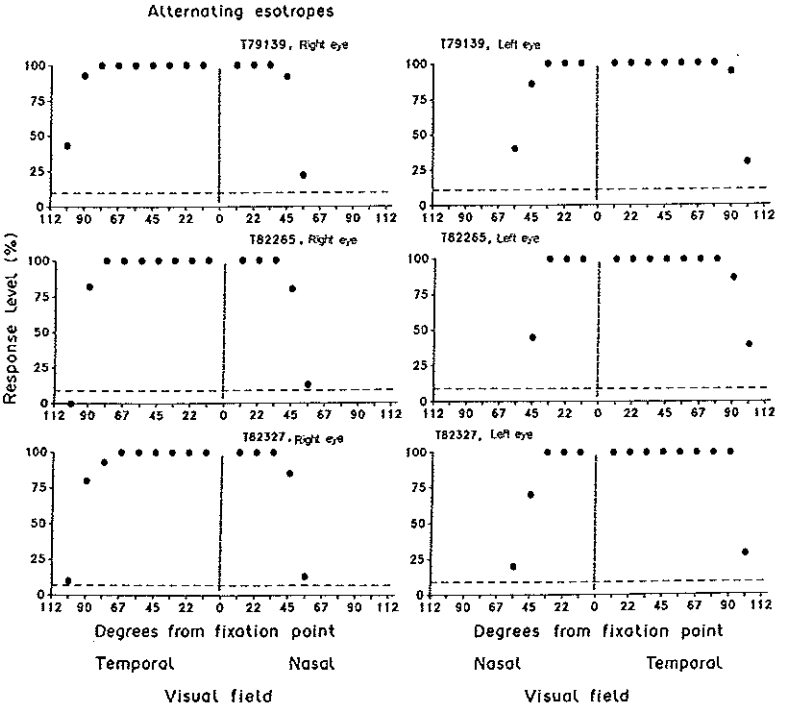
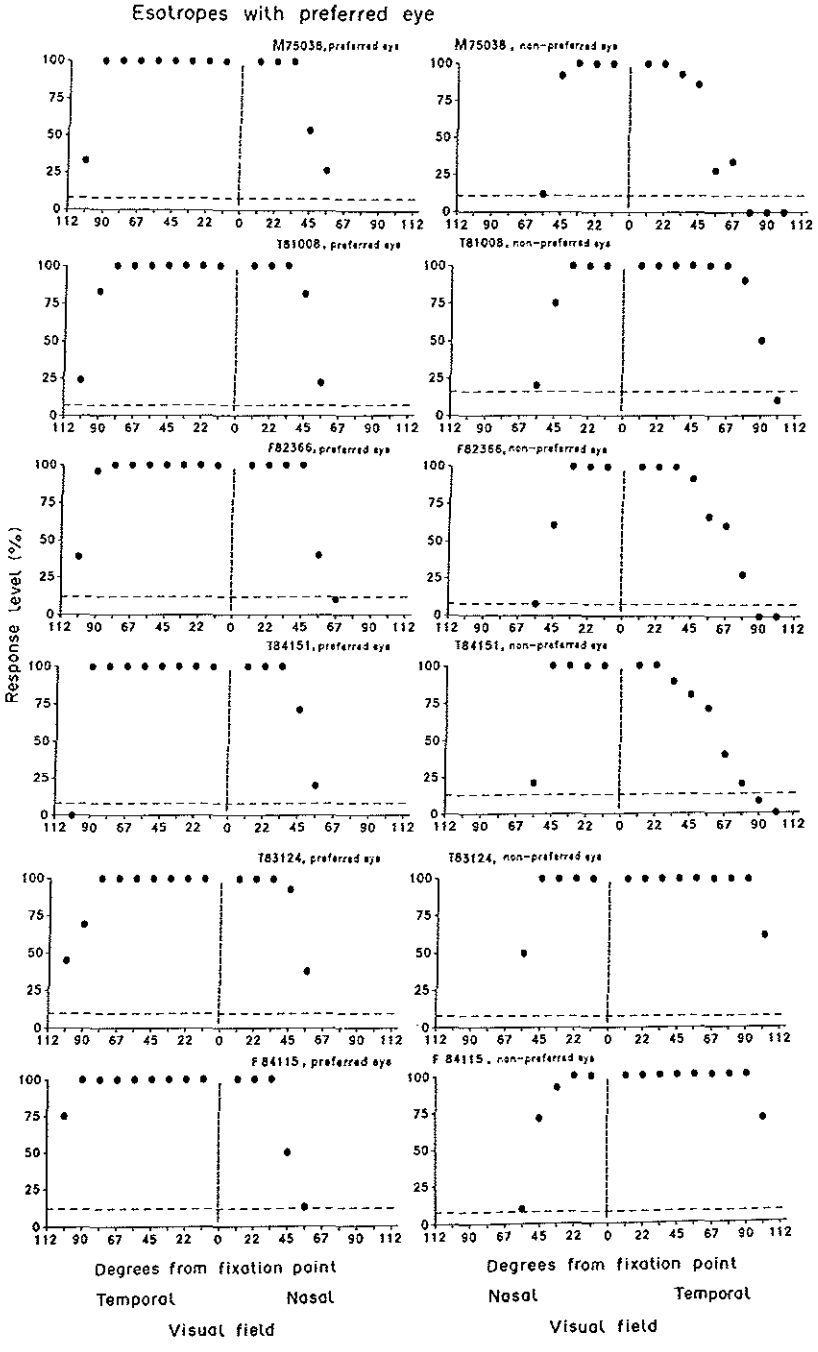


Figure 4 — Response levels of three monkeys with esotropia and alternating fixation between the two eyes. Note that the responses levels and field of views are essentially the same as those of normal monkeys. Other graph representations are the same as Fig. 1.


Esotropes with preferred eye
M75038, preferred eye
M75038 , non-preferred eye
T81008, preferred eye
T81008, non-preferred eye
F82366, preferred eye
F82366, non-preferred eye
T84151, preferred eye
T84151, non-preferred eye
T83124, preferred eye
T83124, non-preferred eye
F 84115 , preferred eye
F 84115 , non-preferred eye
Response Level (%)
100
75
50
25
0
112 90 67 45 22 0 22 45 67 90 112
Degrees from fixation point
Temporal
Nasal
Visual field
Degrees from fixation point
Nasal
Temporal
Visual field

Discussion

None of our strabismic monkeys exhibited the kind of large field losses that have sometimes been reported in the binocular segments of animals reared under conditions of visual deprivation or with experimentally induced strabismus (see Introduction). In this regard, our findings are in agreement with results from humans that have mild strabismic amblyopia.[22] Our monkeys with alternating strabismus and no clear eye preference had normal visual field extents and normal response levels across all segments of the visual field. The only abnormality that we found in any of our animals was that some of our moneys with a clearly preferred eye for fixation showed a small field loss or reduced level of responding in the far temporal periphery of their non-preferred eye's visual field.

The small field deficits that we found in some animals do not appear to be related to the magnitude of the strabismus, current refractive error, or initial refractive error. Correlations between field loss and each of these factors are near zero (r^2=0.3, 0.1 and 0.01 respectively). We speculate that the losses may be related to the visual field expansion that takes place during postnatal development. The visual field expands to its normal adult size during the first postnatal year in humans and during the first 6 postnatal weeks in kittens, but has never been studied in monkeys.[20, 26] The neural basis for postnatal expansion of the visual field is unknown, but several possible mechanisms have recently been discussed.[17] It does not seem unreasonable to speculate that abnormal eye movements during the period when the field is undergoing its expansion, such as might occur under conditions of early onset strabismus, might impair normal development of the visual fields. If this is in fact the mechanism responsable for the deficit, we have no good explanation as to why only some animals are affected. There may be individual differences in susceptibility to field loss, or the field loss may be related to factors such as magnitude and duration of fixation preference during early development.

The deficits that we see in the far temporal periphery are similar in some ways to the visual neglect that is seen contralateral to lesions of various central structures such as the superior colliculus.[1] Our current methods do not allow us to clearly distinguish between a sensory deficit in which the monkeys cannot detect the stimulus, a motor deficit in which the monkeys do not move their eyes into this part of the visual field, or a neglect of this part of the field that is neither strictly a sensory loss nor strictly a motor loss. We rule out a simply acuity loss as the

Figure 5 — Response levels of six monkeys that have an esotropia and a preference for fixation with one eye. Results for the preferred eyes are shown on the left side. Results for the non-preferred eyes are shown on the right side. Other graph representations are the same as Fig. 1.

explanation for three reasons. First, the deficits showed up only at the far periphery and not in the central field of view where strabismic amblyopes would be expected to have an acuity loss. Second, we obtained the same field results whether we used small food stimuli or larger black cardboard targets to elicit responses. Third, the correlation between grating acuity and visual field loss for six eyes on which we have both measures is near zero ($r2=0.1$). Similarly, we can rule out an explanation based on a loss of contrast sensivity because the correlation between peak contrast sensitivity loss and field loss was also near zero ($r2=0.09$).

Asymmetries in extents of the far temporal monocular visual fields have not been previously reported for human strabismic patients, but the magnitude of the field losses that we found in our monkeys were small enough that they would probably not have been previously noted, even if present in human patients. Such losses probably could be detected only by making a careful comparison of the peripheral extents of the far temporal fields in the two eyes of the same patient. The human population that would be most similar to the monkeys which show this deficit would be patients with early onset accommodative strabismus, a clearly preferred eye for fixation, and a mild amblyopia. Future studies with human patients of this type could clarify this issue.

The discrepancy between the results obtained within the binocular segments of our monkeys and those obtained from studies in cats with experimentally induced strabismus[10, 11, 21] might be explained by the fact that naturally occurring early onset accommodative strabismus differs in a number of characteristics from surgically or optically induced strabismus.[15] For example, a surgically induced strabismus immobilizes the eye during the post-surgical period and an optical strabismus results in a constant angle of deviation at all viewing distances rather than just during periods of accommodation, etc. Alternatively, the discrepancy in results could also be due to a species difference. Studies of visual fields in monkeys with experimentally induced strabismus could resolve this issue.

An examination of the results obtained across all of the studies of monocular fields in visually deprived animals and in humans with amblyopia reveals that combinations of field loss in the segments shown in Fig. 1 do not appear to occur randomly, but instead fall into patterns. The pattern of results that is found is consistent with a model that involves a graded effect of deprivation across the three segments of the visual field. With mild deprivation, there are some subjects with no apparent field deficits in any of the three segments. Normal fields can be seen in some cats with surgically induced esotropia,[2] in all three of our monkeys that did not have a preferred eye for fixation, in three of our naturally strabismic monkeys that had a preferred eye, and have also been reported in strabismic human patients that have moderate or no amblyopia.[16, 22]

Deficits that involve only the peripheral extents of the visual field (i.e. deficits in the far monocular temporal segment and/or the binocular nasal segment) have been reported in some cats with form deprivation or experimentally induced strabismus.[2, 7, 10, 11, 26] Deficits confined to the far monocular temporal segment can be seen in some of our naturally strabismic monkeys that have a preferred eye. Mehdorn reported the presence of a nasal hemianopia in some patients with a deep strabismic amblyopia.[16]

In more severe cases, the field losses can extend into the binocular segment, as reported in some cats with form deprivation or experimentally induced strabismus,[18, 21] and in some monkeys with early occlusion.[28] Finally, in the most extreme cases, no responses can be elicited from any of the three segments of the visual field. This condition has been found in some monkeys raised with lid-suture or occlusion.[23, 28]

Humans and monkeys that have a naturally occurring strabismus fall towards the unaffected end of this gradient. For this reason, the large field deficits that are sometimes observed in experimental animals probably have only limited relevance in human strabismic amblyopia.

References

1 Albano J.E., Mishkin M., Westbrook L.E. and Wurtz R.H. (1982) Visuomotor deficits following ablation of monkey superior colliculus. J. Neurophysiol. 48, 338-351.
2 Berman N. and Murphy E. (1981) The critical period for alteration in cortical binocularity resulting from divergent and convergent strabismus. Dev. Brain Res. 2, 181-202.
3 Bisti S. and Carmignoto G. (1986) Monocular deprivation in kittens differently affects crossed and uncrossed visual pathways. Vision Res. 26, 875- 884.
4 Boothe R., Kiorpes L. and Carlson M. (1985) Studies of strabismus and amblyopia in infant monkeys. J. Pediat. Ophthal. Strab. 22, 206 212.
5 Casagrande V.A. and Joseph R. (1980) Morphological effects of monocular deprivation and recovery on the dorsal lateral geniculate nucleus in Galago. J. comp. Neurol. 194, 413- 426.
6 Eggers H.M. and Boothe R.G. (1987) Naturally occurring accomodative esotropia in macaques. Invest. Ophthal. Visual Sci. 28, 103.
7 Elberger A.J., Smith E.L. III and White J.M. (1983) Optically induced results in visual field losses in cats. Brain Res. 26, 147-152.
8 Heitlander H. and Hoffman K.P. (1978) The visual field of monocularly deprived cats after late closure or enucleation of the non-deprived eye. Brain Res. 145, 153-160.
9 Ikeda H. (1979) Physiological basis of amblyopia. Trends Neurosci. 8, 209-213.
10 Ikeda H. and Jacobson S.G. (1977) Nasal field loss in cats reared with convergent squint: behavioral studies. J. Physiol. 270, 367-381.
11 Kalil R.E. (1977) Visual field defects in strabismic cats. Invest. Ophthal. Visual Sci. (Suppl.) 163.
12 Kiorpes L. and Boothe R.G. (1981) Naturally occurring strabismus in monkeys (Macaca Nemestrina). Invest. Ophthal. Visual Sci. 20, 257-263.
13 Kiorpes L., Boothe R., Carlson M. and Alfi D. (1984) Frequency of naturally occurring strabismus in monkeys. J. Pediat. Opthal. Srtab. 22, 60-64.
14 Maurer D., Lewis T. and Brent H. (1990) The effects of deprivation on human development. In Applied Developmental Psychology, Vol. 3, editated by Morrison F.J., Lord C.E. and Keating D.P., in press.

15 Mitchell D. (1988) Animal models of human strabismus and amblyopia: some observations concerning the interpretation of the effects of surgically and optically induced strabismus in cats and monkeys. In Advances in Neural and Behavioral Development, Vol. 3, edited by Shinkman P.G., Ablex Publishing, Norwood, N.J.
16 Mehdorn E. (1985) Nasal hemianopic amblyopia. Invest. Ophthal. Visual Sci. (suppl.) 26, 254.
17 Mohn G. and Van Hof-Van Duin J.(1986) Development of the binocular and monocular visual fields of human infants during the first year of life. Clin. Vision Sci. 1, 51-64.
18 Sherman S.M. (1973) Visual field defects in monocularly and binocularly deprived cats. Brain Res. 49, 25-25.
19 Sherman S.M. and Wilson J.R. (1975) Behavarioral and morphological evidence for binocular competition in the postnatal development of the dog's visual system. J.Comp. Neurol. 161, 183-196.
20 Sireteanu R. and Maurer D. (1982) The development of the kitten's visual field. Brain Res. 22, 1105-1111.
21 Sireteanu R. and Singer W. (1984) Impaired visual responsiveness in both eyes of kittens with unilateral surgically induced strabismus. Invest. Ophthal. Visual Sci. (Suppl.) 26, 216.
22 Sireteanu R. and Fronius M. (1986) Human amblyopia: structure of the visual field. Invest. Ophthal. Visual Sci. (Suppl). 27, 153.
23 Sparks D.L., Mays L.E., Gurski M.R. and Hickey T.L. (1986) Long- and short-term monocular deprivation in the rhesus monkey: effects on visual fields and optokinetic nystagmus. J. Neurosci. 6, 1771-1780.
24 Tieman D.G., Tumosa N. and Tieman S.B. (1983) Behavioral and physiological effects of monocular deprivation: a comparison of rearing with diffusion and occlusion. Brain. Res. 280, 41-50.
25 Tumosa N., Tieman S.B. and Hirsch H.V.B. (1982) Visual field deficits in cats reared with unequal alternating monocular exposure. Exp. Brain Res. 47, 119-129.
26 Van Hof-VanDuin J. (1977) Visual field measurements in moncularly deprived and normal cats. Expl Brain Res. 30, 353-368.
27 Von Noorden G.K. (1985) Amblyopia multidisciplinary approach. Invest. Ophthal. Visual Sci. 26, 1704-1716.
28 Wilson J.R., Lavallee K.A., Joosse M.V., Hendrickson A.E., Boothe R.G. and Harwerth R.S. (1989) Visual fields of monocularly deprived macaque monkeys. Behav. Brain Res. 33, 13-22.

4.2 The monocular visual field in humans with strabismic amblyopia

Introduction

The most striking result of these two field studies in Macaque monkeys with amblyopia is the defect in the far temporal periphery in the eye with early monocular deprivation.[9, 16] In the human literature there have been a small number of studies on the extent of the VF after visual deprivation. Most of these studies were on the effects of strabismic amblyopia on the VF.[1-4, 7, 11, 13, 15] In these studies, there was little emphasis on the far temporal periphery of the visual field. However, Donahue et al. found a reduced sensitivity of the whole temporal half of the visual field as compared with the nasal half in humans with strabismic amblyopia.[3] Unfortunately, they performed static perimetry of only the central 60° of the visual field. Only in 1925 they was a report by Tron of a small field defect in the far temporal periphery in humans with small angle convergent strabismus.[15] He attributed this defect to eccentric fixation. In our monkey studies we found no correlation between the size of the temporal field defects and the amount of eccentric fixation. When present, the size of the temporal field defects exceeded the degree of eccentric fixation.

Patients and Methods

We performed standard Goldmann kinetic perimetry under monocular viewing conditions in 15 patients with convergent strabismus and amblyopia from two ophthalmology departments in the Netherlands (see table). Only patients with amblyopia due to early onset convergent strabismus, including those with consecutive convergent strabismus following surgical undercorrection, were included in the study. Patients had a visual acuity ranging from 0.03 to 0.8 in the amblyopic eye. In all patients at least 4 isopters were measured in both eyes.

Results

Fields of the amblyopic eyes as well as of the normal eyes obtained under monocular viewing conditions extended from 65° nasally to 95° temporally in most cases. In most cases no field defects could be detected in the amblyopic eye. Only in cases 2, 4, 8, 11, 12, 13 and 15 a slight reduction in central sensitivity in the amblyopic eye could be detected. Peripheral constriction of the visual field of the amblyopic eye was found in cases 1, 2, 13 and 14. Nasal shrinkage was found in cases 12 and 15. Temporal shrinkage only occurred in combination with a central reduction in sensitivity in the amblyopic eye of case 13.

Table I — Clinical characteristics of 15 human subjects with convergent strabismus

Case #	age	sex years	eye	refraction	VA	fix.	obj. >	history
1	67	M	R	-2.0	1.0	fovea	10°	L cong.conv.
			L	-2.0	0.6	2°N		surg. at 67 y
2	26	M	R	-0.5 = 3.5 x 125°	0.03	2°N	10°	R cong. conv.
			L	+0.5	1.0	fovea		surg at 18 & 26 y
3	12	F	R	+1.0 = 0.5 x 0°	0.8	fovea	8°	R cong.conv.
			L	+1.5 = 0.5 x 0°	1.0	fovea		surg at 11y
4	53	M	R	+4.0 = 0.5 x 170°	1.0	fovea	2°	prim.L microstrab.
			L	+4.0	0.1	0.5°N		no surg.
5	41	M	R	-4.0	0.25	0.5°N	9°	R cong.conv.
			L	-4.0	0.9	fovea		surg. at 31 & 40 y
6	36	M	R	+0.5	1.0	fovea	3°	prim.L microstrab.
			L	+4.0 = -1.0 x 45°	0.1	1.0°N		no surg.
7	46	F	R	+5.5 = -2.5 x 3°	0.06	1.0°N	10°	R cong.conv.
			L	+4.5 = -1.0 x 0°	1.0	fovea		surg at 13 & 45 y
8	48	F	R	+4.0 = -2.0 x 0°	0.9	fovea	8°	L cong.conv
			L	+3.5 = -2.0 x 0°	0.25	0.2°N		DVD, no surg.
9	76	F	R	-1.0 = -2.0 x 0°	0.9	fovea	3°	prim L microstrab.
			L	+1.5 = -0.5 x 0°	0.04	0.5°N		no surg.
10	14	M	R	-0.75	1.0	fovea	2°	prim. L microstrab.
			L	-1.25	0.6	0.2°N		no surg.
11	43	M	R	+5.0	0.1	5°N	5°	prim R microstrab.
			L	+5.0	1.0	fovea		no surg.
12	65	M	R	+6.0	0.04	12°N	15°	R cong.conv.
			L	+6.0	0.8	fovea		no surg.
13	58	V	R	+4.0 = -2.0 x 90°	0.8	fovea	4°	L cong.conv.
			L	+5.5	0.01	3°N		surg at 21 y
14	71	M	R	+1.5 = -1.0 x 90°	0.1	1°N		R cong.conv.
			L	+1.5	1.0	fovea		no surg.
15	71	M	R	+6.5 = 2.5 x 0°	0.02	12°N		R cong. conv.
			R	+5.0	0.8	fovea		no surg.

VA = visual acuity in percent; obj. > = objective angle of strabismus; M = male, F = female; R = right, L = left; N = nasal; cong. = congenital, conv. = convergent strabismus; surg. = surgery, prim. = primary; microstrab. = microstrabismus (angle < 6°); y = year; DVD = dissociated vertical deviation.

Discussion

We did not detect any field defects in eyes with moderate to severe amblyopia. However we found a slight reduction in central sensitivity in some amblyopic eyes. In some cases we found a slight constriction of the visual field of the amblyopic eye. There was no correlation between the depth of amblyopia and the presence of these slight field abnormalities. Only cases 12 and 15, who had

large angle esotropia with deep amblyopia and extremely excentric fixation (fixation close to or on the optic nerve head, formerly called the blind spot syndrome[14]) had slight nasal constriction of the visual field (respectively 8 and 10° in comparison with the nasal border of the dominant eye). There also was no correlation between the presence of anisometropia and the extent of the field defects.

Our results indicate that binocular competition as found in cats with monocular deprivation does not play a significant role in human strabismic amblyopes. However, it is conceivable that stronger monocular deprivation (eg. congenital cataract, large amount of anisometropia) with subsequently deeper amblyopia might cause field defects like the ones we found in monkeys or those described in cats.[5, 6, 8, 10, 12]

References

1 Bielschowsky, A. (1926). Zur Frage der Amblyopie. Klin. Mbl. Augenheilk. 77: 302-314.
2 Braun, G. (1934). Gesichtsfelduntersuchungen bei Schielenden. Klin. Mbl. Augenheilk. 92, 600-613.
3 Donahue, S.P, Wall, M, Kutzko, K.E., Kardon, R.H. (1999) Automated perimetry in amblyopia: a generalized depression. Am. J. Ophthalmol. 127, 3, 312-321.
4 Duke-Elder, S. (1973). Abnormal ocular motility. Henry Kimpton, London, Volume 6, Chapter 6, pp. 223-317.
5 Elberger A.J., Smith E.L. III and White J.M. (1983) Optically induced results in visual field losses in cats. Brain Res. 26, 147-152.
6 Guillery, R.W. and Stelzner, D. J., The differential effects of unilateral lid closure upon the monocular and binocular segments of the dorsal lateral geniculate nucleus in the rat. J. Comp. Neural., 139 (1970) 413-422.
7 Heine, L. (1905). Uber das zentrale Skotom. Klin. Mbl. Augenheilk. 43,1: 10-40.
8 Ikeda H. and Jacobson S.G. (1977) Nasal field loss in cats reared with convergent squint: behavioral studies. J. Physiol. 270, 367-381.
9 Joosse, M.V., Wilson, J.R., Boothe, R.G. (1990). Monocular visual fields of macaque monkeys with naturally occurring strabismus. Clin. Vision Sci. 5, 2: 101-111.
10 Kalil R.E. (1977) Visual field defects in strabismic cats. Invest. Ophthal. Visual Sci. (Suppl.) 163
11 Mackensen, G. (1959). Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgaenge beim Schielen. v. Graefes Arch. f. Ophthalmol. 160: 573-587.
12 Sireteanu R. and Singer W. (1984) Impaired visual responsiveness in both eyes of kittens with unlateral surgically induced strabismus. Invest. Ophthal. Visual Sci. (Suppl.) 26, 21.
13 Sireteanu R. & Fronius, M. (1990). Human amblyopia: structure of the visual field. Exp. Brain Res. 79: 603-614.
14 Swan, K.C. (1948). The blind-spot syndrome. Arch. Ophthalmol. 40: 371.
15 Tron (1925). Ueber einige Eigentuemlichkeiten des Sehens der Schielenden. Klin. Mbl. Augenheilk.75: 109-118.
16 Wilson, J.R., Lavallee, K.A., Joosse, M.V., Hendrickson, A.E., Boothe , R.G., Harwerth, R.S. (1989). Visual fields of monocularly deprived macaque monkeys. Behav. Brain Res. 33: 13-22.

Quantitative perimetry under binocular viewing conditions in microstrabismus

chapter V

M.V. Joosse,[1] H.J. Simonsz,[1] H.M. van Minderhout,[1] P.T.V.M. de Jong,[2,3] B. Noordzij[1] and P.G.H. Mulder[3]

Vision Res. (1997) 37, 19: 2801-2812

Abstract

In order to elucidate the type, size and depth of suppression scotomata in microstrabismus and small angle convergent strabismus, we performed binocular static perimetry in fourteen subjects with strabismus and four normal observers. The strabismic cases had an objective angle of convergent squint between 1° and 8°, visual acuity between 0.1 and 1.25, and limited stereopsis. During testing the subjects fused pictures on two Friedmann visual field analyzers. Right and left eyes were studied separately under both monocular and binocular viewing conditions.

In five strabismics a suppression scotoma was found in the squinting eye, with a diameter of 5° to 30° and a depth ranging from 4 to 14 dB. No suppression scotomata could be detected in the nine other subjects or in the four normal observers. In conclusion, only 36 percent of subjects with strabismus were found to have a suppression scotoma. These scotomata were centered around the fixation point of the squinting eye, in some cases also encompassing the foveal area, and varying in depth and size.

1 Department of Ophthalmology, University Clinic Dijkzigt, Rotterdam.
2 The Netherlands Ophthalmic Research Institute, Department of Ophthalmology, Academic Medical Center, Amsterdam.
3 Department of Epidemiology and Biostatistics, Erasmus University Rotterdam, The Netherlands.

CHAPTER V

Introduction

It is still not exactly known how strabismic patients perceive the surrounding world. They may suffer from diplopia, confusion, or both. Diplopia is the subjective perception of two identical images next to each other, that arises when an image is projected simultaneously on the fovea of the fixating eye and on an eccentric point of the retina of the squinting eye. The eccentric point in the squinting eye onto which the foveal image of the fixating eye projects under binocular viewing conditions will be called its fixation point. This eccentric location of the fixation point occurs solely under binocular viewing conditions and should not be confused with eccentric fixation, that is seen strictly under monocular viewing conditions in an amblyopic eye. Confusion is the subjective perception that arises when different images are presented to the fovea of the fixating eye and the fovea of the deviating eye. However, it is commonly agreed that patients with early-onset convergent strabismus do not suffer from diplopia or confusion because of two compensatory mechanisms: suppression and anomalous retinal correspondence (ARC). Suppression of the image of the strabismic eye occurs in the form of a suppression scotoma under binocular viewing conditions exclusively. This scotoma is mainly located in the central part of the visual field of the strabismic eye.[7]

Anomalous retinal correspondence (ARC) is the cortical adjustment in directional values supplied by the retinal elements in strabismic eyes. It permits fusion of similar images projected onto non-corresponding retinal areas by object points peripheral to the area of conscious regard.[16] Functionally, ARC can be described as an internal compensation mechanism for external (ocular) squint. Recent work by Sireteanu and Fronius confirmed the clinical observation that in comitant strabismus ARC is present in the peripheral visual field, whereas the central visual field is more likely to show suppression.[22]

Two types of suppression scotomata have been described: a central scotoma and a fixation-point scotoma. A central scotoma is characterized by the fact that the fovea of the squinting eye is the center of the scotoma, while a fixation-point scotoma is centered around the fixation point of the squinting eye. Both scotomata solely occur under binocular viewing conditions and disappear under monocular viewing conditions.

The first report on suppression scotomata in strabismus was performed by Bielschowsky in 1900, who used dissociation by mirrors. He found that the central part of the visual field was predominantly perceived by the fixating eye.[5] Travers found an absolute, circularly shaped fixation-point scotoma in the squinting eye of esotropes.[23]

Harms was the first to use dissociation with red and green glasses for the measurement of suppression scotomata. He found a large fixation-point scotoma and a smaller central scotoma in a group of esotropes with an angle of squint larger than 6° [7] In small angle (< 6°) esotropes he did not find suppression. Using a synoptophore, Lang found scotomata of varying size around the fixation point in the deviating eye of microstrabismic patients.[13] In 1981, Sireteanu and Fronius showed with red-green perimetry in esotropes, that there was suppression of the area that extended from the central to the nasal retina.[22] In 1982, Sireteanu found that esotropes with alternating fixation had temporary suppression in the region centered around the fixation point of the squinting eye.[21] However, depth perception was intact in the far periphery of the binocularly perceived part of the visual field. Mackensen and Pratt-Johnson measured suppression in esotropes using polarizing filters.[14, 17] Where Mackensen found both a fixation-point scotoma and a central scotoma in the squinting eye,[14] Pratt-Johnson found a less well-defined large area of suppression in the non-fixating eye.[17]

Herzau compared various methods of binocular perimetry for the measurement of suppression scotomata. He found a difference in size of the scotomata between the different methods of dissociation between the eyes.8 Also reproducibility varied greatly between methods. With all methods a fixation-point scotoma could be found in patients with esotropia. Herzau[8] and Schuy[19] performed the only quantitative measurements of depth of suppression with a method of profile perimetry using phase difference haploscopy. With this device dissociation is achieved with propellers rotating in a different phase for each eye.[1]

The aim of this paper is to address the following questions. Do microstrabismic and small angle esotropic patients have a suppression scotoma under natural viewing conditions and if so, what are the size and depth and nature of this scotoma? Is it a central scotoma, a fixation-point scotoma or is it a combination of both?

Subjects and Methods

The characteristics of 14 subjects with micro- and small angle convergent strabismus (mean age 26 years), as well as of four normal observers are given in Table 1. All subjects had a standard ophthalmic exam including measurement of best-corrected Snellen visual acuity, slit-lamp examination and indirect fundus examination after pupillary dilatation. The standard orthoptic examination consisted of: cover test, 15 and 4 diopter prism test, measurement of subjective and objective angle of deviation with the synoptophore and prism-cover test at 40 cm and at 6 m, testing of stereopsis with the Titmus fly test and TNO random dot stereopsis tests, Bagolini striated glass test 58 and determination of fixation with

Table I — Table 1. Baseline data on 14 subjects with small angle convergent strabismus and four control subjects

Case #	age years	sex	eye	VA	refraction	fixation	squint type
Case 1	32	M	R	0.8	-0.75 = -2x160	fovea	esotropia L
			L	0.1	-2.0	2°nas	
Case 2	26	M	R	1.25	+2.5 = -1.0x180	fovea	esotropia R
			L	1.25	+2.0	fovea	
Case 3	33	M	R	0.32	+4.0 = +1.5x70	1°nas	microstr. R
			L	1.0	plano	fovea	
Case 4	27	F	R	1.25	plano	fovea	microstr. R
			L	1.0	plano	0.2°nas	
Case 5	26	M	R	1.0	plano	fovea	microstr. R
			L	1.0	plano	fovea	
Case 6	43	M	R	1.25	-4.5	fovea	esotropia L
			L	0.4	-5.0	0.5°nas	
Case 7	36	M	R	0.4	+7.5 = -1.5x180	0.5°nas	microstr. R
			L	1.25	+4.5	fovea	
Case 8	24	M	R	1.6	plano	fovea	esotropia L
			L	1.0	plano	0.2°nas	
Case 9	41	F	R	1.0	+5.0	fovea	microstr. R
			L	1.25	+5.0	fovea	
Case 10	12	M	R	1.25	+2.25	fovea	microstr. L
			L	1.25	+3= -0.5x180	fovea	
Case 11	12	F	R	1.0	plano	fovea	microstr. L
			L	0.5	+3.0	0.5°sup	
Case 12	12	F	R	1.25	plano	fovea	microstr. L
			L	0.4	+2.0	0.5°sup	
Case 13	15	F	R	0.8	plano	fovea	microstr. R
			L	1.0	plano	fovea	
Case 14	17	F	R	1.0	-1.0	fovea	microstr. L
			L	1.0	-1.0	fovea	
Control 1	32	F	R	1.0	-2.0	fovea	orthotropic
			L	1.0	-2.0	fovea	
Control 2	32	M	R	1.2	-0.5	fovea	orthotropic
			L	1.2	plano	fovea	
Control 3	31	M	R	1.0	plano	fovea	orthotropic
			L	1.0	plano	fovea	
Control 4	32	F	R	1.0	plano	fovea	orthotropic
			L	1.0	plano	fovea	

Table 1. M = male, F= female. R = right eye, L = left eye. VA = visual acuity, Bagolini = Bagolini striated glasses test. Stereopsis = Titmus fly test. Angle obj./subj. = objective and subjective angle of squint as measured with the synoptophore. Strab.=strabismus. Conv.=convergent. Acc.=accommodative. Occl.=occlusion

Bagolini	Stereopsis Titmus fly	obj. / subj. squint	angle	diagnosis / history
tot.supp.L	neg.	6°	0°10°	conv.strab.surgery at 3 failed occl. ther.
	pos.	8°	5°	acc.conv.strab. occl. and glasses at 3
part.supp.R	pos.	4°	4°	prim.microstrab, no occl., sec. div., surgery at 32
centr.supp.R	pos.	4°	4°	prim.microstrab. no occl.
centr.sup..R	pos.	4°	4°	conv.strab.surgery at 4 occl. at 3
centr.supp.L	pos.	6°	6	prim.conv.strab., no occl.ther., glasses at 4
part.supp.R	neg.	4	<1°	conv.strab.surgery at 4 failed occl. ther.
centr.supp.L	neg	8°	6°	prim.conv.strab. occl. at 3
centr.supp.R	pos.	5°	<1°	acc.conv.strab. occl. and glasses at 3
centr.supp.L	pos.	2°	<1°	acc.conv.strab. occl. and glasses at 3
centr.supp.L	pos.	1°	1°	prim.microstrab. glasses at 11
centr.supp.L	pos.	1°	<1°	prim.microstrab. glasses at 11
centr.supp.R	pos.	1°	<1°	prim.microstrab. no occl. ther.
centr.supp.L	pos.	1°	<1	prim.microstrab. occl. and glasses at 4
	pos			
	pos.			
	pos.			
	pos.			

direct fundus examination (Cueppers visuscopy). Ten subjects (cases 3-5, 7 and 9-14) had microstrabismus according to Lang's definition,[12] i.e. convergent squint with an objective angle of squint of less than five degrees and ARC. Four subjects (cases 1, 2, 6 and 8) had a slightly larger angle of convergent squint (up to 8 degrees). All subjects had either suppression of the central part of the streaks or partial suppression of the streaks in the squinting eye with Bagolini's striated glasses; suppression of the central part of the streaks on the Bagolini glasses corresponds with a fixation point scotoma. All subjects had reduced stereopsis, and in all the random dot test was negative. In 11 cases only the Titmus fly stereopsis test was positive. In three cases no stereopsis could be found with standard stereoscopic tests. Four cases had an anisometropia of two or more diopters of spherical equivalent. Subjects 11 and 12 were homozygous twins (Note: no DNA tests were performed) and cases 13 and 14 sisters. All subjects or their legal representatives gave their informed consent to participate in the study. The parents of subjects under 18 years of age were in the room during the whole test procedure.

Four normal control observers, between 30 and 32 years, were tested once for each eye under monocular as well as under binocular viewing conditions. Normal observer number one was tested three times on separate days, to determine the reliability of our test results. In this person we performed an analysis of variance with random effects.

Two Friedmann visual field analyzers, designed for static perimetry of the central visual field, each operated by one investigator, were used. Normally, with the Friedmann visual field analyzer two, three or four simultaneous light stimuli can be presented in various patterns (line, triangle or square) to the subject on a black screen, while the subject looks at the central fixation point. During perimetry the subject is asked, after presentation of each stimulus pattern, which flash lights he has seen. The examiner plots these points on a standard form.

For our experiment the black surface of the two field analyzers was modified by mounting identical pictures (penguins in a polar landscape), with a blue fixation dot in the center on the black screen, leaving the original holes in the screens open. The field analyzers were placed facing each other at a distance of 90 cm, with two surface-silvered mirrors halfway in between them. These mirrors were positioned at an angle of approximately 45° toward the Friedmann screens and angled approximately 90° relative to each other with their edges joining in front of the subject. The subject sat with her/his head in a chin rest with the frontal plane parallel to the imaginary line connecting the centers of the Friedmann field analyzers (Fig. 1). During testing the subjects wore their full spectacle correction in spherical equivalent, with reading addition according to age for subjects 7 and 10, who were above forty years of age.

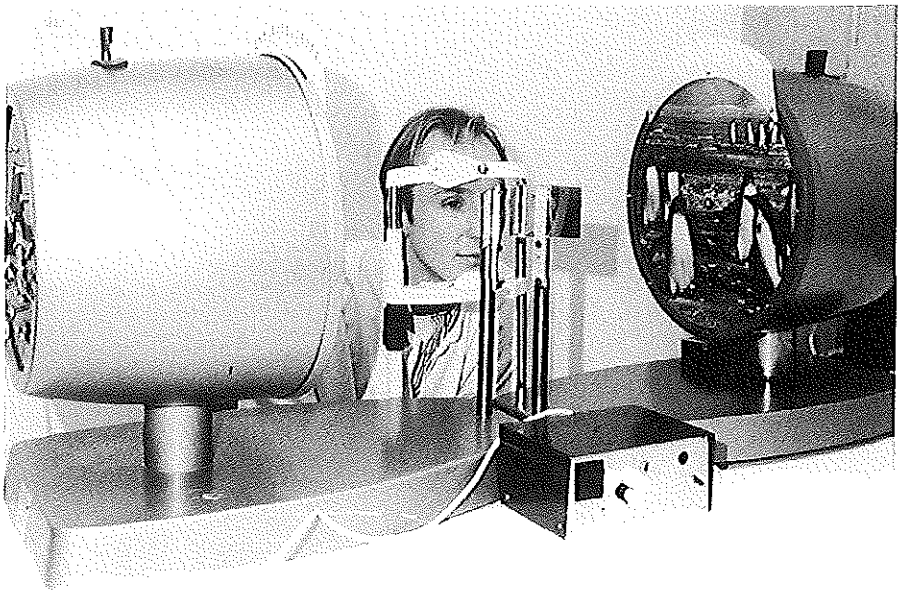


Figure 1 — Picture of the test set-up consisting of two Friedmann visual field analyzers opposite each other, with identical pictures of penguins in the snow on their surface. The subject's head is positioned in the middle of the field analyzers. Via two mirrors angled at 45° the subject can fuse the two screens.

The test person was asked to adjust the mirrors horizontally and vertically so that the images of both perimeter surfaces were fused, i.e. that the subjective angle of squint was compensated and single vision was obtained. Note, that the images were fused mainly in the periphery. The circular screen covered by the pictures subtended 50° of arc. However, only a square of 25° by 25° in the center of the field analyzers could be seen due to the size and placement of the mirrors (Fig. 2). On monocular cover-testing of the non-strabismic eye, a movement of the deviating eye occurred that approximately equaled the angle of ARC. During testing under binocular viewing conditions, the orthoptist regularly performed unilateral cover testing to check if the angle of strabismus remained constant throughout the session.

We substituted the flashlight in the Friedmann field analyzers by a halogen light, because a flashlight presented suddenly to an eye tends to shift attention to this eye and thus will break suppression. Voltage over the halogen light was switched on for a standardized period of 0.3 s., leading to a gradual increase and decrease of luminance lasting both for approximately 0.3 s. (Fig. 3).

Time between light presentations was at least 3 s. The room lights were lowered so that the mean luminance of the screens was 5 apostilbs. A standard test session

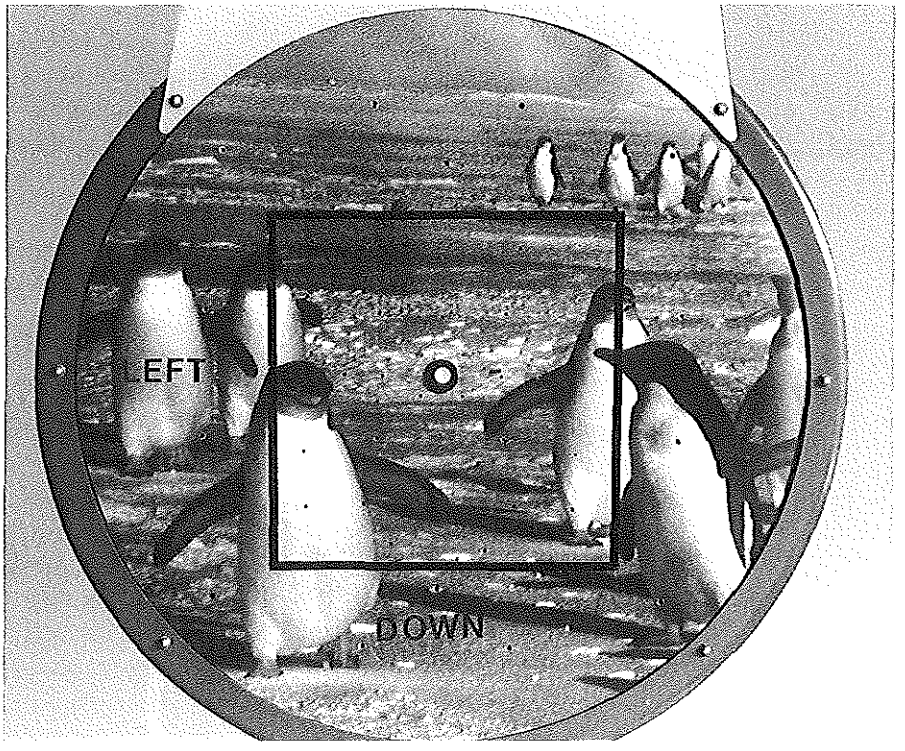


Figure 2 — Picture of one of the test screens, with a black square drawn on the picture to indicate the square of the visual field of 25° vertically by 20° horizontally, as shown in Figs. 4 to 9. In a left eye the label 'Left' indicates the temporal side of the visual field and in a right eye the nasal side of the visual field. In Figs. 4 to 9 this left side is indicated on the y-axis. 'Down' indicates the bottom of the visual field and is shown in figs. 4 to 9 on the x-axis.

would start with testing each eye monocularly. During monocular testing the subject was asked to look with one eye via the homolateral mirror at the corresponding Friedmann screen while the other eye was occluded with a white, non-translucent eye patch. This procedure was performed for both eyes separately. Testing was always begun at the lowest luminance level with a 22 dB filter, an average 4 dB below the central threshold, presenting the central stimuli first, followed by the more peripheral stimuli. Stimulus luminance was increased by steps of 2 dB. Stimuli were presented for three times at most, or less when seen. The final test run was performed with both eyes open with stimuli presented either to the right or to the left eye, while the subject fused both polar landscapes. Again stimuli were presented three times at most for every stimulus position at each luminance level. During this binocular test-run it was difficult for the subject to know to which eye stimuli were presented since binocular single vision of the

surface pictures was maintained. As handling the perimeters was audible, the operators would make clear and audible adjustments to both perimeters simultaneously, whereas actually stimuli were only presented to one eye at a time.

We determined the net suppression in the deviating eye by subtracting the results under binocular viewing conditions from those obtained under monocular viewing conditions. However, this procedure is slightly flawed as during monocular viewing conditions the fovea of the squinting eye fixates the center of the screen, whereas under binocular viewing conditions it is slightly off center, because there is peripheral fusion. In an attempt to make a somewhat valid subtraction we adjusted for the shift in projection of the visual axis between the two viewing conditions by shifting the field results obtained under binocular viewing conditions in a temporal direction by the amount of degrees of the objective squint angle minus the angle of eccentric fixation. Since our field resolution was about 2.5°, we subtracted only those points that were within 1.25° of each other. If by the shift a column of data points would fall outside the tested field by more than 1.25° we would take the sensitivity level of the nearest available data point.

Results

In our four control subjects we found that sensitivity levels for testing under both monocular and binocular viewing conditions ranged between 16 and 20 dB on average. The difference between the results during binocular and monocular viewing conditions was no greater than 2 dB in this control group and thus there was no detectable pattern of suppression in these cases. In the control subject that was tested three times we performed an analysis of variance with random

Figure 3 — Oscilloscopic record of luminance level of a standard stimulus as produced by the halogen light in the perimeters. Horizontal axis: units of 100 ms. Vertical axis: arbitrary luminance units.

effects. We found an average variance of 1.39 for each field position for each viewing condition for each eye leading to an average variance in difference between monocular and binocular viewing conditions for each eye of 2 x 1.39 = 2.78. Averaging across 32 field positions led to a variance in difference between monocular and binocular viewing conditions of 2 x 1.39 / 32 = 0.087 (standard deviation 0.3). Per field position, per eye the variance of the difference between monocular and binocular testing was 2.78. The standard deviation (s.d.) was $\sqrt{2.78} = 1.67$. We considered a difference to be significant if it was larger than 2 s.d. in absolute sense, meaning larger than 2 x 1.67 = 3.34, which, in our device with steps of 2 dB, is a difference of 4 dB or more per field position. Thus we defined an area of suppression as a cluster of points in the visual field where the difference between sensitivity measured under binocular viewing conditions and monocular viewing conditions was 4 dB or more.

In five subjects (subjects 1, 5, 7, 10 and 14) we found, during testing under binocular viewing conditions, a circularly shaped suppression scotoma centered around the fixation point, the foveal projection of the fixating eye in the deviating eye. The test results of these five subjects are summarized in Table 2. The relative depths of these scotomata ranged from 4 to 14 dB, and their radii varied from 2.5 to 15 degrees. In one subject (subject 5) we did not find a suppression scotoma in the deviating eye, but to our amazement we found a scotoma around the fixation point (fovea) of the fixating eye. In the nine other subjects (subjects 2, 3, 4, 6, 8, 9, 11, 12 and 13) we did not find a suppression scotoma. The monocular visual fields of all cases were normal. We will give more detailed information on subjects 1, 5, 7, 10, 11, 12, 13 and 14 below.

In subject 1 we found a deep, small circularly shaped scotoma around the fixation point of the left eye under binocular viewing conditions (Fig 4). Depth was 14 dB and the radius of the deep central part of the scotoma was 2°. Please note that the fovea of the left eye was projected 6° nasally to the centre of the scotoma (fixation point).

Table II

Case #	squint eye	scotoma under binocular viewing conditions				foveal projection	remarks
		eye	*radius*	*depth*	*type*		
Case 1	L	L	2°	14 dB	fix.p.	L 6° N	
Case 5	R	L	5°	4 dB	fix.p.	L 4° N	strabismus R
Case 7	R	R	7.5°	6 dB	comb.	R 4° N	
Case 10	L	L	5°	4 dB	fix.p.	L 2° N	
Case 14	L	L	>25°	4 dB	comb.	L 1° N	

R = right eye, L = left eye. N = nasal. dB = decibel. fix.p. = fixation-point scotoma, comb. = combination of fixation-point and central scotoma.

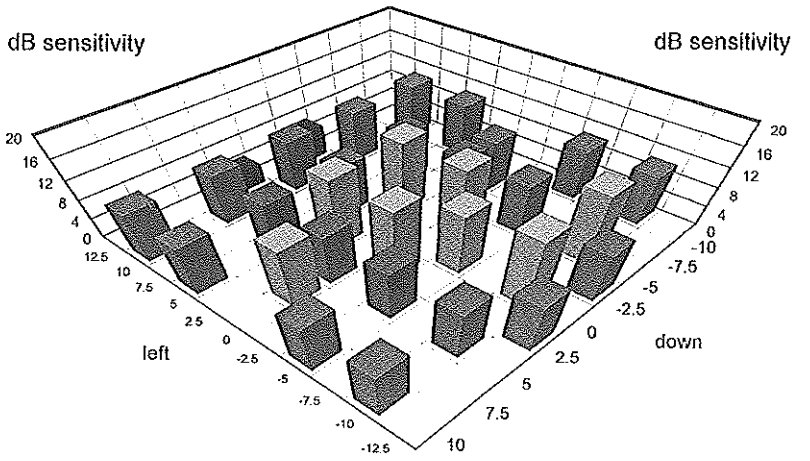


Figure 4a — Case 1. Central 25 by 20 degrees of visual field of squinting left eye under monocular viewing conditions. The z-axis indicates the sensitivity level in decibels.The height of each bar indicates the sensitivity-level for each different stimulus position on the Friedmann visual field analyzer. Here central sensitivity is 18 dB. Sensitivity ranges from 4 to 20 dB. The bars become darker with decreasing sensitivity. Left indicates the temporal side of the visual field of this eye and down indicates down in the visual field.The units for the horizontal (x) axis and vertical (y) axis are degrees from the fixation point.

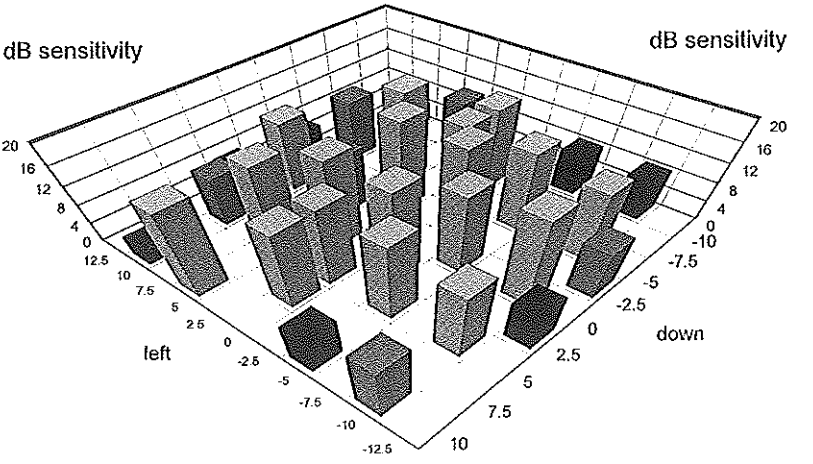


Figure 4b — Case 1. Visual field of non-strabismic right eye under monocular viewing conditions. Left indicates here the nasal side of the visual field. Sensitivity ranges from 4 to 18 dB. Central sensitivity is 18 dB.

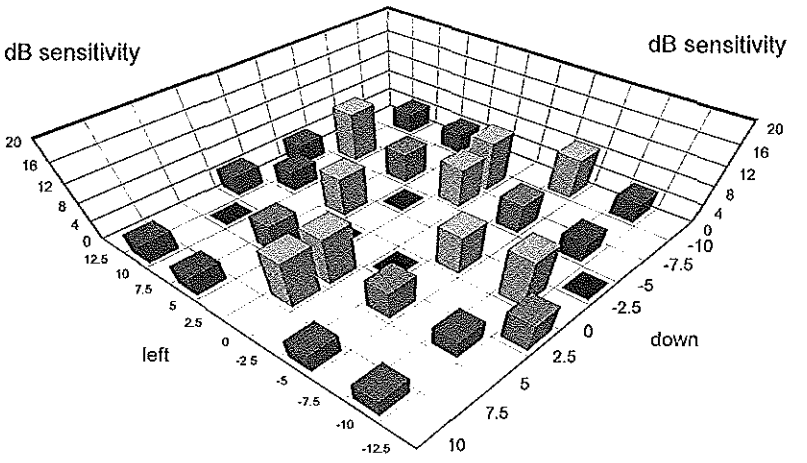


Figure 4c — Case 1. Visual field of squinting left eye under binocular viewing conditions. Sensitivity ranges here from 0 to 10 dB. Central sensitivity is 0 dB. Note that the fovea is located 6° nasally to the centre of the field. The fovea of the squinting eye is shifted nasally under binocular viewing conditions because under these conditions (peripheral) fusion on the basis of ARC occurs and thus the fixation point becomes the centre of the visual field of the squinting eye.

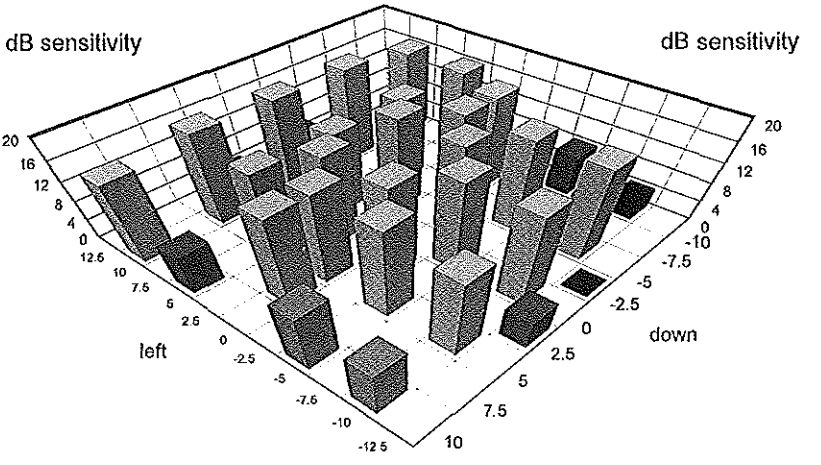


Figure 4d — Case 1. Visual field of right eye under binocular viewing conditions. Sensitiviy ranges here from 0 to 18 dB. Central sensitivity is 18dB.

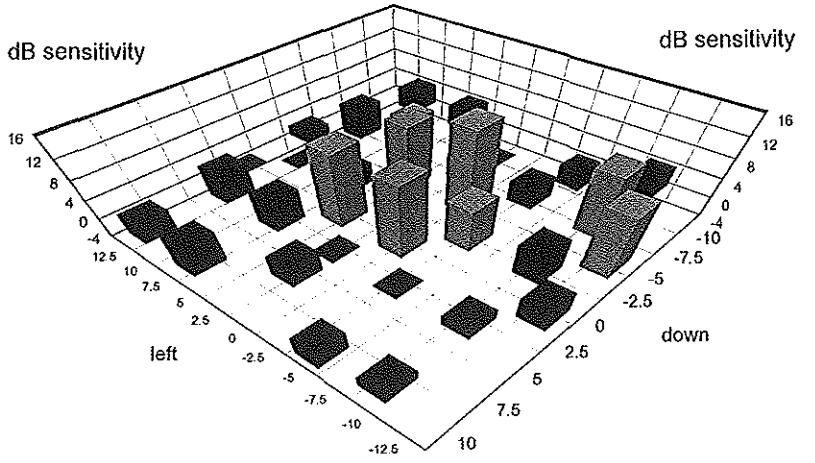


Figure 4e — Case 1. Result of subtraction of the visual field of left eye under binocular viewing conditions from the field under monocular viewing conditions. (ie.'net' suppression). We ask the reader to place an imaginary horizontal zero dB plane in the graph when reading the subtraction figures. This zero plane was necessary because some outcomes of the subtraction of the binocularly obtained results from the monocularly obtained results had a negative value on the z-axis. Note: the more positive the bar, the greater the depth of suppression. The gray bars represent the values greater than 4 dB, ie. the significant (> 4 dB) net suppression (standing bars). The black bars represent the values under 4 dB (either hanging or standingbars). Suppression here reaches to 14 dB in the centre of the field. Also note that the fovea here again is located 6° nasally (right) to the centre of the scotoma or the field. To make this subtraction we shifted the results under binocular viewing conditions 4° temporally (ie. objective angle of squint (6°) minus angle of eccentric fixation (2°)).

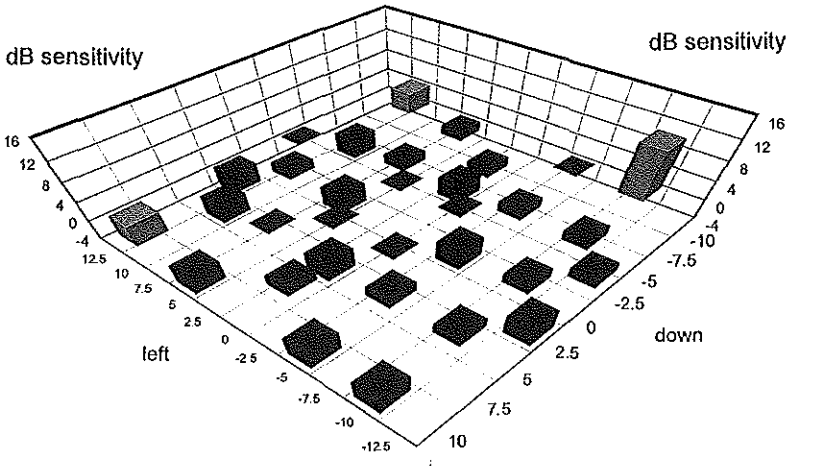


Figure 4f — Case 1. Result of subtraction of the visual field of the right eye obtained under binocular viewing conditions from the field obtained under monocular viewing conditions.

Subject 5 had a 4° microstrabismus of the right eye. Surprisingly we found a circularly shaped fixation point scotoma for the left eye with a depth of 4 dB and radius of 5° (Fig. 5). In subject 7 we found a circularly shaped fixation point scotoma with an average depth of 6 dB and a radius of 7.5° in the right eye under binocular test conditions. The fovea of the right eye was positioned 5° nasally to the centre of the scotoma (Fig. 6). Subject 10 showed a circularly shaped fixation point scotoma with a central depth of 4 dB and a radius of 5° in the left eye under binocular test conditions (Fig. 7).

In subjects 2, 3,4, 6, 8, 9 and 12 there was no significant indication for the existence of a suppression scotoma or any other pattern of suppression.

In subject 11, homozygotous twin sister of subject 12, we found a slight and not significant, overall reduction of sensitivity of 2 dB on average in the left eye under binocular viewing conditions. Subject 13 also showed a not significant overall reduction of sensitivity of 2 dB on average, in the squinting eye under binocular conditions. In the left eye of subject 14 we found an overall reduction of sensitivity, 4 dB on average, under binocular conditions (Fig. 8).

Discussion

In this study we detected a suppression scotoma, centered around the fixation point of the squinting eye in five out of 14 subjects with microstrabismus and small-angle strabismus. In three of these cases we could find only a fixation-point scotoma under binocular viewing conditions. However, in two subjects (subjects 7 and 14) the scotoma was large enough to include both the fixation point as well as the fovea of the squinting eye. Here an overlapping central scotoma and fixation-point scotoma might be present. Thus our results indicate that microstrabismic subjects or subjects with small angle esotropia do not necessarily have two spatially separated scotomas.

In order to measure suppression at its full extent it is important that the eyes look at identical images. This has also been stated by Jampolski[10] and Schor.[18] However, most methods of binocular perimetry have in common that somewhat different images are simultaneously presented to each eye. Examples of these are: coloured filters,[7, 21-23] polarisation filters,[14, 17] phase difference haploscopy,[1, 19] and Bagolini's striated glasses.[2, 3] Bagolini,[3] Herzau,[8] Campos[6] and Mehdorn[15] have compared these methods of binocular perimetry. They all agree that the more dissimilarity between the images, the less suppression will be found. Pratt-Johnson stated that when suppression is measured with more realistic complex patterned stimuli, such as drawings or pictures, a much greater likelihood exists of finding suppression in its full extent.[17]

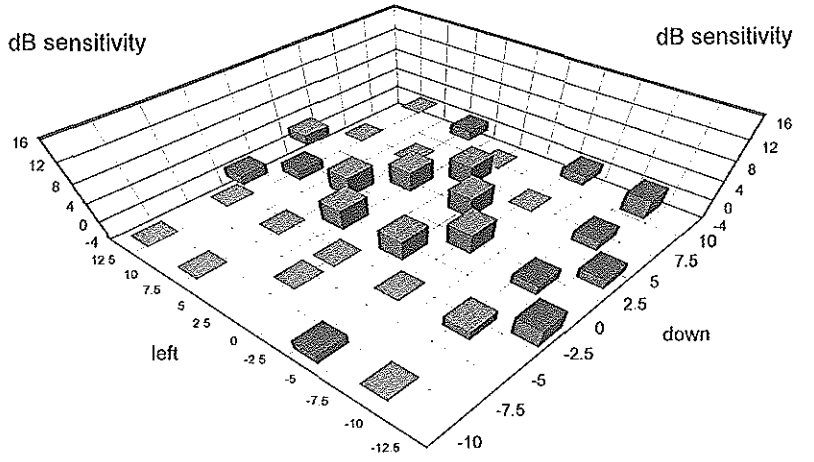


Figure 5 — Case 5. Subtraction of fields of the left non-strabismic eye. A suppression scotoma of 4 dB is shown. The fovea is located 4° nasally (right) to the centre of the field. For the subtraction the results under binocular viewing were shifted 4° temporally.

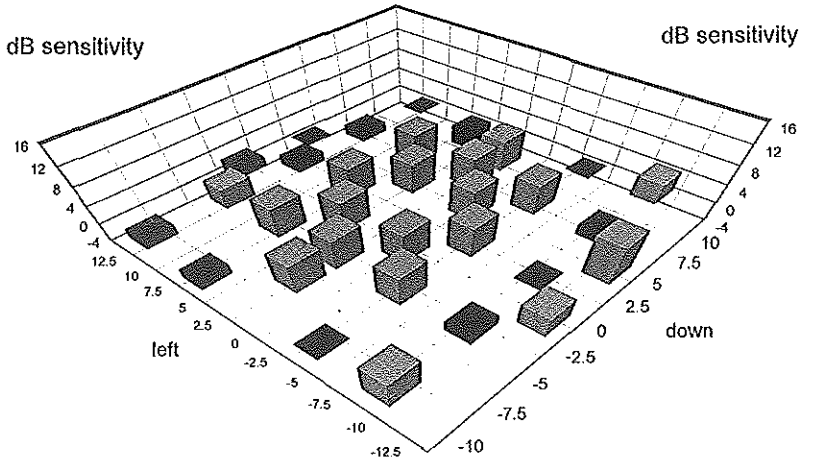


Figure 6 — Case 7. Subtraction of fields of right microstrabismic eye. Fovea is located 4° nasally (left) to the centre of the field. For the subtraction the results under binocular viewing were shifted 3.5° temporally.

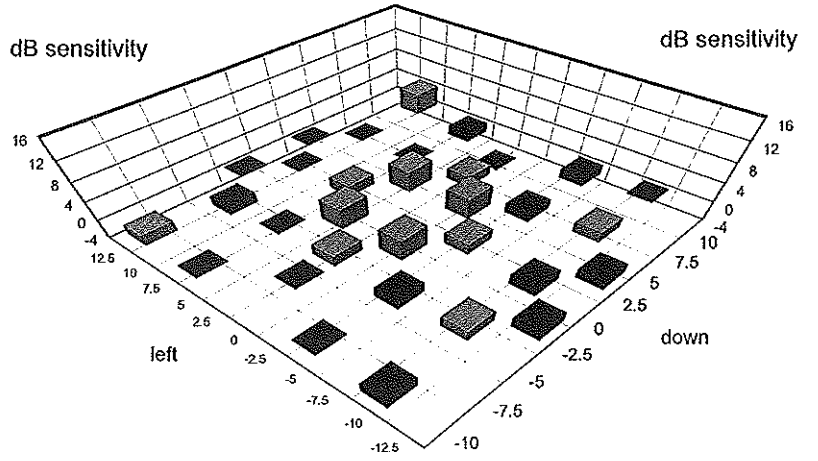


Figure 7 — Case 10. Subtraction of fields of left microstrabismic eye. Fovea is located 2° nasally (right) to the centre of the field. For the subtraction the results under binocular viewing were shifted 2° temporally.

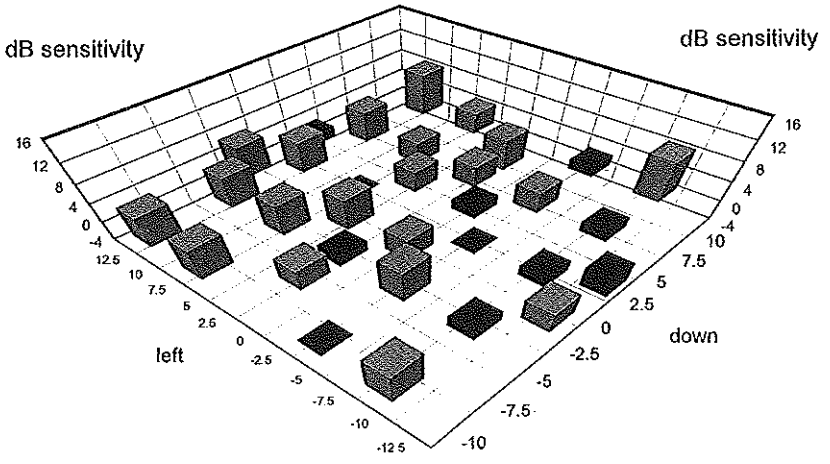


Figure 8 — Case 14. Subtraction of fields of left microstrabismic eye. Fovea is located 1° nasally (right) to the centre of the field. For the subtraction the results under binocular viewing were shifted 1° temporally.

In the measurement of suppression the luminance profile of the stimulus is of great importance. Binocular perimetry employing flash stimuli has the disadvantage that attention is directed to the eye viewing the flash and hence suppression is disrupted. We used a halogen light stimulus that went on and off in a gradual fashion (Fig. 3). In the past decades some studies have been published on the time course of binocular rivalry and suppression.[4, 11, 24, 25] In these studies evidence is given that suppression caused by rivalrous images in normal as well as in amblyopic subjects needs some time to build up. We chose the duration of our light stimuli guided by a study by de Belsunce and Sireteanu.[4] They found that dissimilar images for both eyes, vertical lines for one eye and horizontal lines for the other, shown for periods shorter than approximately 0.1 s., led to a superimposition of the two images, whereas presenting the images for 0.1 to 0.5 s. led to suppression. If the competing images were shown for periods longer than 0.5 s. rivalry occurred. This was the reason that we chose a halogen light stimulus with a triangularly shaped luminance pattern, with a base of 600 ms, leading to an effective stimulus lenghth of approximately 300 ms.

We can only speculate on the reasons for the variability in size and depth of the scotomas we have found. It could be that cases with a history of large-angle strabismus, surgically corrected at the age of 3 to 5 years following amblyopia treatment, as in cases 1 and 7, have total suppression with Bagolini's glasses and large scotomata with our test set up. In fact, it could be possible that these cases had total suppression of one eye; this cannot be demonstrated with our method since our test field only subtended 25 degrees of arc.

Another reason for the large size of the scotomata in subjects 1 and 7 could be anisometropia. There is evidence that subjects with anisometropia have a larger suppression scotoma than subjects with microstrabismus.[9, 20] Maybe the large scotomata in these two subjects are caused by a combined suppression on the basis of both anisometropia and microstrabismus. It is believed by some that the size of the angle of strabismus correlates with the extent of the suppression scotoma.[6, 10] In subjects 5 and 10 this relationship was found. However in subject 1 the radius of the scotoma was smaller than the angle of squint; in subject 7 and 14 the radius of the scotoma was larger than the angle of squint.

Subject 5 had had successful treatment of amblyopia with a central scotoma with Bagolini's glasses for the right eye, whereas we found a small (2.5° radius) shallow (4 dB) scotoma in the other, left eye. Our explanation for this discrepancy between Bagolini testing and our test results is that this subject might have fixated with the left eye during Bagolini testing and fixated with the right microstrabismic eye during our test procedure. This change in fixation between both test situations was possible here because of successful amblyopia treatment and resulting alternating fixation.

We do not know exactly why we found suppression scotomata only in 5 of our 14 subjects and not in all. One reason could be that even though in our test situation identical images were seen with both eyes, pure binocular vision was slightly disturbed by the fact that stimuli were only presented to one eye during our testing under binocular viewing conditions.

A second reason might be that some microstrabismic subjects have a suppression scotoma that is too small to be detected with our set up. Scotomata with a radius of less than 1.5 degrees cannot be detected with our modified Friedmann devices, since the most central stimulus points are at 1.5° eccentricity. We used Bagolini's striated glasses as a predictor of suppression in the primary screening of our subjects. In microstrabismics a central 'hole' in one of the crossed Bagolini streaks correlates with an extremely small part of the visual field, in most cases smaller than the scotomas that can be detected with our method of binocular perimetry. This could be in accordance with the theory that in convergent strabismus ARC occurs in the peripheral visual field and suppression only occurs in the central part of the visual field.[22] It is surmised, that because the receptive fields are larger in the periphery than in the centre of the visual field, and because during early development the receptive fields shrink in size, suppression is needed in the centre of the visual field but binocular vision can be maintained in the peripheral visual field leading to ARC (working hypothesis forwarded by Sireteanu, Bielschowsky Gesellschaft Meeting, Heidelberg, October 1992).

A third reason why we did not find suppression, might be that in some subjects with microstrabismus diplopia is avoided by ARC only, rather than by a combination of suppression in the central visual field and ARC in the more peripheral parts of the binocular visual field.[2,6,15] This could also explain why some subjects with very shallow suppression of only 4 dB (subjects 10 and 14) did not suffer from diplopia while being devoid of amblyopia.

In this study we present a new method of quantitative binocular perimetry, with which we can measure the extent as well as the depth of suppression. Thus the three dimensional 'shape' of the suppression scotoma in strabismus can be shown. With this method we found that subjects with micro- and small angle convergent strabismus have only one scotoma, in all likelihood a fixation-point scotoma.

References

1 Aulhorn, E. (1966) Phasendifferenz-Haploskopie. Eine neue Methode zur Trennung der optischen Eindrücke beider Augen. Kl. Mbl. Augenheilk. 148, 540.

2 Bagolini, B. (1958) Tecnica per l'esame della visione binoculare senza introduzione di elementi dissocianti (test del vetro striato). Boll. d'Oc. 37, 195.

3 Bagolini, B. (1976) Sensorial anomalies in strabismus, Part 1. Doc. Ophthal. 41, 1-22.

4 Belsunce, S de. & Sireteanu, R. (1991) The time course of interocular suppression in normal and amblyopic subjects. Invest. Opthalmol. Vis. Sci. 32, 2645-2652.
5 Bielschowsky, A. (1900) Untersuchungen Åber das Sehen der Schielenden. Albrecht v. Graefes Arch. Ophthal. 50, 406-509.
6 Campos, E.C. (1982) Binocularity in comitant strabismus: binocular visual field studies. Doc. Ophthal. 53, 249-281.
7 Harms, H. (1938) Ort und Wesen der Bildhemmung bei Schielenden. Graefes Arch. Ophthal. 138, 149-209.
8 Herzau, V. (1980) Untersuchungen über das binokulare Gesichtsfeld Schielender. Doc. Ophthal. 49, 221-284.
9 Hess, R.F., Campbell, F.W. & Zimmern, R.C. (1980) Differences in the neural basis of human amblyopias: the effect of mean luminance. Vision Res. 20, 295-306.
10 Jampolski, A. (1955) Characteristics of suppression in strabismus. Arch. Ophthalmol., 154, 683-696.
11 Kaufman, L. (1963) On the spread of suppression and binocular rivalry. Vision Res. 3, 401-415.
12 Lang, J. (1968) Evaluation in small angle strabismus or microtropia. Strabismus Symposium, Giessen, Karger, Basle 219-222.
13 Lang, J. (1973) Mikrostrabismus. BÅcherei des Augenartztes Nr. 62. Enke, Stuttgart 1973.
14 Mackensen, G. (1959) Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgänge beim Schielen. Graefes Arch. Ophthal. 160, 573-587.
15 Mehdorn, E. (1989) Suppression scotomas in primary microstrabismus – a perimetric artefact. Doc. Ophthalmol. 71, 1-18.
16 Parks M.M. (1990) Binocular vision adaptations in strabismus, in Duanes Clinical Ophthalmology, Volume 1, Chapter 8, eds. In Tasman, W. & Jaeger, EA. (Eds), Duanes Clinical Ophthalmology, Vol 1, Chap 8 (pp. 1-7). Philadelphia: Lippincott Company.
17 Pratt-Johnson J.A. & MacDonald A.L. (1976) Binocular visual field in strabismus. Canad J Ophthal. 11, 37-41.
18 Schor, C.M. (1977) Visual stimuli for strabismic suppression. Perception, 6, 583-593.
19 Schuy, K. (1987) Binokulare statische Perimetrie und räumliches Sehen bei Patienten mit Microstrabismus und Normalpersonen mit künstlicher einseitiger Visusherabsetzung. Inaugural-Dissertation, Giessen.
20 Sireteanu, R. & Fronius, M. (1981) Naso-temporal asymmetries in human amblyopia: consequence of long-term interocular suppression. Vision Res. 21, 1055-1063.
21 Sireteanu, R. (1982) Binocular vision in strabismic humans with alternating fixation. Vision Res. 22, 889-896.
22 Sireteanu, R, Fronius, M. (1989) Different patterns of retinal correspondence in the central and peripheral visual field of strabismics. Invest. Ophthalmol. Vis. Sci. 30, 2023-2033.
23 Travers, T. (1938) Suppression of vision in squint and its association with retinal correspondence and amblyopia. Brit. J. Ophthal. 22, 577-604.
24 Wolfe, JM. (1983) Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion on briefly presented dichoptic stimuli. Perception. 12, 447-456.
25 Wolfe, JM. (1986) Briefly presented stimuli can disrupt constant suppression and binocular rivalry suppression. Perception. 15, 413-417.

Quantitative visual fields under binocular viewing conditions in primary and consecutive divergent strabismus

chapter VI

Maurits V. Joosse,[1,2] Huibert J. Simonsz,[1] Ellen M. van Minderhout,[1]
Paul G.H. Mulder[3] and Paulus T.V.M. de Jong[3,4,5]

Graefe's Arch. Clin. Exp. Opthalmol. (1999) 273: 535-545

Abstract

Background. Although there have been a number of studies on the size of the suppression scotoma in divergent strabismus, there have been no reports on the full extent (i.e. size as well as depth) of this scotoma. *Methods.* Binocular static perimetry was used to measure suppression scotomas in five patients with primary divergent strabismus and ten patients with consecutive divergent strabismus. Four control subjects were also included in the study. With two modified Friedmann visual field analyzers, we measured the visual field of both eyes under monocular and binocular viewing conditions. The objective angle of squint ranged from 3 to 25°. Best corrected visual acuity was at least 0.4, but mostly 1.0 in both eyes. *Results.* All subjects had normal visual fields for each eye under monocular viewing conditions. In 12 of the 15 subjects, we found a large area of suppression encompassing the projection of the fixation point as well as that of the fovea in the non-fixating eye under binocular viewing conditions. In two of these twelve patients, one with primary and one with consecutive divergent strabismus, the area of suppression was located nasally to the position of the fovea in the field of

1 Department of Ophthalmology, University Clinic Rotterdam.
2 Department of Ophthalmology, Westeinde Hospital, The Hague.
3 Department of Biostatistics, Erasmus University Rotterdam.
4 The Netherlands Ophthalmic Research Institute.
5 Academic Medical Centre, Amsterdam, The Netherlands.

the non-fixating eye (nasal hemisuppression). In another two patients with divergent squint combined with vertical deviation, a small fixation point suppression scotoma was found. The depth of suppression ranged from 3 to 16 dB. In one subject only, no suppression was found. *Conclusions.* Our findings indicate that the shape of the suppression scotoma is unrelated to the origin of divergent strabismus nor to the angle of squint. Our results also indicate that the critical age for the development of suppression in divergent squint might be up to 14 years.

Introduction

A number of authors have found suppression scotomas in small angle convergent strabismus.[12, 13, 16, 20, 26-28, 30] A strabismic suppression scotoma is an area of reduced sensitivity to stimuli in the deviating eye under binocular viewing conditions. Presently, suppression scotomas are subdivided in central and fixation point scotomas. A central scotoma is centered around the projection of the fovea in the visual field of the deviating eye. A fixation-point scotoma is centered around the point in the visual field of the deviating eye on which the fovea of the fixating eye projects.

In divergent strabismus most authors found suppression of the nasal half of the visual field in both constant exotropia as well as in the divergent phase of intermittent exotropia. In most cases however, the point corresponding with the fovea of the exotropic eye was spared in this nasal hemisuppression.[11-13, 15, 19, 22] Other studies like the famous self-study of Tschermak[31] and studies by Pratt-Johnson and MacDonald[23] and Awaya et al.[1] showed a round suppression scotoma, encompassing both the fovea as well as the fixation-point of the deviating eye. These authors used binocular perimetry with a complex visual background. Bagolini[3] found with the striated glass test[2] in persons with large-angle divergent strabismus without anomalous retinal correspondence (ARC), total suppression of the deviating eye (excluding the strictly monocularly perceived temporal crescent). Contrasting with these results, Cass[8] and Cooper and Feldmann[9] found in intermittent exotropia with large as well as small angles an absence of suppression, an enlarged peripheral field of view and a form of facultative anomalous retinal correspondence. This triad of symptoms was called panoramic viewing.

In a previous study,[16] we quantified the depth and extent of suppression scotomas in convergent strabismus with squint angles between 1 and 8°. For these measurements we used two modified Friedmann visual field analyzers, that were perceived haploscopically. The perimetry results obtained under binocular viewing conditions were subtracted from those obtained under monocular conditions. In five of the 14 subjects tested, we found a circular suppression scotoma, centered around the fixation point of the squinting eye. The depth of the scotomata ranged

from 4 to 14 dB and the diameter from 5 to 30°. In the nine other subjects of this earlier study no evidence of suppression could be found.

A problem with the description of binocularity of subjects with divergent strabismus – as opposed to convergent strabismus – is the variability in the angle of squint and instability of fixation preference. Viewing distance, time of day, physical condition, and complexity of object viewed are of great influence on the binocular status of the subject with divergent strabismus.[21] This is probably true for our subjects with intermittent exotropia as well as for those with consecutive exotropia. For example, it is remarkable that in intermittent exotropia, which accounts for 80% of the manifest divergent deviations,[10] suppression and probably ARC occur during the phase of divergence, whereas no sensory anomalies can be demonstrated during the orthotropic phase.[14]

There is still no agreement on the similarities and differences between perception in convergent and in divergent strabismus. Thus we set out to answer the following questions. Do subjects with divergent strabismus use suppression or panoramic viewing to avoid diplopia? If it is suppression, what are the size and the depth of the suppression scotoma? Are there differences in the type of suppression between primary and consecutive divergent strabismus? Until which age can a divergent type of suppression develop in cases with consecutive divergent strabismus? In this paper we performed quantitative binocular perimetry in 15 patients with divergent strabismus of different origins. Both depth and size of the suppression scotomas were quantified.

Cases and Methods

Included in this study were 15 consecutive patients with divergent strabismus, coming from the outpatient departments of the Rotterdam University Eye Clinic and the Westeinde Hospital in The Hague. Five had primary (congenital) intermittent exotropia, nine constant consecutive (formerly convergent) divergent strabismus and one divergent strabismus, following pineal-gland tumor resection). Ages ranged from 16 to 62 years, with an average of 30 years. Informed consent or parental consent was obtained from all subjects. When testing the subjects that were under the age of 18 one parent was in the room during the whole test procedure. We performed an ophthalmologic and orthoptic examination in all subjects. The standard ophthalmic examination consisted of measurement of best corrected Snellen visual acuity, slit-lamp examination and ophthalmoscopy. The standard orthoptic examination was performed by an orthoptist and consisted of cover test, 15 prism diopter test (base out placed in front of either eye to determine fixation preference and base in to determine ocular correspondence), measurement of subjective and objective angle of deviation with the synoptophore and

prism-cover test at both 40 cm and 6 m, Titmus stereopsis test and random dot stereopsis (TNO) test, Bagolini striated glass test and Cueppers visuscopy. Stereopsis tests at near with prism compensation or bilateral addition of -3 D lenses were performed and the Bagolini test was performed under near and distance viewing conditions. A detailed description of the ophthalmic and orthoptic status of all cases is given in Tab.1.

We measured the visual field of each eye under monocular and binocular test conditions. As a reference we also tested four control subjects, aged between 30 and 32 years. Of these subjects, each eye was examined under monocular as well as under binocular viewing conditions. These were the same control subjects as in our previous study.[16] We tested one strabismic subject, case 7, three times on separate days to determine the precision and the reproducibility of our method. In this subject, we performed an analysis of variance with fixed effects.

We used a slightly modified test-procedure with two Friedmann visual field analyzers as has been described earlier in our previous suppression study in microstrabismic subjects.[16] The Friedmann visual field analyzer is a device designed for static perimetry of the central 50° of the visual field. In its original design, two to four simultaneous flash light stimuli in various patterns can be presented through holes in a black background. The stimulus light intensity can be adjusted manually in steps of 2 dB and the subject was asked which lights he saw on the screen. In our test set-up, on the screen of the two Friedmann field analyzers, identical pictures of penguins in a polar landscape were attached (Fig. 1). These pictures served as complex background for the stimulus light patterns. The pictures were perforated at the original holes in the screens of the Friedmann analyzers.

The field analyzers were positioned facing each other at a distance of 90 cm, with two obliquely positioned surface-silvered mirrors halfway in between them. An orthoptist performed alternating cover tests while the subject's head was in the chin rest to determine the objective angle of squint for the given object distance of 45 cm (i.e. between eye and Friedmann screen via the mirror).

Like in our previous study,[16] our device was designed to allow the most natural binocular viewing conditions. In our small-angle convergent subjects (most cases had strong ARC), we obtained natural viewing by allowing the subject to adjust the mirrors to obtain peripheral fusion (correction of the subjective angle of squint). The only problem with this correction for the subjective angle of squint was that the subtraction of the visual field results obtained under binocular viewing conditions from those obtained under monocular conditions was cumbersome. This was due to the shift of the position of the fovea of the squinting eye on the screen of the perimeter when changing from monocular viewing to binocular viewing.

Thus 'net suppression' could only be calculated with compensation for the shift in foveal position between monocular and binocular viewing.

In those patients with divergent squint, where peripheral fusion was much less profound, supposedly because of the larger suppression areas and less constant ARC, we solved this problem by placing a fixation dot for either eye at an eccentricity of half the objective angle of squint on the surface of both Friedmann screens. For instance, if the objective angle of strabismus was 10°, there would be a fixation dot at 5° temporally from the center of the screen in front of the right eye as well as the other fixation dot at 5° temporally from the center of the screen of the left eye (this situation is shown in Fig. 1). The position of the fixation dot would only be acceptable if no (re)fixation movement occurred during alternate cover-testing. Thus, by dividing the objective angle by two, the subject viewed an identical stimulus background with the same eye under monocular and binocular test conditions (while maintaining his objective angle of squint). In this group, the determination of the net suppression (subtraction of the results obtained under binocular viewing from those under monocular conditions) was much more straightforward since the subjects looked at the exact same eccentric point

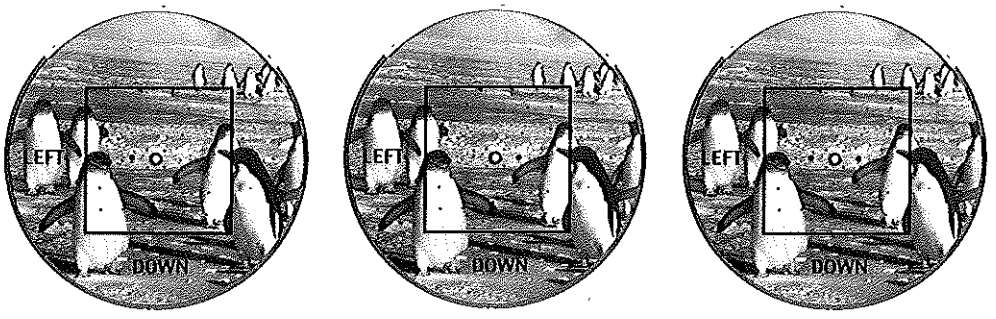


Figure 1a to c — Perceived image under monocular as well as binocular viewing conditions in a 10° exotrope. Left (fig 1a.): Picture of the screen as seen by the left eye under monocular viewing conditions. For clarity, we have drawn a black square on the picture of the surface of the field analyzer, indicating the perceived area during testing (25° horizontally by 25° vertically). In the actual test situation, this black square did not exist. The black dot indicates the foveal fixation spot, here 5° (half the objective angle of squint) temporally, i.e. on the left side of the screen surface. Middle (fig 1b.): Picture of the screen, as seen with the right eye under monocular viewing conditions. Here, the fixation spot is positioned also 5° temporally, i.e. on the right side of the screen surface. The figure on the right (fig 1c.) shows the image as seen by the subject under binocular viewing conditions. Here two fixation dots, one for each fovea are present. This image shows the hypothetical situation where there would be fusion of the two images without diplopia or suppression. In a left eye the label 'Left' indicates the temporal side of the visual field and in a right eye the nasal side of the visual field. In Figs. 1a to c the stimulus holes in the square that could be seen through the mirrors, are indicated by the small black dots. These represent the data points shown in Figs. 2 to 4. Note that data were only obtained in the slightly vertically elongated area of 20° horizontally (x-axis) by 25° vertically (y-axis).

Table I — Baseline data on 15 subjects with divergent squint and four control subjects.

Case #	age years	sex	eye	VA	refraction	squint type
case 1	37	M	R	1.0	+0.75	L consec.div.
			L	1.0	+1.50 = -0.75 x 0°	
case 2	55	F	R	1.2	-1.50 = -0.75 x 0°	R prim.div.int.
			L	1.2	-0.50 = -0.50 x 0°	
case 3	23	M	R	1.0	+1.50	R consec.div.
			L	1.0	+0.75	
case 4	62	M	R	0.7	+1.25 = -1.00 X 90°	R prim.div.int.
			L	0.8	+1.00 = -1.00 x 90°	
case 5	16	M	R	0.8	+0.50	R second.div.
			L	1.0	E	
case 6	24	F	R	0.4	-4.00 = -4.00 x 25°	R consec.div.
			L	0.8	E	
case 7	52	F	R	1.0	E	R consec.div.
			L	1.0	E	
case 8	26	M	R	0.8	+2.00 = -3.50 x 0°	R prim.div.int.
			L	0.8	+0.50 = -3.00 x 0°	
case 9	34	M	R	1.0	-2.25 = -1.50 x 80°	R prim.div.int.
			L	1.0	-3.25 = -2.00 x 80°	
case 10	27	M	R	0.7	+5.00 = -0.75 x 35°	R consec.div.
			L	1.0	+5.00 = -1.00 x 165°	
case 11	20	M	R	1.2	E	L prim.div.int.
			L	1.2	E	
case 12	17	F	R	0.9	+3.00	R consec.div.
			L	1.2	E	
case 13	18	F	R	1.0	+0.50	L consec.div.
			L	1.0	E	
case 14	20	M	R	1.0	+2.50	L consec.div.
			L	0.8	+3.50	
case 15	26	F	R	1.0	-1.50= -0.50 x 90°	R consec.div.
			L	1.0	-1.50= -0.50 x 60°	
Control 1	32	F	R	1.0	-2.00	orthotropic
			L	1.0	-2.00	
Control 2	32	M	R	1.2	-0.50	orthotropic
			L	1.2	plano	
Control 3	31	M	R	1.0	plano	orthotropic
			L	1.0	plano	
Control 4	32	F	R	1.0	plano	orthotropic
			L	1.0	plano	

M = male, F = female. R = right eye, L = left eye; VA = visual acuity; E = emmetropic; prim. = primary, consec. = consecutive, second. = secondary; div. = divergent strabismus; Int. = intermittens; resid. = residual; progr.=progressive; cong. = congenital; Bagolini = Bagolini's striated glasses test, where neg. = negative (meaning no evidence for correspondence, only one streak is seen) and pos. = positive (meaning the presence of correspondence, with or without suppression). Stereopsis = Titmus fly test /

Bagolini	Stereopsis	obj. / subj. squint angle	diagnosis / history
neg.	fly neg.	-22° / -10°	prim.conv.alt., surg. at 4y. consec.div., surg. at 9, 20 & 38y.
pos.	TNO 60"	-9° / var.	progr. prim.div.int. 26° surg. at 53y., resid. R div int.
pos.	fly pos.	-7° / +2°	cong.R conv., occl. ther., surg. at 3 & 4y., progr.R div., surg. at 23y.
neg.	fly neg.	-20° / var.	progr. R. prim.div.int. 20°. with 5° hypotropia. vert. ARC.
pos.	fly pos.	-15° / +1°	prim.microstrab., decomp. to R div. by INO (pineal gland tumor) at 14y.
neg.	fly neg.	-3° / -3°	anisometropia & prim.R div. with surg. at 23y., residual R div.
neg.	fly neg.	-8° / -3°	cong.R conv.str., occl. ther,surg.at 4y, decomp.to R div., surg.at 51y.
pos.	fly neg.	-25°/ var.	moderate symm. hyperopia at 3y. progr.div. alt., L fix. at near.
pos.	TNO 120"	-20°/ var.	anisomyopia, progr.R.div.int.
pos.	fly neg.	-17° / -10°	cong.conv.+ DVD, surg. at 2 and 6y, progr.div.int., pref .L
neg.	fly neg.	-8° / var.	cong.div.+ DVD, surg. at 4 and 17y, progr.div. int.,pref. R
pos.	fly neg.	-8° / var	cong.conv., surg. at 4 and 7y, R progr. div.+ 1°R hypotropia
pos.	fly neg.	-13° / -7°	cong.conv., surg. at 1 and 7y, L progr. div.
neg.	fly neg.	-7° / var.	cong. conv., surg. at 4 and 7y, L div., A-pattern
neg.	fly neg.	-10° / var.	cong.conv., surg. at 6 and 12y, R div.+ slight hypertr.+vert. ARC
	fly pos.		
	fly pos.		
	fly pos.		
	fly pos.		

TNO-test; Angle obj / subj. = objective and subjective angle of squint as measured with prism cover-test at 40 cm; conv. = convergent strabismus, alt. = alternans; cong. = congenital; surg. = strabismus surgery; INO = internuclear ophthalmoplegia; ARC = anomalous retinal correspondance; DVD = dissociated vertical deviation; hypertr. = hypertropia; Y = years of age.

on the Friedmann screen under monocular as under binocular viewing conditions. When present, an objective vertical angle was also corrected with the yellow dots by putting them slightly under and above the vertical midline (by half the vertical angle for each eye).

The maximum size of the visual field that could be seen simultaneously with both eyes through the mirrors was 25° in horizontal diameter. This posed a limitation in the capability of the device to determine the temporal borders of possible suppression scotomata. If for instance the angle of strabismus was 20°, the temporal part of the visual field could not be tested sufficiently. In this instance, the fixation dot would be for both eyes at 10° temporally from the center of each screen, thus almost at the temporal edge of the part of the screen that could be perceived through the mirrors. However, in the subjects with large angles of divergent strabismus the nasal part of the visual field could very well be measured. This part also has our greatest interest, because in persons with divergent strabismus it is mainly in the nasal half of the visual field where the greatest interaction between the eyes (such as e.g. suppression) occurs.

It is not possible to measure suppression with the standard flashlight that the Friedmann field analyzer is normally equipped with, because it will disrupt suppression. In order to break the dissociating effect of this standard flash light, the flash bulb was changed into a halogen light, that glows on and off in a more gradual manner. With this light, an approximately triangularly shaped luminance profile, with a base of 0.6 s, 0.3 s light increase and 0.3 s light decrease, was produced. Time between presentations was at least 3 s. The room lights were dimmed so that the mean luminance of the screens was 5 Asb. A standard test session would consist of three runs. The first two would test each eye separately under monocular viewing conditions. Thus each eye would be tested with the head in the chin rest and with the non-tested eye occluded with a non-translucent eye patch. We would begin testing each eye at a very low stimulus luminance level, presenting the central stimuli first, followed by more peripheral stimuli. The lowest luminance level would be at the 20 dB filter level, but most normals as well as strabismic subjects had a central threshold at the 16-18 dB level. Brightness of the stimulus was gradually increased by steps of 2 dB. Stimuli were presented repeatedly, but for three times at most. The final test run (under binocular viewing conditions) was performed with both eyes open, with stimuli presented either to the right or the left eye, while the subject fused both screens. Here also the stimuli were presented three times at most for every stimulus position at each luminance level. The luminance levels seen during this final test run were scored for each eye separately.

Results

In our group of 15 patients with divergent strabismus we found three types of suppression in the non-fixating eye: (sub)total suppression, nasal hemisuppression or a small fixation-point scotoma. Cases 1, 2, 3, 5, 6, 7, 8, 9, 11 and 13 were of the group that had (sub)total suppression in the non-fixating eye and had a varying depth of suppression, ranging from 3 to 16 dB. In cases 10 and 14 we found nasal hemisuppression. Note that the foveal fixation spot was localized temporally to the center of the screen at an eccentricity of half the objective angle of squint. The nasal hemisuppression had an average depth of 5 dB in case 1, 6 dB in case 10, and 14 dB in case 14. In two cases (cases 4 and 15) we found a small circular scotoma centered around the fixation point, with a depth of 4-6 dB and a diameter of 10°. In case 12 we did not find any indication for suppression (Tab. 2). We did not find any significant abnormalities in the fixating eyes of our subjects under binocular viewing conditions. The monocular visual fields of all cases were normal, varying between 10 and 18 dB (averaged across the visual field). The test results of our 15 divergent subjects are summarized in Tab. 2.

Table II — Characteristics of suppression scotomas in subjects with divergent squint

Case #	preferred eye at near fixation	scotoma (binocular viewing conditions) *eye*	*depth*	*type*	foveal projection (1/2 obj. angle)	
Case 1	R	L	5 dB	total supp.	11°	T
Case 2	L	R	4 dB	total supp.	4.5°	T
Case 3	L	R	5 dB	total supp.	3.5°	T
Case 4	L	R	4 dB	fix. point	10°/2°	T/A
Case 5	L	R	4 dB	total supp.	7.5°	T
Case 6	L	R	4 dB	total supp.	1.5°	T
Case 7	L	R	3 dB	total supp.	4°	T
Case 8	L	R	10 dB	total supp.	12.5°	T
Case 9	L	R	4 dB	total supp.	10°	T
Case 10	L	R	6 dB	nas. hemisupp.	8.5°	T
Case 11	R	L	16 dB	total supp.	4°	T
Case 12	L	—	—	—	4°	T
Case 13	R	L	14 dB	total supp.	6.5°	T
Case 14	R	L	14 dB	nas. hemisupp.	3.5°	T
Case 15	L	R	6 dB	fix. point	5°/1°	T/U

R = right eye, L = left eye; dB = decibel; nas. hemisupp. = nasal hemisuppression; fix. point = fixation point, T = temporal to the centre of the data field; A = above the midline; U = under the midline.

The cases with primary divergent strabismus had either (sub)total suppression (cases 2, 8, 9 or 11) or a fixation-point scotoma (case 4). We did not find nasal hemisuppression in our subjects with primary divergent strabismus. In our group with consecutive divergent strabismus we found three types of suppression: (sub)total suppression, nasal hemisuppression (or a fixation-point scotoma), or panoramic viewing without suppression.

Figures 2-4 show the net suppression, obtained by subtraction of the monocularly from the binocularly obtained perimetry results in the non-fixating eye of three cases (11, 14 and 15) with suppression patterns and objective squint angles of equal to or less than 10°. Case 11 had the deepest total suppression. Case 14 had nasal hemisuppression. Case 15 is the one with the deepest fixation point scotoma. In Figs. 2 to 4 the 25 by 25° segment that is seen with one eye under binocular viewing conditions is shown. Only the eye with suppression is shown in these figures.

Case 7, with the lowest average amount of total suppression of the right eye, was tested three times in order to perform an analysis of variance with fixed effects. We found an average error variance of 1.85 dB2 (349 degrees of freedom) given field position, viewing condition, side of eye, and repetition (averaged across 32 field positions times three repetitions). In the left eye the mean difference for each field position between monocular and binocular viewing conditions was 0.92 dB and for the right, non-fixating eye this difference was 3.96 dB. Thus we found a mean difference in the results of subtraction of the monocularly obtained results from those that were binocularly obtained between the eyes, of 3.96 - 0.92 = 3.04 dB. This is the actual net suppression in the right eye as corrected for the mean difference between monocularly and binocularly obtained results in the left eye. This mean difference has a standard error of $\sqrt{4 \times 1.85/96} = 0.28$; this is significantly different from zero.

In the four control subjects we found sensitivity levels in the visual field fort testing under both monocular and binocular viewing conditions ranging from 16 to 20 dB on average. There was no detectable pattern of suppression in these cases. Thus the difference between the results obtained during monocular and binocular viewing conditions was no greater than 2 dB in this control group.

Discussion

In the current study, we were able to quantify a suppression scotoma in 14 of 15 subjects with divergent strabismus. Our results indicate that there are four mechanisms to avoid diplopia in divergent strabismus: 1. total suppression of the binocularly perceived part of the visual field of the squinting eye (10 cases); 2. nasal hemisuppression in the squinting eye (2 cases); 3. a round fixation point

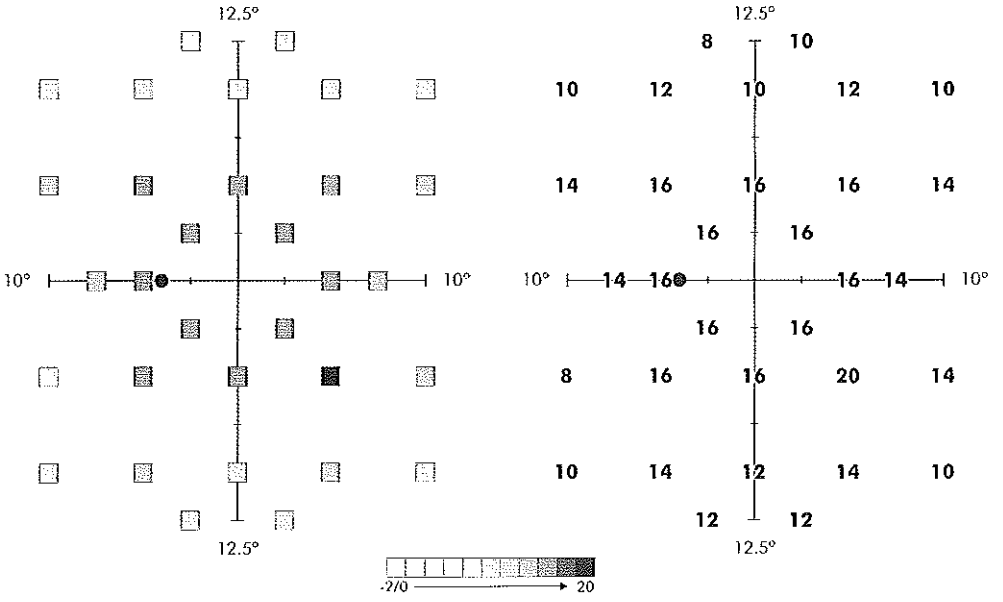


Figure 2 — Case 11. Result of subtraction of the visual field results of left eye obtained under binocular viewing conditions from the field results obtained under monocular conditions (i.e. 'net' suppression). The figure shows the data obtained in the 20 by 25 degree field segment in two slightly different, complementary ways. The left side of the figure is made up from a field of 32 square dots, representing the data points. Depth of suppression is proportional with the amount of greytone of the square dots. A white square indicates that there is no suppression (subtraction led to a value of -2 or 0 dB at that position). The round black dot indicates the position of the fovea. On the right side of the figure, the absolute values obtained across the same 32 data points are shown. Here the position of the fovea also is indicated by the black dot. Note: Levels of 4 dB or more were found to be significant with an analysis of variance with fixed effects as described before. The fovea is located 4 degrees left of the center.

scotoma in the squinting eye (2 cases); or 4. panoramic viewing with simultaneous perception and homonymous ARC, without suppression (1 case).

In this study of divergent strabismus, we chose for two eccentrically placed foveal fixation dots in a haploscopically viewed complex visual background. These fixation dots were placed such that each of them corrected half the objective angle of exotropia. This allowed testing under the most normal exotropic viewing conditions, with easy maintenance of the angle of deviation and straightforward subtraction of the sensitivity thresholds obtained under binocular viewing conditions from those under monocular viewing. If we would have made the test set-up like the one used in our previous study of small angle convergent strabismus,[16] where we asked the patient to horizontally adjust the mirrors to correct

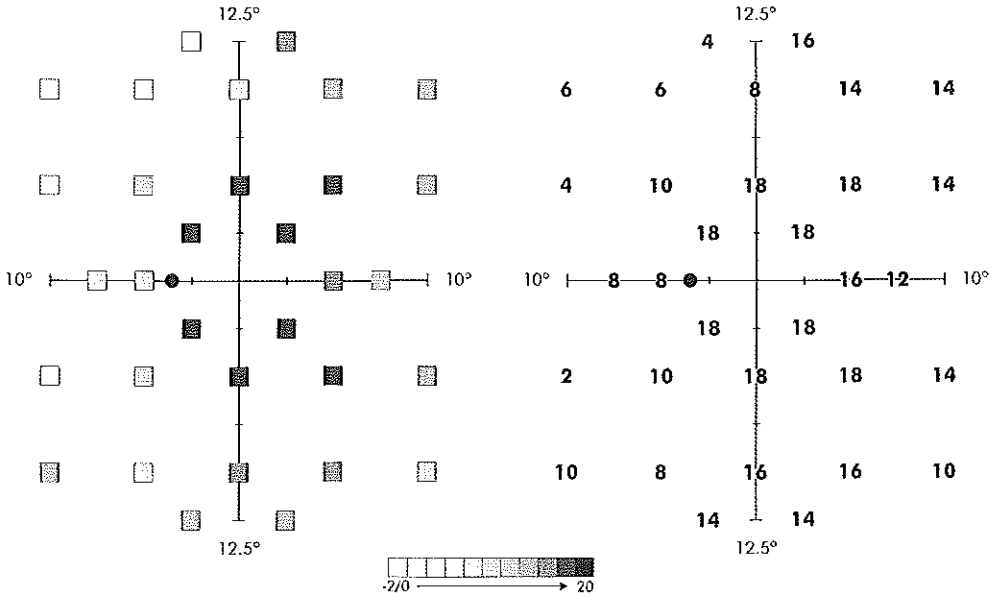


Figure 3 — Case 14. Net suppression of the left eye. The fovea is located 3.5 degrees left of the center.

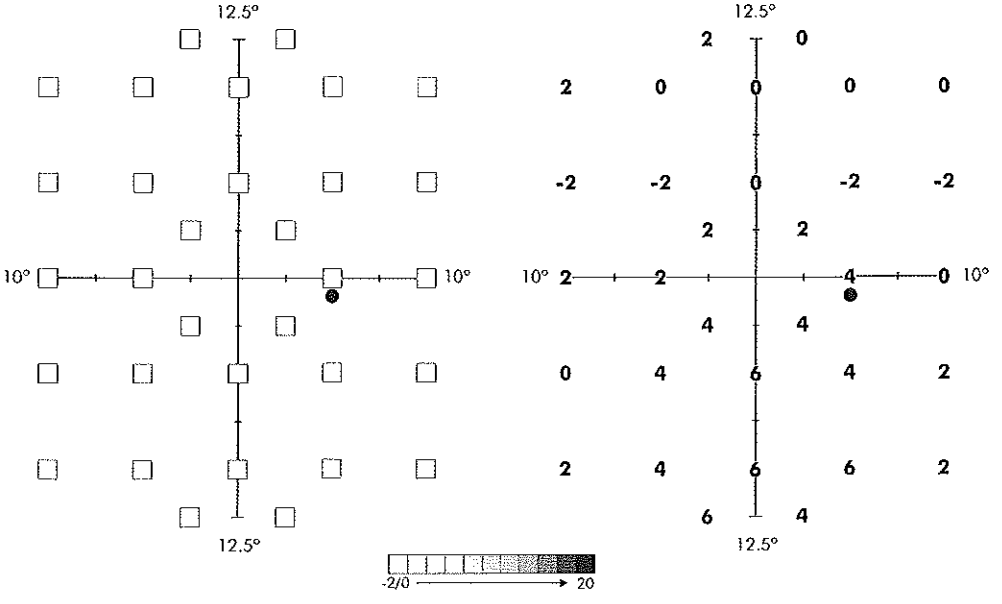


Figure 4 — Case 15. Net suppression of the right eye. The fovea is located 5 degrees right, and 1 degree under the center.

the subjective angle of strabismus, we would most likely have had the same effect as prismatic correction of a divergent squint would produce. The subjects in most cases would suffer from diplopia and would have considerable difficulty to determine how to angle their mirrors, since their subjective angle is much less stable. We are aware however, that the eccentrically placed fixation dots have a somewhat dissociating effect, which might cause artifacts in the measurement of suppression.

Strikingly, we found (sub)total suppression in the majority of our cases with primary or consecutive divergent strabismus, whereas in our group of cases with (small angle) convergent strabismus, we found round fixation point scotomas only in a minority of cases.[16] Probably, there are structural differences between the sensorial status of convergent strabismus as opposed to divergent strabismus. Jampolsky found that peripheral fusion on the basis of ARC is usually much better developed in convergent than in divergent strabismus.[15] Others believe that subjects with divergent strabismus might be in a lower stage of the evolution of their visual sensory-motor system (atavistic theory).[10, 14] Bielschowsky stated that subjects with divergent strabismus might just have a different position of rest, whereas those with convergent strabismus have a deeper pathological defect in their visual system.[5]

Another issue is, why did none of our subjects suffer from diplopia (Fig. 5a). Only three of our subjects stated that they perceived both fixation points simultaneously (without diplopia). They may have had panoramic viewing, with bifoveal perception (Fig. 1c). However, this interpretation does not apply to the other subjects, who stated that they did not see both fixation dots simultaneously. They might have had alternating fixation in which they switched attention between the eyes without fixation movements. It is even possible that those who said to have perceived the fixation points simultaneously in fact alternated. These were also the subjects who asked during testing: 'with which eye do you want me to fixate?' They would direct attention to the image of one eye under binocular viewing conditions, in combination with total suppression of the non-fixating eye. So they would most likely have a type of perception as shown in Figs. 1a or b, but then under binocular viewing conditions. We found this situation in 10 of our cases.

Two cases perceived the image as shown in Fig. 5b. They suppressed only the nasal half of the visual field of the non-fixating eye, with unaltered perception of the temporal half of the visual field of that eye. We can only speculate on what happens with this temporal half. Why is it not perceived diplopically? The bridge of the nose only blocks off perception of the area of the visual field beyond 45° temporally and these two subjects only had relatively small angles of exotropia (7 and 17°). Thus, in these subjects the area temporally to the foveal projection of the deviating eye was perceived for a significant part by the fixating eye, theoretically leading to diplopia. Perhaps, there is panoramic viewing in this segment

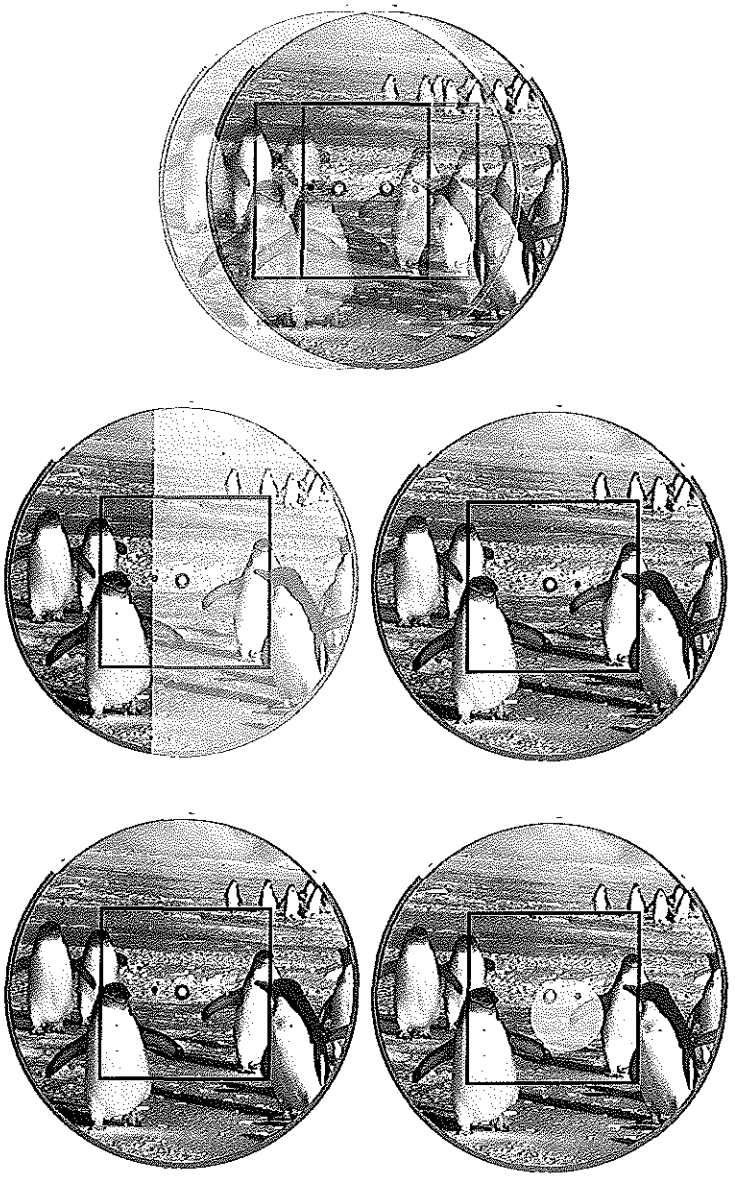


Figure 5 — Top (fig. 5a.), shows the hypothetical diplopic image as might be perceived by a subject with 10° of divergent strabismus. Middle (fig. 5b.), shows the perceived image in the eyes under binocular viewing conditions in the presence of nasal hemisuppression as we found in cases 10 and 14. In this middle figure, the right eye is the fixating eye. Bottom (fig. 5c.), shows the perceived image in the eyes in the presence of a fixation point scotoma, as we found in cases 4 and 15. In this figure, the left eye is fixating.

of the visual field or possibly some sort of facultative ARC. This same question exists for the two cases that had a small fixation point scotoma (see Fig. 5c). They are even more likely to have diplopia, especially in the nasal part of the visual field of their non-fixating eye, because this is the part that overlaps with the nasal part of the fixating eye. We believe that these two subjects might have panoramic viewing without suppression, based on their horizontal deviation, and a fixation point scotoma and vertical ARC, based on their vertical deviation.

Curiously, we found similar types of suppression in consecutive (or secondary) exotropic cases as in cases with (primary) intermittent exotropia. This could indicate that equally large suppression scotomas occur in primary divergent strabismus as in subjects who had primary convergent strabismus that changed into a divergent strabismus at young age. There is discussion on the critical period for the development of suppression.[10, 28] In our study, the findings in case 5 indicate that this critical period might extend up to the age of 14. Case 5 had primary (convergent) microstrabismus that decompensated at the age of 14 into a 15° divergent strabismus secondarily to a pineal gland tumor. Interestingly, he stated that he suffered from diplopia for no longer than a week following this change of direction of the strabismus. Cases 13 and 14, who both became divergent at age 7, following surgery for congenital convergent strabismus, also had a large suppression scotoma based on their divergent strabismus. However, cases 12 and 15, who also had congenital convergent strabismus and became divergent following strabismus surgery, at the ages 7 and 12 respectively, did not show these suppression scotomas.

With rivalrous line gratings shown to the eyes, Wolfe[32] and De Belsunce and Sireteanu[4] have found that suppression can best be measured with exposition times of 100 to 800 ms. The gratings they used, flickered on and off abruptly. Flashes of light or stimuli that are presented abruptly are likely to be dissociating and might break suppression. For this reason we used a stimulus with a triangular luminance-profile with a 600 ms base, like in our former study.[16] Our most recent work indicates that this luminance-profile and stimulus-duration might be the most effective in measuring suppression.[17]

What determines the size and depth of the suppression scotomas in divergent strabismus? Previous research has shown that the degree of suppression strongly depends on the method of measurement[7, 13, 2, 22] According to Campos and Herzau, who mainly performed suppression measurements with devices lacking contour (a filter in front of one or two eyes), the extent of the suppression scotoma in divergent strabismus is highly dependent on the presence of ARC.[7, 23] They state that subjects with divergent strabismus and ARC, in most cases have nasal hemi-suppression, without suppression of the fovea of the deviating eye. However,

with our test set-up using a haploscopically viewed complex visual background, the fovea has only been spared in one of our two subjects with nasal hemisuppression of the non-fixating eye (cases 10). This 17 degree exotrope had ARC as detected with the Bagolini's striated glasses test. Case 14, a 7 degree exotrope, in whom we could not prove any ARC, had nasal hemisuppression without sparing of the fovea, in compliance with Campos and Herzau.[7,13] Ten other subjects with (sub)total suppression, including the fovea, subsequently did not have abnormal correspondence. They were most likely to alternate rapidly between the eyes, without (ab)normal binocular correspondence. Subject 12 is likely to have panoramic viewing, without suppression and bifoveal perception. Subjects 4 and 15, who most likely had a fixation point scotoma on the basis of their vertical deviation, will be left out of this issue.

Large suppression scotomata encompassing the fovea, unrelated to the angle of divergent strabismus have previously been described in studies using a complex visual background viewed through polarizing filters or with the phase difference haploscope.[1,23] In our study, a complex visual background is also used, albeit viewed via mirrors, with an eccentric fixation dot. In most cases, we also find large scotomata, encompassing the fovea. This strengthens our feeling that our test device is not very dissociating, although the eccentrically placed fixation dots are slightly dissociating.

Finally, it has been stated that the size of the angle of strabismus determines the level of suppression and ARC. In small-angle divergent strabismus (< 10°) a small, round suppression scotoma with ARC was found.[3,7] In cases with moderately large-angle divergent strabismus (10°-20°), hemisuppression of the nasal side of the visual field was found.[12-14,19,22] In large angle divergent strabismus (> 20°), panoramic viewing was demonstrated.[6,8,9] Possibly, these persons have bifoveal perception with an enlarged binocular visual field of view.

Others found however, a large fixation point suppression scotoma with ARC or total suppression, in which the size of the scotoma was unrelated to the size of the angle of squint.[23-25] In agreement with these studies, we also did not find a relationship between the size of the angle of squint and the type of suppression. We found total suppression in 10 cases with angles of strabismus varying between 7 and 25°, nasal hemisuppression in two cases with angles of 7 and 17° and a small fixation-point suppression scotoma in two cases with angles of 10 and 20°.

In conclusion, in our study of primary and consecutive divergent strabismus, the shape and depth of the suppression scotoma was unrelated to the etiology of the strabismus nor to the size of the angle of strabismus.

References

1 Awaya S, Nozaki H, Itoh T, Harada K (1976) Moore, Mein & Stockbridge (eds) Orthoptics, Past, Present & Future. Miami, Symposia Specialists, pp 531-546.
2 Bagolini B (1958) Tecnica per l'esame della visione binoculare senza introduzione di elementi dissocianti (test del vetro striato). Boll Ocul 37: 195-204.
3 Bagolini B (1976) Sensorial anomalies in strabismus, Part I. Doc. Ophthalmol. 4:1-22.
4 Belsunce S de & Sireteanu R (1991) The time course of interocular suppression in normal and amblyopic subjects. Invest Ophthalmol Vis Sci 32: 2645-2653.
5 Bielschowsky A (1934) Divergence excess. Arch Ophthalmol 12(2): 157-166.
6 Budd GE & Boyd TAS (1977) Abnormal retinal correspondence and directional values in exotropia. Am Orthoptic J 27: 68-69.
7 Campos EC (1982) Binocularity in comitant strabismus: binocular visual field studies. Docum Ophthalmologica 53:249-281.
8 Cass EE (1937) Divergent strabismus. Br J Ophthalmol 21(11): 538-559.
9 Cooper J & Feldmann J (1979) Panoramic viewing, visual acuity of the deviating eye, and anomalous retinal correspondence in the intermittent exotrope of the divergence excess type. Am J Optometry Phys Optics 56(7): 422-29.
10 De Decker W (1995): Strabismus, Enke Verlag Stuttgart, pp 209-282.
11 Graefe A von (1854) Ueber das Doppelsehen nach Schieloperationen und Incongruenz der Netzhäute. Archiv f Ophthalmol 1: 82-120.
12 Harms H (1939). Ort und Wesen der Bildhemmung bei Schielenden. Albrecht v Graefes Arch Ophthalmol 138: 149-210.
13 Herzau V (1980) Untersuchungen über das binokulare Gesichtsfeld Schielender. Doc. Ophthalmol. 49, 221-284.
14 Jampolsky A (1954) Differential diagnostic characteristics of intermittent exotropia and true exophoria. Am Orthoptic J 4(1): 48-55.
15 Jampolsky A (1955) Characteristics of suppression in strabismus. Arch Ophthalmol 54: 683-96.
16 Joosse MV, Simonsz HJ, Minderhout HM van, Jong PTVM de, Noordzij B, Mulder PGH (1997) Quantitative perimetry under binocular viewing conditions in microstrabismus. Vision Res 37 (19): 2801-2812.
17 Joosse MV, Simonsz HJ, van Minderhout HM, Spekreijse H, de Jong PTVM (1998) Optimal stimulus-duration and – profile for the measurement of suppression in strabismus. Invest Ophthalmol Vis Sci Suppl 39(4): 329.
18 Kaufman L (1963) On the spread of suppression and binocular rivalry. Vision Res 3: 401-415.
19 Knapp P (1953) Intermittent exotropia: Evaluation and therapy, Am Orthoptic J 3: 27-33.
20 Mackensen G (1959) Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgänge beim Schielen. Graefes Arch Ophthalmol 160: 573-587.
21 Mein J & Trimble R (1994) Blackwell Science. Diagnosis and management of ocular motility disorders. Second Edition, Section 1, chapter 7, pp. 116-143.
22 Parks MM (1990) Philadephia: Lippincott Company. Binocular Visual Adaptations in Strabismus, Duanes Clinical Ophthalmology, Volume 1, chapter 9, pp. 1-13.
23 Pratt-Johnson JA & MacDonald AL (1976) Binocular visual field in strabismus. Can J Ophthalmol 11: 37-41.
24 Pratt-Johnson JA, Tillson G and Pop A (1983) Suppression in strabismus and the hemiretinal trigger mechanism. Arch Ophthalmol 101: 218-224.
25 Schor C (1978) Zero retinal image disparity: a stimulus for suppression in small angle strabismus. Doc Ophthalmol 46(1): 149-160.
26 Schuy K (1987) Binokulare statische Perimetrie und räumliches Sehen bei Patienten mit Microstrabismus und Normalpersonen mit künstlicher einseitiger Visusherabsetzung. Inaugural-Dissertation, Giessen.
27 Sireteanu R & Fronius M (1981) Naso-temporal asymmetries in human amblyopia: consequence of long-term interocular suppression. Vision Res 21: 1055-1063.

28 Sireteanu R (1982) Binocular vision in strabismic humans with alternating fixation. Vision Res 22: 889-896.
29 Smith EL, Levi DM, Manny RE, Harwerth RS, White JM (1985) The relationship between binocular rivalry and strabismic suppression. Invest Ophthalmol Vis Sci 26: 80-87.
30 Travers T (1938) Suppression of vision in squint and its association with retinal correspondence and amblyopia. Brit J Ophthalmol 22: 577-604.
31 Tschermak A (1899) Ueber anomale Sehrichtungsgemeinschaft der Netzhäute bei einem Schielenden. Albrecht v Graefes Arch Ophthal 47: 508-550.
32 Wolfe JM (1986) Briefly presented stimuli can disrupt constant suppression and binocular rivalry suppression. Perception 15: 413-41.

The optimal stimulus to elicit suppression in small angle convergent strabismus

chapter VII

M.V. Joosse,[1,2] H.J. Simonsz,[1] H. Spekreijse,[3] P.G.H. Mulder,[1]
H.M. van Minderhout[1] and P.T.V.M. de Jong[3,4,5]

(submitted)

Abstract

We determined the optimal stimulus duration as well as the most appropriate luminance profile to elicit suppression in small-angle convergent strabismus. Suppression was found in 5 subjects with small-angle convergent strabismus, when tested haploscopically under binocular viewing with peripheral fusion. Three control subjects were also included in the study. Stimuli were shown randomly in the central 3° of the visual field of either eye. Stimulus durations were varied in seven steps from 50 to 1000 ms and three luminance-time profiles were used: square wave, triangle and half-sinus, thus yielding 21 different stimuli. The peak light intensity was the same for all stimuli. Suppression, defined as the difference in the threshold sensitivities under monocular vs. binocular viewing, was found with our test device in five of the ten subjects, and ranged between 3 and 33 dB. Suppression was deepest with triangular or half-sinusoidal stimuli of 400 ms duration. Square wave stimuli showed the smallest difference.

1 Department of Ophthalmology, University Clinic Rotterdam, The Netherlands.
2 Department of Ophthalmology, Westeinde Hospital, The Hague, The Netherlands.
3 The Netherlands Ophthalmic Research Institute, Amsterdam, &Academic Medical Centre, Amsterdam, The Netherlands.
4 Department of Biostatistics, Erasmus University, Rotterdam, The Netherlands.

CHAPTER VII

Introduction

Persons with strabismus without suppression are confronted with two visual disturbances: diplopia or confusion. Diplopia is the subjective perception of two identical images next to each other, that arises when an image is projected simultaneously on the fovea of the fixating eye as well as on an eccentric point of the retina of the squinting eye, or in general, when an image is projected on any other pair of non-corresponding points of the retina. Confusion is the subjective perception that arises when different images are projected on the fovea of the fixating eye as well as on the fovea of the deviating eye, or when two images are projected on any other pair of corresponding points of the retina. Based on studies performed decades ago, we now commonly agree that subjects with early-onset strabismus do not suffer from diplopia or confusion because under binocular viewing conditions they have suppression of the central part of the visual field of the deviating eye.[4, 10, 21] In small-angle convergent strabismus the ocular misalignment is compensated by a cortical mechanism called anomalous retinal correspondence (ARC) in the more peripheral part of the visual field so that binocular vision remains possible.[18]

Many authors state that suppression develops from rivalry between the dissimilar images falling onto the two retinas.[2, 5, 9, 12, 13, 16, 20] Rivalry occurs when images with different contours or colours are projected onto corresponding retinal points of the eyes. The observer sees parts of the image of either eye alternating over time. This has been very effectively demonstrated by Panum in 1858.[13] He presented a line grating to one eye and an orthogonally directed grating to the other eye. However, the literature is not conclusive whether the rivalry elicited in orthoptically normal subjects or persons with alternating strabismus, can be compared with the suppression (and rivalry) found in persons with constant angle strabismus. Some authors think it does,[2, 8, 15] whereas others believe it does not.[1, 3, 14, 19, 24]

Orthoptically normal subjects viewing orthogonally presented line gratings for presentation times of less than 150 ms, experience superposition of the images to the eyes. They see a mosaical pattern, consisting of an image composed of parallel lines seen by one eye, and orthogonally directed lines seen by the other eye.[23] For longer stimuli, Wolfe found fusion and suppression. In 1986, Wolfe showed that the time-course of the intermittent rivalry suppression in normals strongly resembles that of the more steady suppression in esotropes.[24] Belsunce & Sireteanu found that rivalry, suppression and superposition elicited by line gratings, occurred at other presentation times for normals than for strabismic amblyopes.[1] They found that suppression in esotropes can occur after 80 ms, whereas rivalry suppression occurs in normals after 150 ms. With single cell

recordings from binocularly driven cells in primary visual cortex of normal cat, Sengpiel et al. showed that suppression of rivalrous images occurs after 60 to 250 ms, thus leading to the conclusion that rivalry and suppression might indeed follow the same pathways.[16]

The issue addressed in the present study is whether in subjects with small angle strabismus the depth of suppression depends on the duration and luminance profile of the stimulus.

Methods and Subjects

In this study we present data obtained in five subjects with microstrabismus or small-angle convergent strabismus, as well as in three normal observers (their ophthalmic and orthoptic characteristics are given in Table 1). In all subjects, we performed a standard ophthalmic examination, including best corrected Snellen visual acuity, slit-lamp examination and indirect fundus examination after pupillary dilatation. An orthoptist performed an orthoptic examination consisting of cover test, 4 and 15 D prism test, prism cover test at 40 cm and at 6 m, measurement of objective and subjective angle of strabismus with the Synoptophore assessment of stereopsis with the Titmus fly test, Bagolini striated glasses test, and determination of fixation with direct fundus examination (Cueppers visuscope).

Four of the five subjects had microstrabismus according to Lang's definition,[7] i.e. convergent strabismus with an objective angle of squint less than 5° and ARC. All 8 persons were tested identically. In this testing, the subject had a haploscopic view via two surface silvered mirrors of two identical images of penguins in the snow mounted on the front plates of two Friedmann visual field analyzers. This identical haploscopically viewed visual background was also used in an earlier study on the size and depth of suppression scotomas in small angle esotropia and microstrabismus.[6] The viewing distance via the mirrors was 40 cm for each eye, with the surface-silvered mirrors halfway in between the screens. The mirrors were positioned at an angle of approximately 90° towards each other and at an angle of approximately 45° towards the screen as well as to the frontoparallel plane of the subject. The circular screens covered by the pictures subtended 50 degrees of arc. In the centre of the screens a blue fixation dot was placed, around which a square of four small holes (0.1 degree of arc in diameter) was positioned. The four holes were positioned at a distance of 1.5 degree of arc from the fixation dot. The mirrors could be adjusted horizontally and vertically, such that the subjective angle of squint could be corrected for and peripheral fusion could be obtained. Upon covering of the non-strabismic eye, a movement of the deviating eye occurred, that equalled the angle of ARC. During testing, full correction of

the refractive error was given with spectacles. For those who were above 40 years (cases 3 and 5) reading addition was given of +1.0D.

Each circular picture plate was mounted on a square box containing an electronically controlled circular fluorescent lamp (L4W/20, cool white). The baseline luminance level of these lamps gave a mean luminance across the screens of 5 Asb (in combination with illuminance by the room lights). With a pulse generator (Hewlett-Packard 3312 A) various luminance profiles could be presented: a square wave, a triangle and a half-sinusoid. For each stimulus profile, seven durations were used: 50, 100, 200, 400, 600, 800 and 1000 ms. All stimuli had the same peak light intensity and were randomly presented.

The baseline luminance level produced by the four stimulus holes was maintained at 0.1 log fL; the peak luminance of the four dot stimuli amounted to 1.55 log fL and could be reduced with neutral density (nd) filters in front of the centre of the screens. Filters of 3, 6 and 9 dB or multiples of them were used (0.3 nd equals 6 dB).

A standard test session consisted of firstly determining the threshold of each eye for each luminance profile and stimulus duration under monocular viewing, with the other eye occluded by a black non-translucent patch. During testing,

Table I — Orthoptic characteristics of 5 cases with suppression, 5 cases without suppression and 2 control subjects

Case #	age years	sex	eye	VA	refraction	fixation	squint type
Case 1	33	M	R	1.0	-2.75	fovea	L esotropia
			L	0.8	+1.75	fovea	
Case 2	28	M	R	1.0	plano	fovea	R microstr.
			L	1.0	plano	fovea	
Case 3	42	M	R	1.2	+1.0	fovea	R microstr.
			L	1.2	+1.0	fovea	
Case 4	30	M	R	0.5	+2.0	0.5° nas.	R microstr.
			L	1.2	+1.0	fovea	
Case 5	49	M	R	0.4	+4.0	0.5° nas.	R microstr.
			L	0.9	+2.5	fovea	
Contr.1	32	F	R	1.0	-5.0	fovea	ortho
			L	1.0	-4.5	fovea	
Contr. 2	34	M	R	1.0	plano	fovea	ortho
			L	1.0	plano	Fovea	
Contr.3	25	F	R	1.0	-3.0	Fovea	ortho
			L	1.0	-3.0	Fovea	

alt. = alternating; Bagolini = Bagolini's striated glasses test; centr = central; conv. = convergent strabismus; div. = divergent strabismus; DVD, dissociated vertical deviation; F = female, M = male; L = left; R = right; microstr. = microstrabismus; nas. = nasal; temp. = temporal; neg. = negative; pos. = positive; obj./subj. angle = objective/subjective angle of strabismus; tot. = total; supp. = suppression; occl. = occlusion therapy; surg. = surgery; VA = visual acuity

the subject was asked to fixate the blue dot in the centre of the screen. Following testing of each eye separately, both eyes were tested under binocular viewing with unrestrained cross eyedness. Under that condition stimuli were presented randomly to either eye. During this testing, the orthoptist performed regular unilateral cover testing to check whether the angle of strabismus remained constant. Under both monocular as well as binocular viewing, the stimuli were attenuated until they were just seen (just above threshold), and that value was noted. This was done by locking-in with filters of supra- and infra-threshold density in front of the tested eye. A positive response was scored if the subject saw all four light dots simultaneously. All responses were rechecked at least once at a different moment during the procedure. There was randomization to the luminance profile that was presented for each stimulus duration. There was also randomization as to which eye received the stimulus under binocular viewing conditions. During testing we simultaneously held filters in front of the tested and the non-tested eye so the subject would not know beforehand to which eye stimuli would be presented. Time between presentations was at least 3 s.

For each stimulus duration and luminance profile the results of testing under binocular viewing were subtracted from the results obtained under monocular

Bagolini	Stereopsis	obj. / subj. squint	angle	history
L tot. supp.	Fly neg.	6°/	varying	alt.conv.,str. at 4,no occl.
R centr. supp.	Fly pos.	4°/	4°	occl.at 3, conv. str. surg at 4
R centr. supp.	Fly pos.	1.5°/	1.5°	occl. at 3, conv surg. at 41
R centr. supp.	Fly pos.	0.5°/	0.5°	occl. at 4, div. surg at 28
R centr. supp.	Fly pos.	1°/	1°	occl. at 3. no surg.
neg.	Fly pos.	0°/	0°	glasses at 4
neg.	Fly pos.	0°/	0°	none
neg	Fly pos.	0°/	0°	glasses at 6

viewing to obtain the amount of 'net suppression' in dB. Two situations may occur. In the first the projection of the (pseudo) fovea shifts from the central blue fixation dot under monocular viewing to a more nasal position in the field under binocular viewing. The magnitude of this shift equals in degrees the objective angle of squint minus the angle of eccentric fixation. This situation applies to cases 1 and 2. In earlier tests we found that both cases 1 and 2 both have a suppression scotoma with a diameter of respectively 20° and 10° probably centered around the fixation point. Even with a shift of 6° (case 1) or 4° (case 2) the four stimulus dots would still be well within the borders of the suppression scotoma. In the second situation, the angle of eccentric fixation is identical to the objective angle of strabismus. In that situation, as exists in cases 3 to 5, there is no shift of the point of fixation under monocular vs. binocular viewing.

One subject (case 1) was tested two times on separate occasions and one control person (control 3) was tested three times on separate occasions to determine the precision and the reproducibility of our method. In these two persons we performed an analysis of variance. Reproducibility is defined as the absolute difference between two consecutive measurements within a patient that is only exceeded in 5% of the times. It is calculated as 1.96 times the square root of two times the within subject variance.

Results

In five subjects (cases 1-5) we were able to quantify the depth of suppression and found differences in this depth with duration and luminance profile of the stimuli. We found a maximal difference between the threshold sensitivities under binocular viewing and monocular viewing for stimulus lengths of 200 to 600 ms, irrespective of the luminance profile of the stimulus. In all five subjects there was a small difference between the depths of suppression: triangular stimuli showed slightly stronger suppression than the half-sinusoidal ones. With square wave stimuli the suppression was much weaker for nearly all stimulus durations.

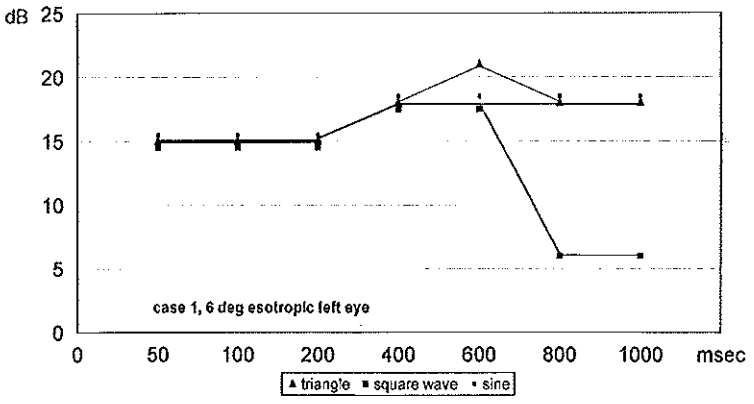
Cases 1 to 3 had under monocular viewing the same sensitivities (respectively 27, 33 and 36 dB) for each eye irrespective of luminance profile and stimulus duration. Only cases 4 and 5 showed a 3 dB sensitivity difference between the eyes under monocular viewing conditions. For the eyes without suppression, the sensitivity determined under monocular viewing was the same as under binocular viewing, except for case 4. He had a difference between monocular and binocular viewing of 3 dB in the left eye, compared to 30-33 dB in the right eye. Table 2 gives the sensitivities of the eyes with suppression measured under monocular as well as binocular viewing. Net suppression or the difference in sensitivity levels between monocular and binocular viewing are shown in Figs. 1 to 5.

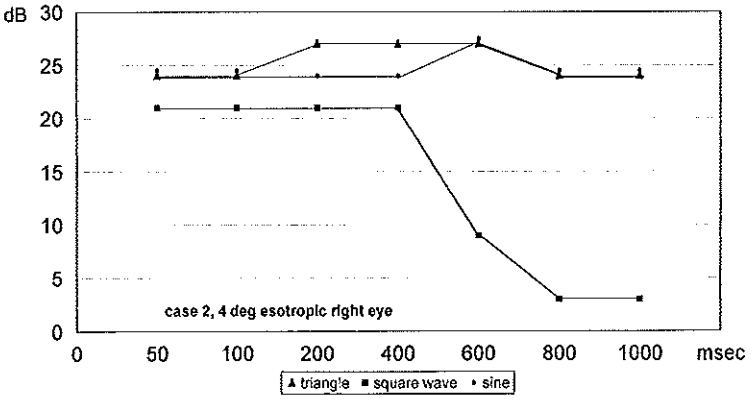
Case 1 was tested two times on separate occasions and an analysis of variance for each luminance profile was performed. Within-subject variance was 1.5 for triangular as well as sinusoidal stimuli and 1.125 for square wave stimuli. By regression analysis we found in his left, non-fixating eye an average difference between monocular and binocular viewing of 16.6 dB for triangular (standard error 0.986), 16.2 dB for sinusoidal (standard error 0.851) and 12.9 dB (standard error 1.105) for square wave stimuli, which is highly significant. In the right, fixating eye we found an average significant difference of 1.385 (std. error 0.697 and 0.601 respectively) for triangular and sinusoidal and 0.923 (std error 0.782) for square wave stimuli, which is also significant. In this case the reproducibility was 4.25 dB for sinusoidal and triangular stimuli and 3.90 dB for square wave stimuli. In the three control subjects we found sensitivity levels of 30-33 dB under monocular viewing conditions for all stimulus-durations and luminance-profiles. With binocular viewing we found a sensitivity level of 30-33 dB for either eye for all stimulus-durations and luminance-profiles. Control subject 3 was tested three times on separate occasions to perform analysis of variance for each luminance

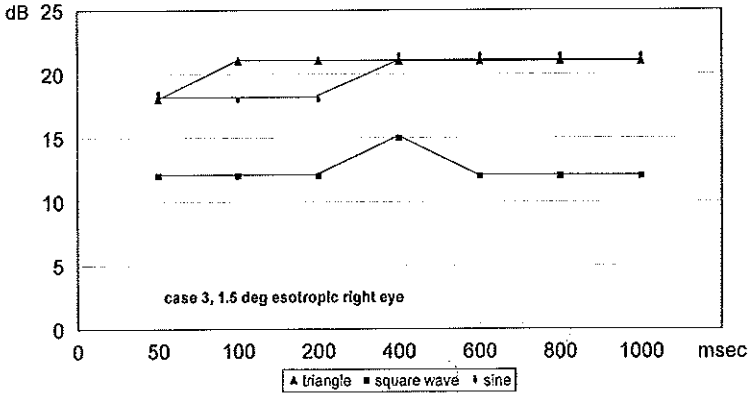
Table II — Sensitivity thresholds in dB under monocular and binocular viewing conditions for various stimulus durations and Luminance profiles in the five subjects with suppression.

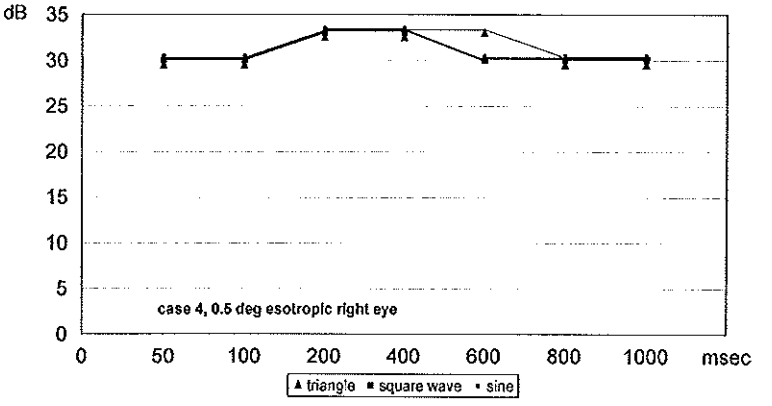
Case no. (Eye)		50 ms. mon/bin	100ms. mon/bin	200ms. mon/bin	400ms mon/bin	600ms. mon/bin	800ms. mon/bin	1000ms. mon/bin
Case 1	triangle	27/12	27/12	27/12	27/9	27/6	27/9	27/9
(LE)	sine	27/12	27/12	27/12	27/9	27/9	27/9	27/9
	square wave	27/12	27/12	27/12	27/9	27/9	27/21	27/21
Case 2	triangle	33/9	33/9	33/6	33/6	33/6	33/9	33/9
(RE)	sine	33/9	33/9	33/9	33/9	33/6	33/9	33/9
	square wave	33/12	33/12	33/12	33/12	33/24	33/30	33/30
Case 3	triangle	36/18	36/15	36/15	36/15	36/15	36/15	36/15
(RE)	sine	36/18	36/18	36/18	36/15	36/15	36/15	36/15
	square wave	36/24	36/24	36/24	36/21	36/24	36/24	36/24
Case 4	triangle	33/3	33/3	36/3	36/3	36/3	36/6	36/6
(RE)	sine	33/3	33/3	36/3	36/3	36/6	36/6	36/6
	square wave	33/3	33/3	36/3	36/3	36/6	36/6	36/6
Case 5	triangle	30/27	30/27	30/27	30/24	30/27	30/27	30/27
(RE)	sine	30/27	30/27	30/27	30/24	30/27	30/27	30/27
	square wave	30/27	30/27	30/27	30/27	30/27	30/27	30/27

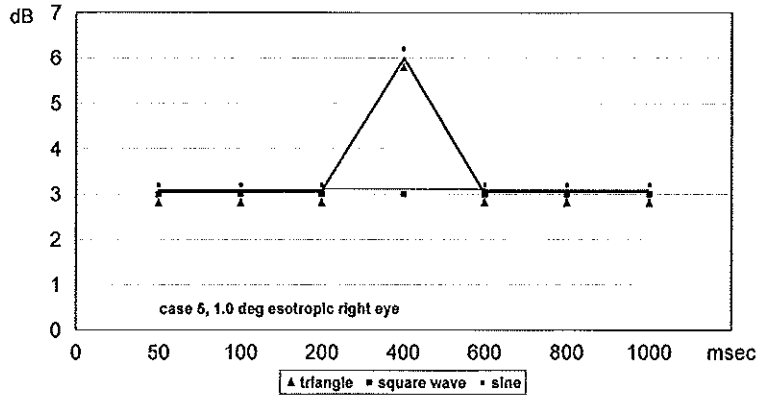
dB = decibels; ms. = milliseconds; mon = monocular viewing conditions; bin = binocular viewing conditions; LE = left eye; RE = right eye. Note, the net suppression levels for each luminance profile and stimulus duration can be easily obtained by subtraction of the sensitivities under binocular viewing from those under monocular viewing conditions.


dB 25
20
15
10
5
0
case 1, 6 deg esotropic left eye
0 50 100 200 400 600 800 1000 msec
triangle square wave sine


dB 30
25
20
15
10
5
0
case 2, 4 deg esotropic right eye
0 50 100 200 400 600 800 1000 msec
triangle square wave sine


dB 25
20
15
10
5
0
case 3, 1.5 deg esotropic right eye
0 50 100 200 400 600 800 1000 msec
triangle square wave sine





Figures 1, 2, 3, 4 and 5. Levels of 'net suppression' (dB) measured in the deviating eyes of cases 1-5 for stimulus durations between 50 and 1000 ms. Note that in order to validly make a subtraction of sensitivity thresholds obtained under binocular viewing conditions from those obtained under monocular viewing conditions a shift of the position of the fovea has to be taken into account; only for reasons mentioned in the methods section of this article, in cases 1-5 this subtraction could be performed without any adjustments. The data points are indicated by a black triangle for triangular stimuli, a, small round black dot for half-sinusoidal stimuli and a black square for square wave stimuli.

profile, stimulus duration and eye. For triangular stimuli we found a mean within subject variance of 1.071 (sd 1.464), and for sinusoidal and square wave stimuli of 1.179 (sd 1.54). Thus, for triangular stimuli the reproducibility was 2.87 dB, and for sinusoidal and square wave stimuli 3.02 dB.

Discussion

The main finding in this study is that a stimulus with a triangular or sinusoidal luminance-time profile and a duration of 400 ms elicits the strongest suppression in convergent strabismus. For stimuli of 200 ms or less, or longer than 600 ms, the depth of suppression was somewhat smaller. Triangular stimuli seemed to be more effective than half-sinusoidal stimuli; this was only significant when compared with the reproducibility of control 3 (2.87 dB for triangular and 3.02 dB for sinusoidal and square wave stimuli), when compared with the somewhat higher reproducibility of case 1 (4.25 dB for sinusoidal and triangular stimuli and 3.90 dB for square wave stimuli) there was no significant difference between these stimuli. Square wave stimuli were the least effective when compared with the reproducibility of control 3 in cases 1-3 and 5 and in cases 1-3 when compared with the reproducibility of case 1. Strikingly, under monocular viewing we did not find any change in sensitivity variations with stimulus profile and duration, except for case 4, in which a small increase in sensitivity was found with increasing stimulus duration. Although the amount of net suppression in case 5 seems rather small, it is especially striking that in this subject significant suppression was only detected with triangular and square wave stimuli of 400 ms (when compared with the reproducibility of control 3 as well as case 1).

We found a slightly biphasic stimulus-time relationship in depth of net suppression, with the greatest net suppression for stimulus durations ranging from 100 to 800 ms. What could be an explanation for our results? Summarizing the results of Wolfe[24] and Belsunce & Sireteanu[1], it can be stated that three situations can be observed when linear gratings positioned at right angles are presented for various time periods to the eyes of a person with strabismus. For presentation times shorter than 150 ms, there is superposition, for periods between 150 and 600 ms suppression prevails, and for times longer than 600 ms most strabismic subjects perceive rivalry between the orthogonal directed images.

Our test set-up differs strongly from the classical rivalry suppression experiments, with orthogonal line gratings, presented simultaneously to both eyes.[1, 23, 24] We presented a complex background to both eyes with light dots to only one eye. Therefore, it is particularly interesting that we found a time-course for the build-up of suppression, parallelling the one found by de Belsunce and Sireteanu.[1] This is a strong indication that rivalry and suppression in strabismus follow the same neuronal pathways.

In order to measure suppression, undisturbed binocular viewing is important, without dissociating factors that may shift attention to either eye. Flash stimuli are likely to have such a dissociating effect. Stimuli with a steep increment, like

square wave stimuli, behave flash-like and thus might be less effective to elicit suppression in contrast to triangular stimuli that behave the least flash-like. This most likely is the reason why stimuli with a triangular or a half-sinusoidal shape are the most effective to elicit suppression.

For very short presentation times, all luminance profiles can be considered flashlike. This might explain why we found the smallest difference between the three stimulus profiles in net suppression for durations as small as 50 ms. For longer stimulus durations, the triangular stimulus has the most gradual increment in luminance and thus would be most likely to be the stimulus with the least dissociating effect and hence the most effective to elicit suppression. The fact that we found a somewhat reduced level of suppression with short stimuli can be correlated with studies by Wales & Fox[22] and by Makous & Sanders[11] who found suppression in normals viewing rivalrous images with flash stimuli presented to one eye. However these authors agree that the level of suppression measured with a flash stimulus is lower than with a more steady stimulus.

In 2 subjects (cases 1 and 2) net suppression diminished for square wave stimuli with durations exceeding 600 ms. This may have been caused in these subjects by the occurrence of alternating fixation, which possibly may be more easily initiated by square wave stimuli, than by the other stimuli. Thus, square wave stimuli may because of their steep increment, behave similarly to short flash-like stimuli, in the sense that they draw attention to the fixating eye and are thus likely to break suppression.

In two subjects (cases 1 and 5) there was considerable anisometropia. It is possible that part of the suppression was caused by the anisometropia or by the aniseikonia caused by the spectacle correction thereof. Although there are no reports on suppression in strabismus and anisometropia, there is evidence that normals with one defocused eye, have suppression of stimuli presented to this eye while fixating with the other eye.[17] To separate the effects on suppression of strabismus from those of anisometropia a study of a larger group would be necessary, containing subjects with aniseikonia, with strabismus and with a combination of these conditions.

In this study, we determined the optimal stimulus for the quantitative measurement of suppression in convergent strabismus. Triangular and sinusoidal stimuli with a duration of 400 ms proved to be the most effective, and square wave stimuli of the same duration were the least effective. This result might be useful for future quantitative studies on suppression in strabismus.

References

1 Belsunce, S. de & Sireteanu, R. (1991). The time course of interocular suppression in normal and amblyopic subjects. Invest. Ophthalmol. Vis. Sci. 32, 2645-2652.

2 Blake, R. (1989) A neural theory of binocular rivalry. Psychol. Review, 96: 145-167.

3 Cogan,A.I. (1982). Monocular sensitivity during binocular viewing. Vision Res. 22: 1-16.

4 Harms, H. (1938). Ort und Wesen der Bildhemmung bei Schielenden, Albr. V. Graefe's Arch. F. Ophthalmol. 138, 149-210.

5 Hering, E. (1920). Grundzüge der Lehre vom Lichtsinn. Berlin, Verlag von Julius Springer.

6 Joosse, M.V., Simonsz, H.J. , Minderhout, H.M., Jong, P.T.V.M. de, Noordzij, B., Mulder, P.G.H. (1997). Quantitative perimetry under binocular viewing conditions in microstrabismus. Vision. Res., 37,19: 2801-2812.

7 Lang, J. (1968). Evaluation of small angle strabismus or microtropia. Strabismus Symposium, Giessen, Karger, Basle, pp. 219-222.

8 Leonards, U., Sireteanu, R. (1993). Interocular suppression in normal and amblyopic subjects: the effect of unilateral attenuation with neutral density filters. Perception & Psychophysics, 54, 1: 65-74.

9 Levelt, W.J.M.: On binocular rivalry, Soesterberg, The Netherlands, 1965, Institute for Perception RVD-TNO.

10 Mackensen, G. (1959). Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgänge beim Schielen. V. Graefe's Arch. F. Ophthalmol. 160:573-587.

11 Makous, W. and Sanders, R.K. (1978). Suppressive interactions between fused patterns. In Armington et al., Eds., Visual Psychophysics and Physiology, Academic Press, 167-179.

12 Ogle, K.N. (1962). The optical space-sense, In Davidson, H., ed: The eye. Vol. 4, New York, Academic Press.

13 Panum, P.L. (1858). Physiologische Untersuchungen über das Sehen mit zwei Augen. Schwerssche Buchhandlung, Kiel.

14 Schor, C.M. (1977). Visual stimului for strabismic suppression. Perception,6: 583-593.

15 Sengpiel, F, Blakemore, C, Kind, P.C., Harrad, R. (1994). Interocular suppression in the visual cortex of strabismic cats. J. Neurosci. 14, 11: 6855-6871.

16 Sengpiel, F., Blakemore, C., Harrad, R. (1995). Interocular suppression in the primary visual cortex: a possible neural basis of binocular rivalry. Vision Res. 35, 2: 179-195.

17 Simpson, T. (1992). Monocular acuity in the presence and absence of fusion. Optom. Vis. Sci. 69: 405-410.

18 Sireteanu, R. & Fronius, M. (1989). Different patterns of retinal correspondence in the central and peripheral visual field of strabismics. Invest. Ophthalmol. Vis. Sci. 30: 2023-2033.

19 Smith,E.L., Levi, D.M., Manny, R.E., Harwerth, R.S., White, J.M. (1985). The relationship between binocular rivalry and strabismic suppression. Invest. Ophthalmol. Vis. Sci. 26: 80-87.

20 Tour, E.F., du. (1760). Discussion d'une question d'optique. Mémoires de mathematique et Physique d'Académie Royale Science (Paris), 3: 514-530.

21 Travers, T.B. (1938). Suppression of vision in squint and its association with retinal correspondence and amblyopia. Brit. J. Ophthal. 22: 577-604.

22 Wales, R. and Fox, R. (1970). Increment detection thresholds during binocular rivalry suppression. Perception & Psychophysics, 8: 90-94.

23 Wolfe, J.M. (1983). Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion on briefly presented dichoptic stimuli. Perception. 12: 447-456.

24 Wolfe, J.M. (1986). Briefly presented stimuli can disrupt constant suppression and binocular rivalry suppression. Perception. 15: 413-417.

General discussion

chapter VIII

This thesis consists of five studies on the visual field in amblyopia and suppression in strabismus. For the sake of clarity, I will describe what amblyopia and suppression are. Amblyopia is partial loss of vision under monocular viewing conditions, following early onset monocular visual deprivation or strabismus in the absence of other ocular abnormalities. After the age of twelve it is usually permanent. Suppression is a fleeting partial loss of vision of one eye when looking with both eyes as an adaptation to unequal images to the eyes as in strabismus

Firstly, I measured the extent of the monocular visual field in primates with amblyopia induced by strabismus or by monocular occlusion (Chapters 3 and 4). Secondly, I measured the extent of the suppression scotoma in subjects with small-angle convergent strabismus (Chapter 5). Thirdly, I measured the extent of the suppression scotoma in subjects with divergent strabismus (Chapter 6). Finally, as a control study to check the methods employed in the latter two studies I defined the best presentation time and light profile to detect suppression in the squinting eye (Chapter 7).

The visual field is defined as that part of the environment that can be seen with an unmoving eye (relative in position to that eye). It extends upward, downward, temporally and nasally from the fixation point. The visual field of one eye extends in the horizontal meridian to 65 degrees on the nasal side and on the temporal side to 95°. The visual fields of both eyes overlap centrally. The visual field of one eye can therefore be divided in two segments: a central area that potentially can be seen by both eyes, the binocular segment, and a segment that is not seen by the other eye, the monocular temporal segment (the temporal crescent).

In lower vertebrates like fish, the eyes are positioned laterally in the skull and thus there is little or no overlap between the visual fields of the eyes, whereas the eyes of primates are pointing anteriorly, with a large area of overlap between the visual fields.[3] The advantage of this overlap is that it allows higher functions such as fusion and depth perception. How this advantage becomes a disadvantage, becomes clear when there is misalignment of the eyes, strabismus. It is commonly believed that in the case of strabismus, chronic suppression of a central part of the visual field of the deviating eye leads to amblyopia of that eye.

8.1 What are the effects of binocular interaction on the monocular visual field in strabismus and monocular deprivation: *Is amblyopia only a consequence of binocular competition?* (Chapters 3 and 4)

Wiesel and Hubel postulated that binocular competition is instrumental for amblyopia to occur and, thus, that amblyopia would only cause a defect in the binocular segment of the visual field.[11] This theory was based on their work in cats with amblyopia by early monocular deprivation through occlusion. It is commonly agreed that amblyopia due to monocular occlusion as well as due to strabismus may cause field defects in the binocularly perceived central part of the monocular visual field.

The question is, however, whether the monocularly perceived segment is unaffected in amblyopia. Our observations in primates with amblyopia due to strabismus as well as to early monocular occlusion do not fit completely with the model of binocular competition. In several monkeys with monocular deprivation or strabismus we found a defect in the monocularly perceived temporal crescent. This finding leads to the conclusion that apart from the mechanism of binocular competition, there has to be another mechanism responsible for these temporal field defects in monkeys.

The reduction of the sensitivity across the whole monocular visual field in some monkey eyes with monocular occlusion also cannot be explained by Wiesel and Hubel's model alone. This could be more in concordance with the cell shrinkage in both the monocularly as well as the binocularly driven cells of the lateral geniculate nucleus as described by Vital-Durand et al.[10] and Lin & Kaas[6] in monkeys with monocular occlusion.

As a general observation, it can be stated that there seems to be a species difference in the effect of deprivation amblyopia on the extent of the visual field obtained under monocular viewing conditions. Cats have the largest defects, mainly in the binocularly perceived nasal half of the visual field,[8,9] monkeys have smaller defects,[4,12] and humans the smallest to none.([2,7] and our own observations).

Although the effects of severe monocular deprivation have not been studied systematically in humans it might still be possible that the defects in the binocularly perceived part of the visual field as found in cats might also occur in humans with severe monocular deprivation (e.g. congenital unilateral cataract). Our own observations in humans indicate that early-onset strabismus does not have any effect on the visual field obtained under monocular viewing conditions. However, we did not test patients with a visual acuity below 0.03. Thus the possibility that even deeper strabismic amblyopia might still cause field defects cannot be ruled out. It is also possible that some cases with untreated amblyopia and convergent strabismus might still have a central visual field defect. However, we did not come across such patients. Our data could lead to the conclusion that humans (and monkeys) might be more resistant to visual deprivation than cats.

8.2 What is the extent of the visual field under binocular viewing conditions in small angle convergent strabismus; *how does binocular competition affect the visual field under binocular viewing conditions?*

(Chapter 5)

Chapter 8.1 dealt with the problem we have with the application of the principle of binocular competition on our findings in the monocular crescent of the monocular visual field. The chapter below concerns the application of this principle to the central part of the binocular visual field in microstrabismus, defined as small convergent strabismus (< 6°) with a low degree of binocular functions.

In a number of subjects with microstrabismus we found a small approximately circular suppression scotoma in their strabismic eye. In the following I will give our explanation why we specifically found round or slightly oval scotomas. This shape can fully be explained by the working hypothesis communicated to us by Sireteanu at the Meeting of the Bielschowsky Gesellschaft in Heidelberg, 1992. For this hypothesis it is important to explain the concept of the receptive fields. A receptive field is an area in the visual cortex corresponding with a small round part of the visual field of one or both eyes (2-8° in diameter). In the receptive fields there are three types of cells: those corresponding with the right eye, the left eye and those corresponding with both eyes simultaneously. These receptive fields are greater in the periphery of the visual field than for the center. During early postnatal development, the receptive fields shrink and become mature by the end of the first year of life.

For microstrabismus, Sireteanu suggested that in the center of the visual field where the receptive fields are smallest there can be no overlap of the receptive fields of the eyes (because of the small angle of strabismus) so suppression of

the deviating eye is needed. In the more peripheral part of the visual field, where the receptive fields are larger, overlap between the receptive fields of the fixating and the microstrabismic eye is possible because the angle of strabismus is smaller than the size of the peripheral receptive fields. This permits some binocular vision, however with a slightly horizontally shifted image in the deviating eye. The latter is called anomalous retinal correspondence (ARC). As mentioned in the Introduction, this is an internal squint on a cortical level, which compensates for an external squint of up to 6°. ARC can result in paradoxical diplopia in some adult strabismus patients, following cosmetically perfect surgical alignment of the eyes. This result has puzzeled strabismus surgeons ever since the first operation. But Sireteanu's hypothesis explains this very well. In a way, Sireteanu's hypothesis can be considered as an application of Hubel and Wiesel's general principle of binocular competition.

Upon closer analysis of our data in small angle strabismus it could be possible that the suppression scotomas we found are slightly oval (with horizontal elongation). This would be in concordance with the early work by Wertheim. He mentioned in 1894 that measured from the fovea, visual acuity drops off steeper in the vertical direction,than in the horizontal direction.[11] This again could correlate with the fact that the receptive fields increase more rapidly in size in the vertical than in the horizontal direction.

Between subjects the extent of the suppression scotoma varied significantly. In part, we think that the size of a suppression scotoma varies with individual variations in the size of the receptive fields and thus also with the angle of strabismus. In some of our subjects we found this correlation, in others we did not. In part the size of the scotoma might correlate with the amount of anisometropia. It is a clinical fact that anisometropia is very common in microstrabismus. Indeed, two out of four of our subjects with a measurable suppression scotoma had anisometropia greater than 1 diopter. Larger groups of microstrabismic subjects with and without anisometropia are necessary to confirm any conclusions on the effects of anisometropia on the size of the suppression scotoma in microstrabismus. Also the size and the depth of suppression scotomas might vary for reasons unknown and might just be individually determined. Some people need strong suppression to protect them against diplopia, whereas others need little to none.

8.3 What is the nature of the suppression scotoma in divergent strabismus; *are there differences between primary and consecutive divergent strabismus?* (Chapter 6)

In subjects with divergent strabismus there is less overlap between the visual fields of the eyes than in normals. This situation gives less interaction or competition

between the eyes. This might be the reason that we did not find such well-defined scotomas in the center of the field of the non-fixating eye as we observed in subjects with small angle-convergent strabismus. In many cases our subjects with divergent strabismus had total suppression of one eye. We believe that most persons with divergent strabismus might have alternating total suppression. As a matter of fact the majority of our subjects could readily shift fixation to either eye and thus simultaneously might suppress the non-fixating eye. Since there is less overlap between the visual fields of the eyes, there is also less need for abnormal correspondence between the eyes.

8.4 What is the optimal stimulus to elicit suppression in strabismus? (Chapter 7)

In order to validate our methods of measurement of suppression we also determined the optimal stimulus to perform perimetry under binocular viewing conditions and measure suppression. We found that a light stimulus with a triangular profile and a duration of 400 ms is best to detect suppression in strabismus.

In simultaneous perception five situations can be described. The first situation occurs, when identical images are seen by straight eyes (orthotropic). Here, fusion and stereopsis are possible. The second occurs, when rivalling images are presented to straight eyes, such as a field of parallel lines shown to one eye and a field of orthogonallly directed (parallel) lines to the other eye for a very brief period of time (<100 ms). Here the subject sees parts of the image of one eye mixed with parts of the image of the other eye. The third, when rivalling images are shown to straight eyes for a prolonged period of time (> 800 ms). Here, the subject alternately sees the image shown to the one eye followed by the image shown to the other eye (rivalry). These three situations have been described by Wolfe[14] and by De Belsunce and Sireteanu.[1] The fourth situation occurs when similar images are briefly shown to crossed (strabismic) eyes. Here, a combined, probably diplopic image is seen. The fifth situation occurs when similar images are shown to crossed eyes for a period greater than 500 ms. These situations have been described by Wolfe[15] and by De Belsunce and Sireteanu[1] and Leonards and Sireteanu.[5] These findings are in concordance with our results. We found that suppression needs some time to build up and and can optimally be detected with light stimuli of 400 ms.

In order to measure suppression, undisturbed binocular viewing is important. Factors that shift attention to one eye are likely to break suppression. Flash stimuli tend to have such a dissociating effect. In a way, all stimuli with a steep increment like square wave stimuli or short triangular stimuli behave flash-like, and thus are likely to be dissociating. To put it differently, the more gradual the increment of the luminance profile of the stimulus, the better suppression can be

elicited. This might lead to the conclusion that the amount of suppression might be inversely correlated with the value of the first derivative (the differential value obtained by integration) of the luminance profile of the stimulus. This could explain why square wave stimuli which ideally have an infinite derivative value as well as short triangularly shaped stimuli with obviously also a high derivative are less effective to elicit suppression.

Flash stimuli as are often present in visual field analyzers (e.g. the Humphrey field analyzer) are too dissociating. The Humphrey field analyzer uses square wave stimuli of 200 ms. This makes this device less appropriate for the quantitative measurement of suppression. Also, orthoptists measuring suppression with a synoptophore (amblyoscope) should make an effort not to alternate too quickly between the eyes, but present the images at least for a period of 400 ms.

References

1 Belsunce S de & Sireteanu R (1991). The time course of interocular suppression in normal and amblyopic subjects. Invest Ophthalmol Vis Sci 32: 2645-2653.
2 Braun, G. (1934). Gesichtsfelduntersuchungen bei Schielenden. Klin. Mbl. Augenheilk. 92, 600-613.
3 Crone, R.A. (1973). Diplopia. Excerpta Medica, Amsterdam.
4 Joosse, M.V., Wilson, J.R., Boothe, R.G. (1990). Monocular visual fields of macaque monkeys with naturally occurring strabismus. Clin. Vision Sci. 5, 2: 101-111.
5 Leonards, U. and Sireteanu, R. (1993). Interocular suppression in normal and amblyopic subjects: The effect of unilateral attenuation with neutral density filters. Perception & Psychophysics, 54,1: 65-74.
6 Lin, C.S. and Kaas, J.H. (1980). Effects of monocular deprivation on geniculocortical pathways in the owl monkey, Actus trivargatus, Neurosci. Lett. 18 267-273
7 Mackensen, G. (1959). Monoculare und binoculare statische Perimetrie zur Untersuchung der Hemmungsvorgaenge beim Schielen. v. Graefes Arch. f. Ophthalmol. 160: 573-587.
8 Sherman, S.M. (1973). Visual field defects in monocularly and binocularly deprived cats.Brain Res. 49, 25-45.
9 Van Hof-van Duin, J (1977). Visual field measurements in monocularly deprived and normal cats. Exp. Brain Res. 30, 353-368.
10 Vital-Durand, F., Garey, L.J. and Blakemore, C. (1978) Monocular deprivation in the monkey: morphological effects and reversibility. Brain Res. 158: 45-64.
11 Wertheim, T. (1894). Ueber die indirekte Sehschärfe. Zeitschrift für Psychologie und Physiologie Sinnesorgane. 7, 172-241.
12 Wiesel, T.N. & Hubel, D.H. (1963). Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. J. Neurophysiol. 26: 978-993.
13 Wilson J.R., Lavallee K.A., Joosse M.V., Hendrickson A.E., Boothe R.G. and Harwerth R.S. (1989). Visual fields of monocularly deprived macaque monkeys. Behav. Brain Res. 33, 13-22.
14 Wolfe, J.M. (1983). Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion on briefly presented dichoptic stimuli. Perception. 12: 447-456.
15 Wolfe, J.M. (1986). Briefly presented stimuli can disrupt constant suppression and binocular rivalry suppression. Perception. 15: 413-417.

Summary

It is not exactly known how people with strabismus with or without amblyopia perceive the world. The work presented in this thesis tries to elucidate this issue by means of visual field analysis. In other words, we determined the effects of binocular interaction or competion on the visual field. When applied under monocular viewing conditions, visual field analysis can help in the quantification of the amount of amblyopia. When applied under binocular viewing conditions, visual field testing can give insight in the exact amount of suppression in persons with strabismus. In short, our work aims to answer three questions.

1 What is the effect of deprivation amblyopia on the extent of the visual field under monocular viewing conditions in primates?
2 What is the optimal stimulus to elicit (strabismic) suppression?
3 What is the effect of strabismic suppression on the extent of the visual field under binocular viewing conditions in humans?

In Chapter 2 an overview of the literature on perception in strabismus with special emphasis on the visual field is given. Most studies on the extent of the visual field in monocular deprivation were performed in cats. In these animals an amblyopic visual field defect was found in the binocularly perceived part of the visual field of the deprived eye. This finding is in concordance with Hubel & Wiesel's theory on amblyopia. They stated that the effects of amblyopia are the consequence of binocular competition in the geniculate body and the visual cortex. Thus according to this theory, amblyopia can only cause a field defect in the binocular segment of the visual field and not in the far temporal periphery (temporal crescent).

In Chapters 3 and 4 three studies are presented on the visual field under monocular viewing conditions in amblyopia in primates. The first study involved Macaca nemestrina monkeys with monocular occlusion early in life. When testing only the horizontal axis of their visual field we found a range of field defects across the study groups. Animals with prolonged occlusion from birth on, lasting at least 12 months, had total absence of perception across the field of the affected eye. In cases with later onset of occlusion (3 weeks to 1 year) it resulted in only a defect in the temporal periphery. Three conclusions can be drawn from these data: the earlier occlusion was given, the more extensive the field defect would be; the longer the duration of deprivation, the greater the field defect; binocular competition cannot explain amblyopic field defects found in monkeys.

The same method of horizontal profile perimetry under monocular viewing conditions was also performed in Macaque monkeys with naturally occurring convergent strabismus. We found a field loss in the far temporal periphery of the squinting eye of three out of six cases with non-alternating convergent strabismus. In the three cases with alternating strabismus we did not find any field defect. On the basis of these results it can be stated that the mechanism of binocular competition also does not play an active role in strabismic amblyopia in monkeys.

In human subjects with convergent strabismus and amblyopia with a visual acuity (VA) ranging between 0.03 and 0.8 we performed kinetic Goldmann perimetry under monocular viewing conditions. In these subjects we did not find field defects. Therefore it can be stated that strabismic amblyopia with the above mentioned visual acuities is not associated with any visual field defects in humans.

In Chapter 5 data are presented on the visual field under binocular viewing conditions in human subjects with small angle convergent strabismus. Most studies determined the size of the suppression scotoma, some others measured the depth across the horizontal meridian. Our study aimed at quantifying both the depth as well as the size of the suppression scotoma. We performed our tests with two Friedmann visual field analyzers that were viewed haploscopically via mirrors. On the surfaces of each field analyzer a complex picture was attached, which facilitated peripheral fusion on the basis of ARC. This imitated natural viewing conditions as much as possible. By subtracting data obtained under binocular viewing conditions from those obtained under monocular viewing, the extent of the suppression scotoma in these cases could be quantified. In five out of 14 cases with small angle convergent strabismus we were able to find a well-defined suppression scotoma in their strabismic eye. These scotomas had a diameter of 5° to 30° and a depth ranging from 4 to 14 dB. These scotomas were centered around the fixation point of the squinting eye, in some cases also

encompassing the foveal area. No suppression scotomata could be detected in the nine other subjects or in four normal observers.

Chapter 6 deals with the extent of the suppression scotoma in subjects with primary and consecutive divergent strabismus. The cases with consecutive divergent strabismus developed their divergent status following strabismus surgery up to the age of 14 years. Again a set up with two haploscopically viewed Friedmann field analyzers was used. Since subjects with divergent strabismus do not have ARC, the most natural viewing conditions were obtained by placing an eccentric fixation spot on each screen of both field analyzers. Again, by subtracting data obtained under binocular from those obtained under monocular viewing, the amount of net suppression could be determined. In 12 of the 15 subjects, we found a large area of suppression encompassing the projection of the fixation point as well as that of the fovea in the non-fixating eye under binocular viewing conditions. In two of these 12 cases, one with primary and one with consecutive divergent strabismus, the area of suppression was located nasally to the position of the fovea in the field of the non-fixating eye (nasal hemisuppression). In another two cases with divergent squint combined with vertical deviation, a small fixation point suppression scotoma was found. The depth of suppression ranged from 3 to 16 dB. In one subject only, no suppression was found. Two conclusions can be drawn from our data: the shape of the suppression scotoma is neither related to the origin of divergent strabismus nor to the angle of squint; the critical age for the development of suppression in divergent squint might be up to 14 years.

In Chapter 7 we determined which stimulus is optimal to elicit suppression in small angle convergent strabismus. In most reports on the measurement of suppression scotomas in the literature no emphasis has been put on the duration or the luminance profile of the stimulus. On the basis of rivalry experiments it has been found that rivalry-induced suppression takes some time to build up. Under 100 ms there is superposition of rivalrous images, between 100 and 500 ms suppression can be found, for durations longer than 500 ms there is rivalry of the images shown to the eyes.

In our test set up, stimuli with seven durations ranging from 50 to 1000 ms and with three luminance-time profiles were used: square wave, triangle and half-sinus, thus yielding 21 different stimuli. Suppression was found in five out of ten subjects, and ranged between 3 and 33 dB. Suppression was most outspoken with triangular stimuli of 400 ms duration. Half-sinusoidal stimuli of 400 ms were slightly less effective and square wave stimuli elicited the smallest amount of suppression.

With the studies presented in this thesis I think to have given more insight into how people with strabismus perceive the world and I hope it will stimulate future research into the field of perception in strabismus. Our findings might be of help to both clinical ophthalmologists as well as orthoptists in prescribing prism glasses or planning strabismus surgery.

Samenvatting

Het is niet geheel bekend hoe personen met scheelzien met of zonder amblyopie de wereld zien. Het onderzoek beschreven in dit proefschrift tracht dit deels op te helderen door middel van gezichtsveld analyse. In andere woorden, we bepaalden de invloed van binoculaire interactie of competitie op het gezichtsveld. Gezichtsveld onderzoek, verricht onder monoculaire omstandigheden, kan naast meting van de gezichtsscherpte de mate van amblyopie nader kwantificeren. Gezichtsveld onderzoek verricht onder binoculaire omstandigheden verschaft inzicht in de de exacte mate van suppressie in personen met scheelzien. In het kort beoogt ons onderzoek de volgende vragen te beantwoorden:

1. Wat is het effect van deprivatie amblyopie op de omvang van het gezichtsveld onder monoculaire omstandigheden in primaten?
2. Wat is de optimale stimulus om (scheelziens-)suppressie op te wekken?
3. Wat is het effect van scheelziens suppressie op de omvang van het gezichtsveld onder binoculaire omstandigheden in mensen?

Hoofdstuk 2 geeft een overzicht van de literatuur op het gebied van de perceptie bij scheelzien. Hierbij is speciale aandacht gegeven aan het gezichtsveld. De meeste studies naar de omvang van het gezichtsveld bij monoculaire deprivatie zijn verricht bij katten. Bij deze dieren is het amblyope gezichtsveld defect met name gevonden in het binoculair waargenomen deel van het gezichtsveld van het oog met deprivatie. Deze bevinding komt overeen met de theorie van Hubel

en Wiesel over amblyopie. Zij stellen dat de effecten van amblyopie de consequentie zijn van binoculaire competitie in het corpus geniculatum laterale en de visuele cortex. Daarom kan volgens deze theorie amblyopie alleen een gezichtsvelddefect geven in het binoculaire segment van het gezichtsveld en niet in de temporale periferie.

In de hoofdstukken 3 en 4 worden drie studies gepresenteerd over het gezichtsveld onder monoculaire omstandigheden bij amblyopie in primaten. De eerste studie betrof Macaca nemestrina apen met monoculaire occlusie kort na de geboorte. Bij het testen van de horizontale as van het gezichtsveld vonden we diverse gezichtsvelddefecten voor de verschillende studiegroepen. Dieren waarbij vanaf de geboorte langer dan 12 maanden occlusie was toegepast, hadden een totaal afwezige waarneming over het gehele gezichtsveld van het aangedane oog. In gevallen met latere aanvang van de occlusie (3 weken tot 1 jaar) werd slechts een defect in de temporale periferie gevonden. Naar aanleiding van deze resultaten kunnen drie conclusies getrokken worden: hoe vroeger de occlusie wordt gegeven, hoe groter het gezichtsvelddefect zal zijn; hoe langer de duur van de deprivatie, hoe groter het defect; binoculaire competitie kan de amblyope gezichtsvelddefecten in apen niet verklaren.

Dezelfde methode van horizontale profiel perimetrie onder monoculaire omstandigheden werd ook toegepast in makaken met aangeboren convergent scheelzien. Wij vonden een gezichtsvelddefect in de uiterste temporale periferie van het schele oog in drie van de zes apen met niet-alternerend scheelzien. In drie gevallen met alternerend scheelzien, vonden wij geen gezichtsvelddefect. Op basis van deze resultaten kan gesteld worden dat het mechanisme van binoculaire competie ook geen actieve rol in scheelziens amblyopie bij apen speelt.

In personen met convergent scheelzien en amblyopie met een gezichtsscherpte reikend van 0,03 t/m 0,8, werd kinetische Goldmann perimetrie verricht onder monoculaire omstandigheden. In deze personen vonden we geen gezichtsvelddefecten. Dit leidt tot de conclusie dat een amblyopie met deze gezichtsscherpte bij de mens niet geassocieerd is met gezichtsvelddefecten.

In Hoofdstuk 5 worden resultaten gepresenteerd van studie naar het gezichtsveld onder binoculaire omstandigheden in personen met convergent scheelzien met kleine hoek. In de meeste studies werd de grootte van het suppressiescotoom onderzocht, terwijl in sommige studies juist alleen de diepte van de suppressie in de horizontale meridiaan werd getest. Onze studie had juist het doel om zowel de grootte als de gehele omvang van het suppressie scotoom te bepalen. Wij hebben onze tests verricht met twee Friedmann field analyzers, die simultaan via spiegels waargenomen konden worden. Op het oppervlak van de field analyzers was een

foto aangebracht, welke perifere fusie op basis van anomale retinale correspondentie mogelijk maakte. Hierdoor werden natuurlijke visuele omstandigheden zoveel mogelijk gesimuleerd. Door subtractie van de uitkomsten verkregen onder binoculaire omstandigheden van die verkregen onder monoculaire, kon de afmeting en de diepte van het suppressiescotoom bepaald worden.

In vijf van de 14 gevallen met convergent scheelzien met kleine hoek kon een goed afgrensbaar rond suppressiescotoom in het scheelziende oog worden gevonden. Deze scotomen hadden een diameter van 5 tot 30° en een diepte varierend van 4 tot 14 dB. De scotomen waren gecentreerd rond het fixeerpunt van het scheelziende oog, in sommige gevallen het foveale gebied omvattend. Er kon geen suppressiescotoom worden gevonden in negen andere proefpersonen noch in vier normale controle personen.

Hoofdstuk 6 behandelt de omvang van het suppressiescotoom in personen met primair en consecutief divergent scheelzien. De personen met consecutief divergent scheelzien hadden hun divergente stand ontwikkeld na scheelziens operatie voor de leeftijd van 14 jaar. Wederom werd een opstelling toegepast bestaande uit twee haploscopisch waargenomen Friedmann field analyzers. Omdat personen met divergent scheelzien gewoonlijk geen anomale retinale correspondentie hebben, werden de meest natuurlijke omstandigheden verkregen, door plaatsing van een eccentrische fixatie stimulus op het scherm van beide Friedmann Field analyzers. De mate van suppressie werd weer bepaald door middel van subtractie van de data verkregen onder binoculaire omstandigheden van die verkregen onder monoculaire. In 12 van de 15 patienten, vonden wij een groot gebied van suppressie dat zowel de projectie van het fixeerpunt als ook die van de fovea omvatte in het niet-fixerende oog onder binoculaire omstandigheden. In twee van de 12 patienten (een met primair en een met consecutief divergent scheelzien) was het supressie gebied gelocaliseerd nasaal van de projectie van de fovea in het gezichtsveld van het niet-fixerende oog (nasale hemisuppressie). In twee andere patienten met divergent scheelzien in combinatie met een verticale deviatie, werd een klein fixeerpunt suppressie scotoom gevonden. De diepte van de suppressie varieerde tussen de verschillende personen van 3 tot 16 dB. In één persoon kon geen suppressie worden aangetoond. Aan de hand van onze bevindingen kunnen twee conclusies worden getrokken: de vorm van het suppressiescotoom is niet gerelateerd aan de oorzaak van het divergente scheelzien, noch aan de grootte van de scheelzienshoek; de kritische leeftijd voor de ontwikkeling van suppressie in divergent scheelzien reikt tot de leeftijd van 14 jaar.

In Hoofdstuk 7 wordt bepaald welke stimulus het meest geschikt is om suppressie in personen met convergent scheelzien te detecteren. In de meeste studies van

suppressiescotomen is geen nadruk gelegd op de duur of het luminantie-profiel van de stimulus. Op basis van de rivaliteits experimenten, is gebleken dat de suppressie die optreedt bij rivaliteit enige tijd nodig heeft om op te bouwen. Voor stimuli met een duur van minder dan 100 ms bestaat superpositie van de rivaliserende beelden, bij stimuli van 100 tot 500 ms treedt suppressie in en bij stimuli langer dan 500 ms ontstaat rivaliteit van de beelden.

In onze onderzoeksopstelling werd gebruik gemaakt van stimuli met zeven tijdsduren en drie luminantie profielen: blokvormig, driehoekig en half sinusoidaal, resulterend in 21 verschillende stimuli. Suppressie werd gevonden in vijf van de tien onderzochte personen en varieerde tussen 3 en 33 dB. Suppressie was het sterkst aanwezig bij driehoekige stimuli met een lengte van 400 ms. Half-sinusoidale stimuli van 400 ms waren iets minder effectief, gevolgd door blokvormige stimuli, welke de geringste suppressie konden oproepen.

Door middel van de studies beschreven in dit proefschrift denk ik meer inzicht te hebben gegeven in hoe mensen met scheelzien de wereld waarnemen en ik hoop dat de resultaten een stimulans zullen zijn voor verder onderzoek op het gebied van perceptie bij scheelzien. Onze bevindingen kunnen behulpzaam zijn bij het werk van oogartsen en orthoptisten bij het voorschrijven van prismaglazen of bij de planning van scheelziens-chirurgie.

Dankwoord
Acknowledgements

In de twaalf jaar voorafgaande aan de verschijning van dit proefschrift heb ik met zeer veel mensen een prettige en vruchtbare samenwerking gehad.

Professor de Jong. Paulus, ik wil je bedanken voor je niet aflatende inzet en coaching bij de tot stand koming van dit proefschrift. Jouw nuchtere blik op soms complexe vraagstukken heeft mij altijd veel steun gegeven. Zonder jou zou het veel langer geduurd hebben.

Doctor Simonz. Huib, ik weet niemand die meer kennis bezit over dit onderwerp dan jij. Jouw vernieuwende inzichten zijn zeer belangrijk voor de strabologische gemeenschap in zijn geheel. Ik kan nog steeds veel van je leren.

Professor Boothe. Ron, if it was not for you and Jim, I would not have entered the field of research on the visual system. While I really enjoyed working in your lab, I laid both a basis for this PhD research project as well as for my choice to work in the field of ophthalmology. I also want to thank the wonderful people at Yerkes Research Center, that I have worked with for their support.

Professor Sireteanu. Ruxandra, you are an example to researchers in the field of visual science. Your work has always fascinated and inspired me.

Professor Collewijn, dank u voor de ondersteuning bij de eindfase van de totstandkoming van mijn proefschrift.

Professor van Rij. Riel, jou ken ik eigenlijk het langste van iedereen. Dank je voor de tijd die je gegeven hebt om mijn proefschrift te beoordelen.

Professor Spekreijse. Henk, ik bewonder jouw kennis van en inzicht in visual science. Jij hebt me de waarde getoond van bondige en heldere wetenschappelijke

taal. Jouw ideeen zijn zeer belangrijk geweest bij de totstand koming van met name het zevende hoofdstuk van dit proefschrift.

Dr. van Osch en Drs. Sterfanovic. Loes en Maja, ik ben blij dat ik jullie als collega's heb. Zonder jullie steun bij mijn promotie-werkzaamheden was het zeker niet gelukt.

Drs. Dobbe. Lia, het enthousiasme waarmee jij het oogheelkundige vak maar ook het dagelijkse leven benadert, heeft op mij altijd een aanstekelijk effect.

Mevrouw van Minderhout, orthoptiste. Ellen, jouw inzet en inzicht hebben mij altijd zeer veel geholpen.

Professor Marani. Enrico, hoewel we elkaar nu niet zo vaak meer zien, wil ik je bijzonder bedanken voor de ondersteuning die je mij hebt gegeven in de beginfase van het onderzoek.

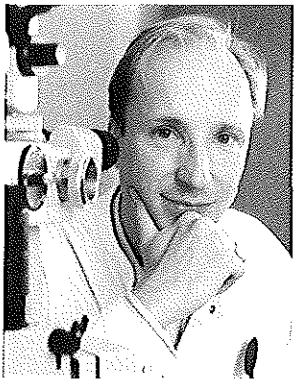
BOOST-R. Marieke, Chris en Jerry, zonder jullie hulp zouden de laatste loodjes wel erg zwaar zijn geweest.

Alle proefpersonen en apen wil ik danken voor hun medewerking.

Tot slot wil ik ook de niet met naam genoemde personen die direkt of indirekt hebben bijgedragen aan de totstand koming van dit proefschrift bedanken.

Bovenal Arjan.

Curriculum Vitae



Maurits Victor Joosse was born on november 15th, 1962 in the Hague, the Netherlands. He passed secondary school 1981 at the 'Eerste Vrijzinnig Christelijk Lyceum' in the Hague. From 1981 to 1982 he studied Law at Leiden University.

In 1982 he started his medical training at Leiden University. From 1987 to 1988 he performed research on the visual field in monkeys with strabismus and amblyopia at Yerkes Regional Primate Research Center in Atlanta, Georgia, U.S.A under the supervision of Prof. Dr. R.G. Boothe. This work constituted the basis for this thesis. In 1990 he graduated from Leiden Medical School (cum laude). From 1990 until 1991 he worked as a resident at the Department of Neurology of the Leyenburg Hospital in the Hague. From 1991 until 1995 he took his training in ophthalmology at the Department of Ophthalmology of the Dijkzigt Academic Hospital in Rotterdam under the supervision of Prof. Dr. P.T.V.M. de Jong. In this clinic he continued his research on the visual field in strabismus and amblyopia together with Dr. H.J. Simonsz, ophthalmologist. From 1995 he works together with colleagues L.D.M. van Osch and M. Stefanovic as an ophthalmologist at the Department of Ophthalmology of the Westeinde Hospital in the Hague.