Binocular Eye Movements in Humans: From Optimal Binocularity to Strabismus

Binoculaire oogbewegingen bij mensen: van optimale binoculaire coördinatie tot scheelzien

Proefschrift
ter verkrijging van de graad van doctor
aan de Erasmus Univeristeit Rotterdam op gezag van
de Rector Magnificus Prof.dr.ir. J.H. van Bemmel
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 26 juni 2002 om 13.45 uur

door

Anna Frederika van Leeuwen
geboren te Rotterdam

Promotiecommissie

Promotor:	Prof.dr. H. Collewijn
Overige leden:	Prof.dr. C. J. Erkelens Prof.dr. G. van Rij Prof.dr. C.I. de Zeeuw
Copromotor:	Dr. J. van der Steen

Drukwerk verzorgd door drukkerij Macula bv, Boskoop, www.macula.nl
De specialist in minder milieubelastend drukwerk.

The studies presented in this thesis were performed at the Neuroscience Institute (member of the Helmholtz Institute), Medical Faculty of the Erasmus University Rotterdam and at the Rotterdam Eye Hospital.

All described studies were funded by NWO-MW (903-47-007).

Dit proefschrift kwam tot stand door vrijwillige deelname van menselijke proefpersonen aan de beschreven experimenten.

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Voor Fay en Roos

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Introduction

GENERAL INTRODUCTION

Binocular vision and stereopsis is one of the major characteristics of frontal eyed species, such as humans. Binocular vision results from the projection of 3D-objects on corresponding area's of the retina's of the two eyes. An individual with binocular vision perceives one single image of the object containing depth information (binocular vision). The minute differences between the left and the right image (disparity) ideally give rise to stereoscopic vision. This entity of the binocular system has been used for artificial stereopsis in 3-D pictures and movies.

The importance of binocular vision in daily life becomes clear when individuals with optimal binocular coordination are forced to use mostly one eye (e.g. because of an eye infection). Their loss of binocular visual information causes difficulties with simple tasks, like shaking hands. Individuals who have sub-optimal binocularity for a longer period can function very well due to adaptive mechanisms and the use of non-stereoscopic depth cues. Many people are unaware of their slight sub-optimal binocularity which only a stereopsis test reveals. People with low vision in one of their eyes, have less binocularity but the use of both eyes can still be very useful for the detection of large moving objects such as approaching cars. They usually have no impairments in their daily tasks. Individuals with vision in one eye only adapt mainly by making more head movements. With this adaptation they have no difficulties, even with tasks like driving a car.

Patients with strabismus (or squint) with low vision in the deviated eye still use this (amblyopic) eye to detect changes (e.g. movement or ligth) in the visual field of that eye. Binocular coordination seems almost or completely absent. Strabismus is often associated with social problems, either from prejudice about the appearance or from difficult eye contact. The latter is often a problem in group meetings when it is unclear whom a person is looking at.

Many visual complaints can be related to disturbed binocularity as well. These functional complaints usually occur when the equilibrium of a person's habitual binocularity is disturbed. This thesis describes the binocular eye movements of persons with optimal binocularity, with sub-optimal binocularity and of strabismus patients with abnormal binocular coordination.

BINOCULAR COORDINATION AND STEREOPSIS

Sensory binocular coordination

During binocular viewing, the retinal images in the two eyes are normally perceived, through sensory fusion, as one single image. In the clinic, tests are often based on this principle. For instance, in a synoptophore, two different images can be presented to the left and the right eye simultaneously to test if they can be fused (e.g. a tree and a house) and to test under wich circumstances fusion breaks down. It has been shown that the visual circumstances of the images play a role in fusion or suppression. For instance light intensity, visual acuity and blur influence the perception of the images. Furthermore, individual monocular preferences or 'sighting preference' play an important role in suppression of the image of the weaker eye when the two retinal images can not be fused (e.g. looking trough a monocular microscope with both eyes open). A preference for one of the eyes can be detected in about 90 per cent of the population (Purves and White, 1994).

Binocular motor coordination

Sensory binocular coordination depends strongly on binocular motor coordination to direct the foveae of the two eyes at a given object in 3-D space. Moving targets are normally kept on the foveae through version eye movements (smooth pursuit or saccades, depending on target speed) and vergence eye movements.

Shifts between binocular fixation objects are usually accomplished by a combination of version (saccades) and vergence eye movements. Version is defined as the average change in direction of the two eyes. Fast version movements (saccades) account for the shift between targets in different directions. Horizontal vergence eye movements, which are by definition horizontal rotations of the left and the right eye in opposite directions, serve to keep objects fixated binocularly at the correct distance. The vergence angle is defined as the angle between the lines of sight of the left and the right eye. When fixation is changed from a distant target to a near target, a convergence movement (the vergence angle becoming larger) is essential for correct fixation of the new target. When fixation changes again towards the distant target, a divergence movement is necessary. Small residual errors in vergence may exist; they are compensated by sensory fusion (von Noorden, 1996). It has been shown that horizontal version and vergence movements can enhance each other's dynamics. In chapter 2 we further address the issue of facilitation of vergence by version. A specific question was, whether vergence is enhanced only by simultaneous saccades in the plane of the vergence, i.e. only by horizontal saccades, or also by vertical saccades, that are oriented orthogonally to the vergence plane. The answer to this question has implications for theories that address the nature and possible location of the version-vergence interaction.

Coupling between sensory and motor coordination

Accommodation of the eye lens, to focus nearby details, is associated with convergence of the eyes. The process of accommodation is coupled between the left and the right eye and is coupled with a convergence movement. For instance, when focussing on a text with the right eye open and the left eye occluded, the left eye turns inward. The other way around, fusional convergence enhances accommodation when the eyes move towards a near target (Ciuffreda and Kenyon, 1983). Therefore, our image of distant objects becomes blurred when we converge our eyes at will. During the process of ageing, the ability of lens accommodation decreases. Consequently, the facilitation of vergence by accommodation decreases, with a reducing effect on overall vergence ability (Fry, 1939; Alpern, 1962). Vergence difficulties can cause many complaints such as painful eyes, headaches, diplopia, blurring of vision and fatigue, altogether called "asthenopia".

CONVERGENCE INSUFFICIENCY

Convergence Insufficiency (C.I.), a diminished ability to fixate nearby targets binocularly, is observed in all age groups from the age where reading gets important (Daum, 1988). The diagnosis of C.I. is based on the existence of asthenopic complaints and the inability to fixate targets closer than 10 cm to the eyes (Von Noorden, 1996). C.I. patients often close one eye during reading to reduce their complaints. In the clinic, patients with asthenopia and/or C.I. are usually treated with vergence training exercises. Studies have indicated that patients benefit from these exercises (Cooper, Selenow, Ciuffreda, Feldman, Feverty, Hokoda and Silver (1983)). Training diminishes complaints and probably increases vergence range. Although it is usually assumed that subjects without manifest strabismus or defects of vergence fixate all attended objects within the physiological binocular oculomotor range accurately, with both of the foveae, this assumption lacks firm experimental verification until now. In chapter 3 questions are addressed about the quality of vergence and, thus, the accuracy of binocular fixation, in subjects without and with complaints of asthenopia. The effects of task (viewing of point targets vs. reading), oculomotor training exercises and existing ocular preferences are also addressed.

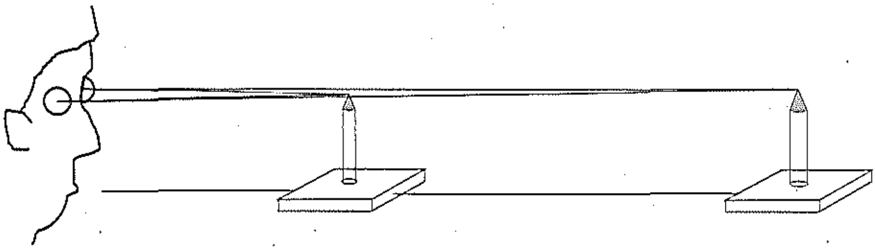

Fig. 1.1
The training device we designed for the experiment in chapter 3.

STRABISMUS

Individuals with manifest strabismus (squint) can not direct both eyes simultaneously towards a single visual target. The non-fixating eye is deviated outward in exodeviations (exotropia or divergent strabismus) or inward in esodeviations (esotropia or convergent strabismus) (Von Noorden, 1996). In latent strabismus the deviation does not occur constantly but can be evoked, for instance, by occlusion of one of the eyes or by fatigue. In intermittent strabismus, there are periods of strabismus and periods of normal eye alignment. Usually one of the eyes is the deviating eye during binocular viewing; this is most often the non-dominant or amblyopic eye. Sometimes, individuals with strabismus use each eye in turn, at will or unconsciously, as the eye of fixation. In chapter 4, the oculomotor strategies of such alternators are investigated in conditions of gaze-shifting between distinct targets. As they can fixate one distinct target only with one of the two eyes, the question is if and how their gaze-shifting behavior is related to their switching of fixation between the eyes.

Binocular alignment and binocular vision are not present at birth (Thorn, Gwiazda, Cruz, Bauer and Held, 1994), but develop in early life. This process seems to be disturbed in individuals who develop strabismus. Strabismus can result from disease or trauma (secondary), but often starts during the first 6 months of life (infantile or primary) (Von Noorden, 1996). There is a hereditary component and the aetiology seems multi-factorial.

Binocular single vision of fixation targets is disturbed by a strabismus angle. This potentially gives rise to diplopia (double vision). A number of investigators (Steinbach, 1981; Sireteanu, 1982; Travers, 1938; Schor, 1977; Joosse, 1999) have shown that suppression may play an important role in preventing diplopia. Whereas individuals with micro-strabismus (strabismus of only a few degrees) often have binocular fusion, sometimes even with gross stereopsis, subjects with large angle strabismus have suppression of the fovea of the non-fixating eye to avoid diplopia. If early strabismus is untreated, no diplopia occurs. Either, one of the eyes becomes dominant and other eye fails to develop good function, or the eyes obtain a kind of alternating dominance. Constant or alternating suppression of the fovea, or a larger area, of the non-fixating eye can cause these two possible outcomes. If strabismus patients with constant suppression of one of the eyes, are not treated with occlusion therapy before the age of 7, a deep amblyopia (acuity of 1/10 or less) in the deviating eye is the result. Usually, occlusion therapy (patching of the dominant eye) establishes optimal acuity in each eye, even though binocular coordination remains sub-optimal. Amblyopia can have other causes than strabismus. It can, for instance, result from recurrent eye infections in childhood, occlusion through ptosis and from anisometropia. These causes can also occur in combination with strabismus of other origin and make it complex to determine the primary cause of the amblyopia or strabismus. Oculomotor studies in strabismus have until now been limited largely to ocular misalignments or instabilities under conditions of static gaze in various directions. Little is known about binocular motor coordination under dynamic conditions, i.e. during saccadic gaze shifts. This issue is addressed in chapter 5. The main questions investigated are how the accuracy, speed and conjugacy of binocular saccades, under conditions of binocular or monocular viewing, compare between normals and various subgroups of strabismics (with various degrees of retained acuity in the two eyes vs. amblyopia). Specifically, it is asked whether a degrading of binocular vision is parallelled by a degrading of dynamic binocular oculomotor control.

EXPERIMENTAL SETUP

All experiments were conducted with subjects who wore scleral search coil contact annuli while sitting in an a.c. magnetic field. The voltages that are induced in the eye-coils by the magnetic field are a function of the ocular angular orientations. In this way, accurate measurements of vertical and horizontal eye rotation were obtained. The subjects kept their heads still, aided by a chin- and forehead rest that kept the eyes in the centre of the magnetic field. The targets were always light emitting diodes arranged in one or two iso-vergence circles in a darkened room. All points on a circle trough the eyes - within the oculomotor range - require the same convergent angle between the eyes, although the distances differ. Details about the experimental setup are discussed in each chapter.

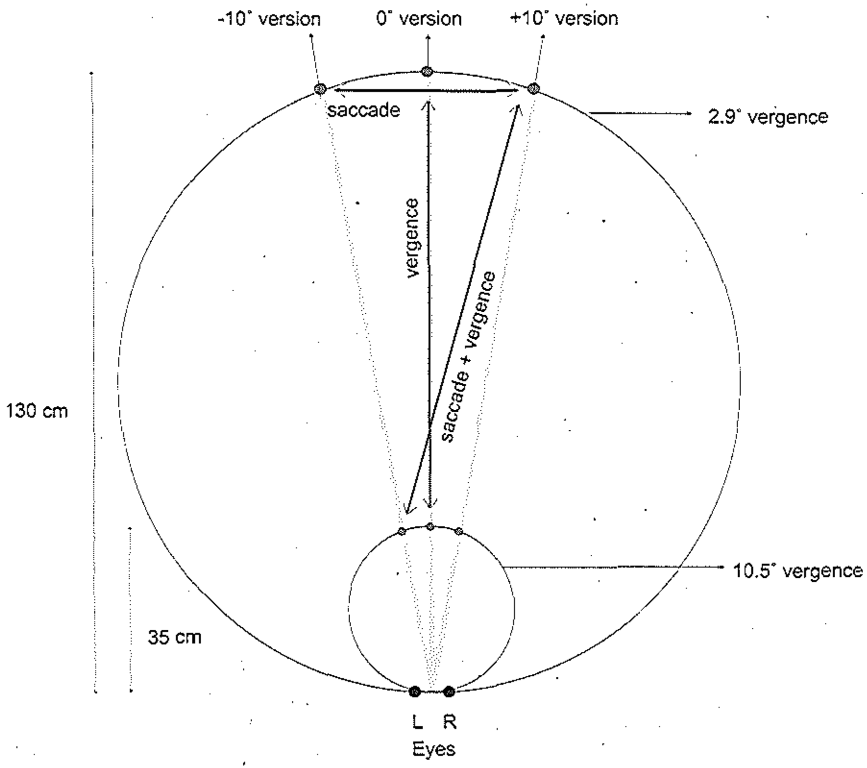

Fig. 1.2
Top view of the two iso-vergence circles on wich we arranged the light emitting diodes as visual targets. The eye movement types we studied are schematically depicted as arrows between start and end fixation points of the eyes.

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Dynamics of horizontal vergence movements: interaction with horizontal and vertical saccades and relation with monocular preferences

Anna F. van Leeuwen, Han Collewijn & Casper J. Erkelens

This chapter was published in Vision Research 38: 3943-3954 (1998)

SUMMARY

We studied the dynamics of pure vergence shifts and vergence shifts combined with vertical and horizontal saccades. It is known from earlier studies that horizontal saccades accelerate horizontal vergence. We wanted to obtain a more complete picture of the interactions between version and vergence. Therefore we studied pure version (horizontal and vertical), pure vergence (divergence and convergence) and combinations of both in 5 adult subjects with normal binocular vision and little phoria (<5°). The visual targets were LED's in isovergence arrays presented at two distances (35 and 130 cm) in a dimly lit room. Two targets were continuously lit during each trial and gaze-shifts were paced by a metronome. The two subjects with a strong monocular preference made vergence eye movements together with small horizontal saccades during pure vergence tasks. The other subjects, who did not have a strong monocular preference, made pure vergence movements (without saccades). These findings suggest that monocular preferences influence the oculomotor strategy during vergence tasks. Vergence was facilitated by both horizontal and vertical saccades but vergence peak-velocity during horizontal saccades was higher than during vertical saccades.

INTRODUCTION

The switching of binocular fixation between objects of interest is usually accomplished by a combination of version and vergence eye movements. The versional component, a saccade, accounts for the fast directional shift and the vergence component of the movement re-aligns the eyes to compensate for changes in distance. In natural environments, targets normally differ in direction and in distance. In experimental conditions it is theoretically possible to isolate version and vergence eye movements to study them separately.

Collewijn, Erkelens and Steinman (1988 a, b) found that saccades between isovergent targets were accompanied by a transient change in vergence. Horizontal and upward vertical saccades were accompanied by a divergence-convergence sequence while downward saccades showed initial convergence. From the latter, they concluded that changes in vergence during vertical saccades could not (as previously suggested) be caused by a temporary loss of the vergence signal. What causes these changes in vergence during saccades is still unclear. Collins, Carlson, Scott and Jampolsky (1981) measured a 30% greater eye rotation stiffness in the nasal than in the temporal direction. On the other hand, they showed a 40% greater maximum active force for the medial rectus muscle than for the lateral rectus muscle. We do not know if these maximum forces are representative of the forces during normal eye movements. The difference in stiffness could, in contrast to the force profiles, explain transient divergence during horizontal saccades. Enright (1989) suggested that the up-down transient vergence asymmetry could be explained by co-contraction of the vertical recti and (at the same time) changes in tension of the superior oblique muscles during vertical saccades. Whether transient vergence has a useful purpose during 3-D gaze shifts is unclear.

Slow non-conjugate eye movements can occur when two targets are, for instance, aligned in front of one of the eyes (Enright, 1992, 1996). If only one eye moves, a change in vergence and a small change in version result. This type of movement does fit neither into the definition of version nor the definition of vergence. If one wants to fit the movement into Hering's Law, one should describe it as a combination of symmetrical vergence and slow version (Enright, 1996). In this paper we assume that this type of movement is functionally a vergence movement and we will refer to this movement and other slow non-conjugate horizontal movements as "asymmetrical vergence".

The historical view, that combined gaze-shifts are simply the result of summed outputs of the saccadic and the vergence subsystem, has been gradually abandoned and transformed into a view of interaction between the subsystems. In 1986, Enright reported that both horizontal and vertical saccades were effective in mediating large fractions of intended vergence changes. He also reported that residual (post-saccadic) vergence was usually asymmetrical or even monocular. This complex behaviour of vergence and version movements was difficult to fit into simple summation of the two movements.

Enright (1992) studied asymmetrical horizontal vergence by aligning two targets in front of the non-preferred eye. He found that these targets elicited both vergence and saccadic movements. He proposed that the step component for each eye depended only on that eye's visual input; and that the pulse components generated for each eye depended on weighted averaging of visual stimuli of both eyes. In 1996, Enright found that symmetrical and asymmetrical convergence tasks could be accomplished without saccades. He concluded that convergence movements could not be accounted for by a single generator of binocular symmetrical input to the eye muscles but that convergence consisted of two synchronous monocular components.

Erkelens, Steinman and Collewijn (1989), Zee, Fitzgibbon and Optican (1992) and Collewijn et al. (1994, 1995) all found that combining vergence and version accelerated vergence and slowed down version. They proposed the existence of strong interactions between the saccadic and the vergence subsystem. They rarely observed pure vergence movements. Most subjects made horizontal small saccades when targets were set to elicit only vergence. A possible function of the occurrence of small horizontal saccades during pure vergence tasks could be the enhancement of vergence so that a new target is fixated more quickly. Another explanation could be that the small saccades bring one of the eyes close to or even on the target while the fellow eye follows later. Furthermore, small saccades are simply necessary if targets are not aligned exactly in a line protruding from the cyclopean eye (the point centrally between the eyes on the isovergence circle through the eyes) in any direction. Therefore, experimental settings to elicit pure vergence eye movements need great precision.

A well-known interaction exists between accommodation and vergence eye movements (Ciuffreda and Kenyon, 1983; Eadie and Carlin, 1995). During monocular viewing, accommodation of the viewing eye produces accommodation in the occluded eye and a vergence movement. Enright (1986) showed, by comparing monocular and binocular gaze-shifts, that about one quarter of intra-saccadic vergence could be the result of accommodation cues. Han, Seideman and Lennerstrand (1995) compared dynamics between the accommodative vergence movements triggered by the preferred eye and the fellow eye of subjects. They found a different accommodation-vergence relationship when the non-preferred eye was fixating with the other eye occluded, compared to the opposite. We did not investigate this relationship in the present study but accommodative vergence plays a role in the vergence shifts that we measured. The assumption that this accommodative vergence component remained constant within subjects during the experiment justifies comparing gaze shifts within subjects.

Considering previously reported asymmetries (Barbeito, 1981, 1986; Peli and McCormack, 1983; Erkelens et al. 1996) related to eye preferences, we hypothesised that also the dynamics of vergence movements could relate to these preferences. A preference for one of the eyes can be detected in about 90 per cent of the population (Purves and White 1994). This preference is often called "monocular preference" or "sighting dominance". We use the terms "preference" and "preferred eye" in this paper to avoid confusion with the clinical term "dominant eye", the counterpart of the "amblyopic eye".

In 1997, Collewijn and colleagues described gaze-shift trajectories and found pre-saccadic vergence movements while directional changes did not start until the saccade began. From this they concluded that control of the vergence and version components of a gaze-shift can be dissociated to some degree. Ocular vergence and version systems could, therefore, process target vergence and target direction separately. They proposed a strong interaction between the two oculomotor activities whenever they occurred at the same time. Comparing the vertical version-horizontal vergence relationship to the horizontal version-vergence relationship within one experiment could show the interactive mechanisms more clearly.

In our present experiment, we looked at version and vergence eye movements

Table 2.1: Main subject characteristics
For the 'tube-test', L/R means that there was a symmetrical response and, therefore, no strong monocular preference. For the 'ring-test', L (left eye) or R (right eye) indicates the preferred eye (fixating 6-8 times out of 8), '?' indicates inconclusive test-results (no preference detected).

Subject	sex	age	correction	phoria	tube-test	ring-test	IPD	experience
1	M	33y	-4.5/-4.5	eso	R/R	R	66 mm	++
2	F	30y	none	exo	L/R	L	63 mm	++
3	M	30y	none	exo	L/R	?	65 mm	++
4	M	25y	none	?	L/L	L	65 mm	-
5	F	31y	none	exo	L/R	R?	65 mm	+

during gaze-shifts between targets positioned such as to elicit pure vergence, vertical version, horizontal version and combinations of these types of movements. From our results it seems likely that there are separate systems for horizontal vergence and saccades with a strong interaction. Horizontal and vertical saccades both facilitate vergence but not necessarily in the same way. Furthermore, we found support for a relation between eye movement asymmetries and monocular preferences during vergence tasks.

METHODS

Subjects

Five adult subjects participated in our experiments. Four of them had previous experience with visual tasks in search coil measurements. All subjects underwent ophthalmic and orthoptic examinations in the Rotterdam Eye Hospital and additional tests in our department. The main results are shown in Table 2.1.

They all had a visual acuity of at least 20/20 in each eye and a stereo-acuity of 40 sec. according to the Titmus stereo-test. All were emmetropic except subject 1 who wore his contact lenses during the measurement. None of the subjects had a phoria larger than 5° (at near or far fixation) as measured with the cover test. Each subject showed alternating dominance of the eyes when tested with the prism-test. Subject 1 had a slight leftward rotation and tilt of his head of which he had never been aware. Because of his completely normal binocular functions, we accepted this as a normal

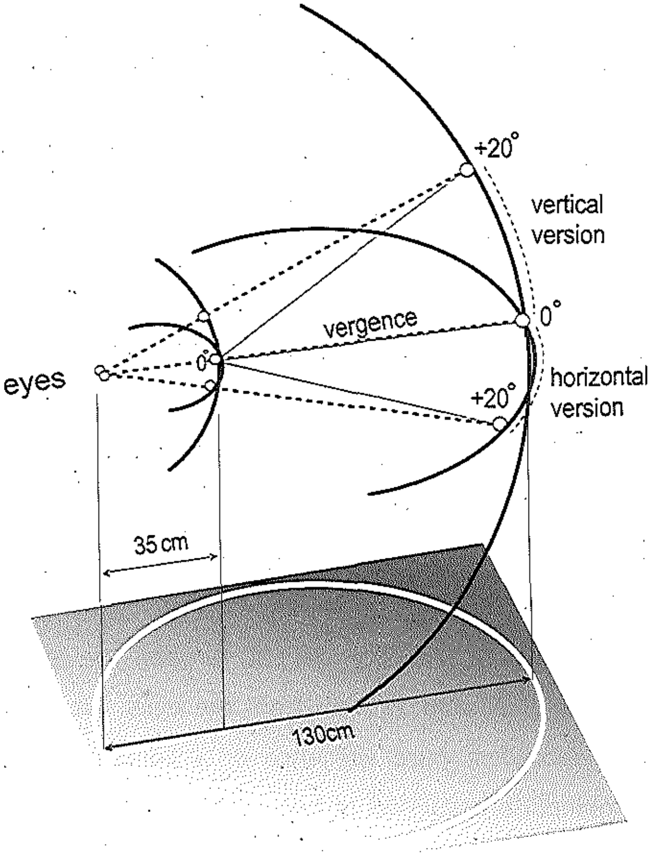


Fig. 2.1
Schematic drawing of the two isovergence arrays. For reasons of clarity, only three targets are drawn here, which would elicit eccentric saccades upward and rightward from the central target. Thick dotted lines show theoretical paths of vergence between these targets; thin dotted lines represent version and thin solid lines combinations of version and vergence.

variation and did not exclude him from our experiment.

To detect if subjects had a monocular preference, we designed a 'tube-test', which was comparable to classical preference tests, such as described by Barbeito (1981). In our test we gave the subjects two tubes, one in each hand. We then asked them to look at a target through each tube consecutively. We used two tubes instead of one because we wanted to prevent subjects from using their dominant hand each time they looked trough the tube. Subjects were instructed to keep each tube in the hand that we gave it in and were told that it did not matter which eye they used for fixating the target. Looking through both tubes with the same eye was taken as a sign of strong preference for that eye. Putting the left tube before the left eye and the right tube before the right eye was taken as absence of a strong preference. To detect weaker preference, we designed a separate test that we called the 'ring-test'. In this test, subjects had to fixate a self-chosen distant object through a ring (diameter: 3 cm) that was adhered to the window of our office on the fifteenth floor (distance between circle and eyes: 50 cm). We instructed the subjects to keep both eyes open and to select a distant object that fitted completely in the circle. Then we covered one of the eyes and asked if the object was still in the circle. This test was repeated 8 times; four times standing in front of the circle, twice standing left of the circle and twice standing right of the circle. Because of the large distance, even subjects who could normally choose between suppressing the left and the right image, partly suppressed one of the ring-images. If the subject used the same eye to fixate an object through the ring at least six times, we concluded that there was a mild monocular preference for that eye. The results of both tests are shown in Table 2.1. Two of the subjects (no. 1 and 4) showed a strong monocular preference, two a mild preference (no. 2 and 5); in subject 3, we could not detect any preference with these tests.

Visual conditions

We used vertical and horizontal isovergent arrays of real LED targets. The central targets were straight-ahead at distances of 35 and 130 cm from the eyes. We chose LED combinations to elicit versional saccades, pure vergence or a combination of both (see Fig. 2.1). Each target combination consisted of two continuously lit LED's, presented in dimly lit surroundings. The required vergence shift between the two isovergence arrays was 7.7° for an inter-pupillary distance (IPD) of 6.5 cm (7.1° for IPD of 6 cm, 8.2° for IPD of 7 cm). The near and far LED's were perceived equally luminous and comparable in angular size. In this way we minimised convergence-divergence differences due to target inequality. The farther targets were not occluded by the nearer isovergence array.

Experimental procedure

Target combinations elicited saccades of 20° and 30°, symmetrical around the centre. We used target combinations that elicited versional saccades (vertical and horizontal) at both distances, version-vergence combinations and pure vergence shifts.

To establish correct alignment with the targets, we made the subjects aware (if necessary) of the physiological diplopia of non-fixated targets. We positioned them centrally according to the symmetry of images perceived with either eye of the central target and targets 15° in all 4 directions, both near and far. We adjusted chin and forehead rests to minimise head movements. After positioning and fixation of the head we anaesthetised each eye with two drops of a topical anaesthetic (oxybuprocaine 0.4%) and inserted the coils. We instructed the subjects to keep their heads in the central position, to refrain from blinking during each trial and we asked them particularly not to blink during the gaze-shifts. All subjects were well aware of the importance of correct alignment during the experiment. They initiated each trial themselves by pressing a button when they felt ready. Gaze-shifts were paced by a metronome at intervals of 2 seconds. Trials lasted 23 seconds to obtain at least five complete gaze-shifts in each direction.

Data collection and analysis

We recorded the orientation of both eyes with scleral coils (Skalar, Delft) in an a.c. magnetic field (Robinson, 1963). We used chin and forehead rests to minimise head movements. Signals were low-pass filtered with a 250 Hz cut-off frequency, before being sampled at 500 Hz with an A-D converter (CED 1401, Cambridge Electronic Design, Cambridge) and digitally stored. Search coils were pre-calibrated and, in addition, monocular fixations of the central target and targets 10° out of the centre in each direction at the start and end of the experiment were used for off-line calibration. To minimise effects of small coil displacements, we used the first set of fixations for the first half of the trials and the second set for off-line correction of the second half.

We analysed the data off-line with custom software written under PV WAVE (Visual Numerics). We defined 0° eye rotation as the orientation of both lines of sight straight-forward and parallel. Because of this definition, fixation of the central target at 130 cm distance resulted in a +1.45° left eye orientation and a -1.45° right eye orientation, when the IPD was 6.5 cm. All ocular angles were expressed in Helmholtz co-ordinates (elevation and azimuth; see Carpenter, 1988). Leftward and downward rotations were signed as negative, velocities were signed correspondingly. Vergence was calculated as left eye orientation minus right eye orientation (vergence angles thus being positive during normal convergent fixation and vergence velocity being positive when vergence angles increased).

Saccades were detected based on the following criteria in both eyes: velocity exceeding 12°/s, acceleration exceeding 2000°/s^2, duration between 12 and 200 ms and amplitude exceeding 3°. After rough detection of a saccade, the exact starting point of each saccade was determined by our software as described earlier by van der Steen and Bruno, 1995. We defined saccadic amplitude as the difference between orientations at the start and end of a saccade. Only primary saccades larger than 60% of the target amplitude were analysed. We defined pre-saccadic vergence as the change in vergence angle during the 400 ms preceding the saccade-start and post-saccadic vergence as the change in vergence angle during the 400 ms following the saccade.

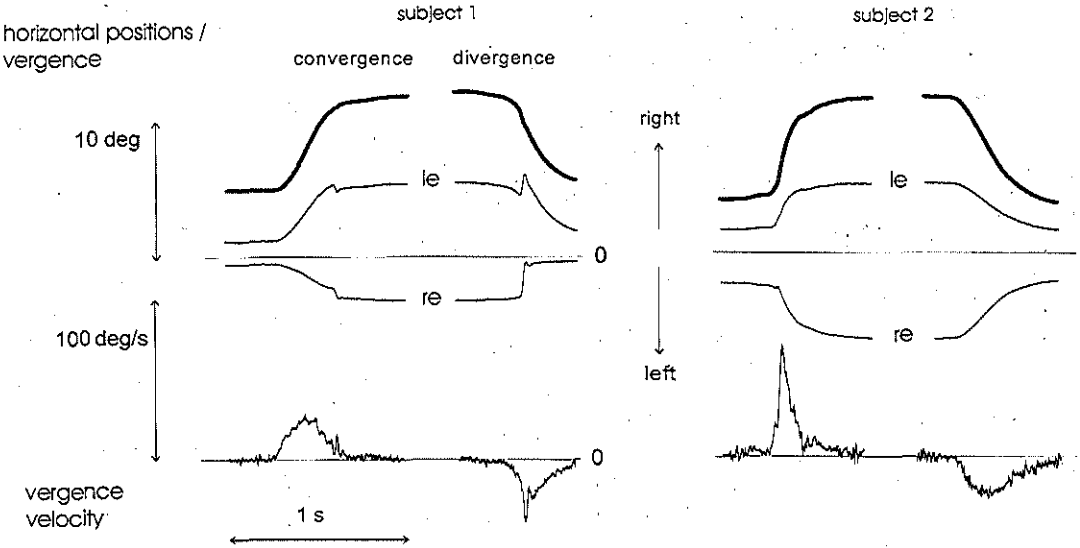


Fig. 2.2
Representative examples of horizontal eye orientations during pure vergence tasks of 2 subjects. The thin lines represent the left eye and the right eye, the thick line vergence. Upward going traces represent either rightward movements or convergence movements. The lower panel shows the vergence velocities. Subject 1, who has a preferred right eye, makes small saccades during vergence shifts. During the divergence shift, his right eye is on the target first. Subject 2, who has no strong monocular preference, makes smooth pure vergence movements.

RESULTS

Pure vergence

Three of the five subjects (no. 2, 3 and 5) made pure vergence movements without any saccades during most of the trials that required pure vergence. The other two subjects added small horizontal saccades in most of the trials.

Convergence was faster than divergence in three subjects while the other two subjects showed no consistent difference in peak-velocity between convergence and divergence. The duration of pure vergence shifts ranged between 150 and 650 ms, was slightly shorter for convergence than for divergence and was not dependent on the vergence peak-velocity. Fig. 2.2 shows a representative example of two subjects' vergence shifts in a trial with pure vergence targets. Subject 1 usually added small saccades while subject 2 usually did not.
Subject 1 made rightward saccades of around 3° during pure divergence tasks in all directions (0°, 10° and 15° eccentric, left, right, up and down). Only in the 15° leftward direction were his divergence movements pure. The small disjunctive saccades put his preferred eye on or within 1° of the target. Convergence movements were executed mostly without any saccades by this subject. Subject 4 showed leftward saccades during divergence shifts and rightward saccades during convergence shifts in pure vergence tasks in all directions. In this case the disjunctive saccades (of 2-3° version) usually aligned the preferred eye within 1° of the target. These small disjunctive direction-dependent saccades occurred consistently in these two subjects.

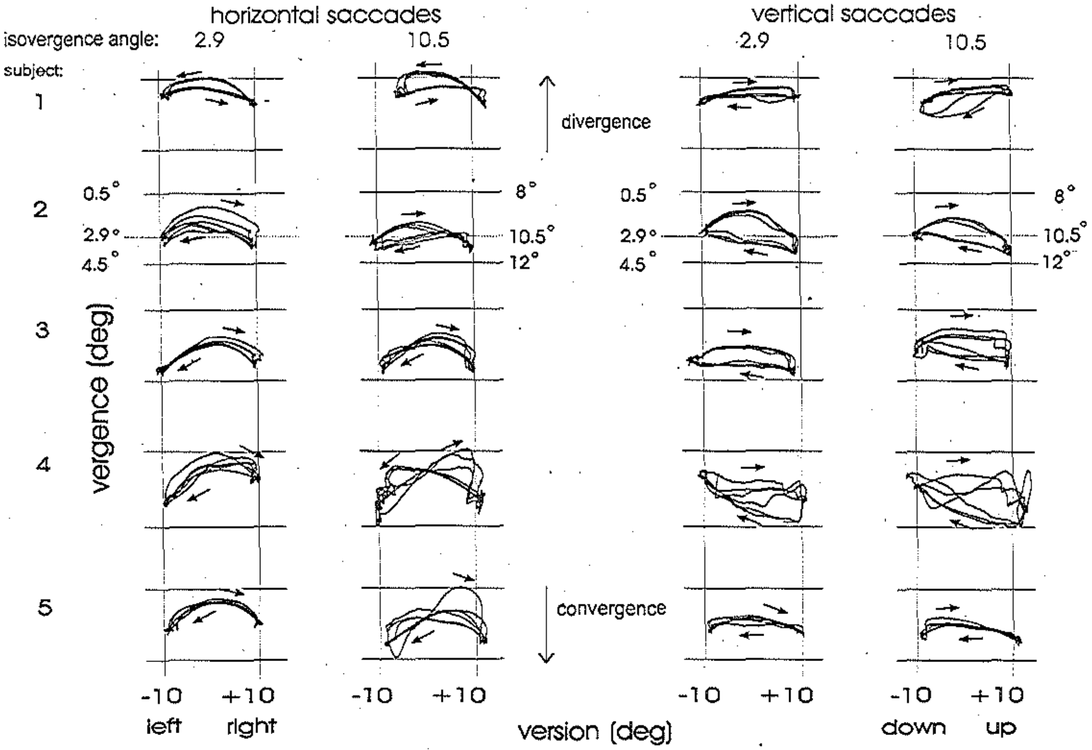
The other subjects (no. 2, 3 and 5) made small saccades only occasionally during pure vergence tasks. These saccades were usually smaller, more conjugate and more variable in direction. They seemed of a more directionally corrective nature, comparable to small saccades during fixation. The subjects showed idiosyncratic changes in vertical vergence that were dependent on direction and horizontal vergence angle; these changes never exceeded 2° and were not further analysed.

Vergence angles during steady fixation were not the same for all subjects. Part of this variation between the subjects could be explained by differences in IPD. We assume that some of the inaccuracy was due to the size of the stimuli and to small variations in head position. Small fixation errors are normal and not perceived because of sensory fusion.

'Pure' version

During saccades between isovergent targets, there was always a transient divergence component as found in earlier studies (Collewijn et al. 1988 a, b). The magnitude and timing of this transient divergence was strongly idiosyncratic and varied also with direction. Fig. 2.3 shows vergence-version plots during 20° horizontal (left panel) and vertical (right panel) isovergent saccades. Multiple gaze-shifts for 5 subjects for two isovergence angles (2.9 and 10.5°) are plotted. Vergence-version traces did not differ much during saccades at the two distances. We found slightly more rightward vs. leftward asymmetry in horizontal saccades between the nearer targets than between the farther targets.

Subjects 1, 2 and 3 had on average a longer duration of 30° horizontal saccades at 10.5° isovergence than at 2.9° isovergence with, on average, equal peak-velocities. These differences in duration were almost statistically significant (t-test) in subject 2 (P<0.1), significant in subject 3 (P<0.05) and highly significant in subject 1 (P<0.01). The other two subjects showed a large variability in saccade duration. Vertical saccades at the two distances also showed slight (usually non-significant) differences in duration but these were more subject- and direction specific.



2-D Plots of horizontal vergence and version during 20° symmetrical saccades between isovergent LED's for all 5 subjects. The left panel shows horizontal saccades at the two distances, the right panel vertical saccades at the two distances. In this figure divergence is depicted positive and convergence negative. In this way the plots resemble top-view trajectories. Leftward and downward version are depicted negative, rightward and upward version are depicted positive. The wrong start and end-position during horizontal saccades at 10.5° isovergence of subject 1 are probably due to an accidental misplacement of the targets.

During horizontal saccades, all subjects showed initial divergence starting together with the saccade and followed by compensatory convergence. At the end of a saccade, some subjects had already re-attained the required vergence angle whereas others needed post-saccadic convergence to fixate the target binocularly. Upward saccades showed approximately the same transient vergence sequence but downward saccades usually showed different transient vergence traces. The behaviour of subject 4, transient convergence with upward saccades and transient divergence with downward saccades, was compliant with the findings of Collewijn et al. (1988 b, 1995) and Enright (1989).

The other 4 subjects showed transient divergence with all vertical saccades but of a smaller magnitude during upward than during downward saccades (as reported by Zee et al. 1992). The transient vergence during 30° vertical and horizontal saccades had typically the same characteristics as for 20° saccades for each subject, being only slightly larger during larger saccades (see Fig. 2.7).

As described previously (Collewijn et al. 1988 a, b, 1996), saccades symmetrical about the mid-position of these sizes were usually faster in the horizontal than in the vertical direction. Unlike previous results, all subjects showed peak-velocity differences between symmetrical upward and downward saccades of equal amplitudes. Subjects 1, 2, 3 and 4 had significantly faster and shorter upward than downward saccades, but subject 5 had much faster downward than upward saccades.

Horizontal saccades with horizontal vergence

Fig. 2.4 shows representative traces for 2 subjects of 20° horizontal saccades with vergence shifts (of about 7° amplitude). The binocular saccades were unequal in amplitude, yet none of the saccades produced the demanded vergence angles for fixation of the target. After the saccade the vergence angle was corrected by a pure symmetrical or asymmetrical vergence movement and/or small disjunctive corrective saccades. Fig. 2.4 also shows that vergence velocities often had a double peak during saccades.

The left panel of Fig. 2.5 shows vergence-version plots for each subject during horizontal saccades with vergence shifts. When a convergence shift was required with a saccade some initial divergence, as during versional saccades, was still present. Also,

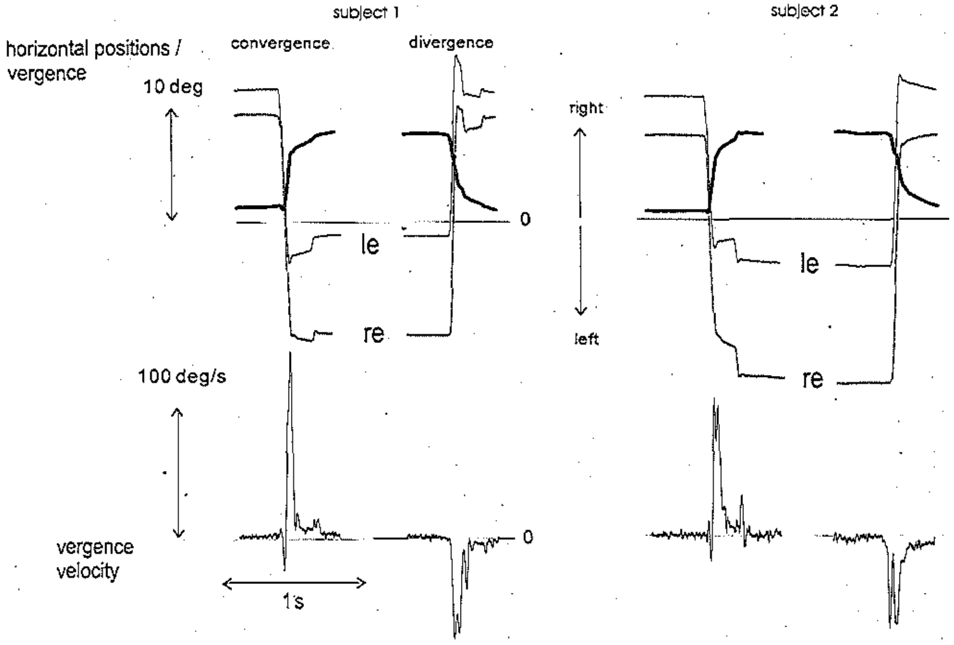


Fig. 2.4
Representative examples of horizontal eye orientations during 20° horizontal saccades between a near right target and a far left target of 2 subjects. The thin lines represent the left eye and the right eye, the thick line vergence. Upward going traces represent either rightward movements or convergence movements. The lower panel shows the vergence velocities. Notice the presence of pre-saccadic vergence in both examples.

this transient divergence component was larger during 30° than during 20° convergent saccades (Fig. 2.7). When a gaze-shift was divergent, the transient divergence seemed to be incorporated in the total vergence shift during both 20° and 30° saccades. As a consequence, all subjects showed a fairly rectilinear version-vergence trace during divergent horizontal saccades and a more curved version-vergence trace during convergent saccades.

Fig. 2.5 shows that usually a substantial part of the required vergence was accomplished *after* the initial saccade. The post-saccadic divergence shifts were smaller after 30° saccades than after 20° saccades. During the larger saccades, the combined version-vergence movements lasted longer and more divergence was accomplished during the saccade. This can be seen in Fig. 2.7, that shows disconjugate gaze-shifts of 20° and 30° version of one subject. Post-saccadic *con*vergence was not smaller after larger saccades, probably due to the larger transient divergence that had to be overcome.

Similar to findings by Takagi, Frohman and Zee (1995) and by Collewijn et al. (1997), we found small vergence movements in the required direction preceding the horizontal saccades; so-called pre-saccadic vergence. We found pre-saccadic *di*vergence prior to all divergent saccades in subjects 2, 3 and 5. Subject 1 only showed consistent pre-saccadic divergence preceding rightward divergent saccades and subject 4 showed no consistent pre-saccadic vergence before horizontal gaze-shifts. The average pre-saccadic divergence movements per subject averaged 0.1° to 0.6° in magnitude. Pre-saccadic *con*vergence was usually much smaller (subject averages 0.02 - 0.2°) but, nevertheless, consistently present in subject 1, 2 and 3. The asterisks in figure 2.5 point out all occasions of consistent pre-saccadic vergence in the required direction.

As expected, all the subjects had higher vergence peak-velocities during horizontal

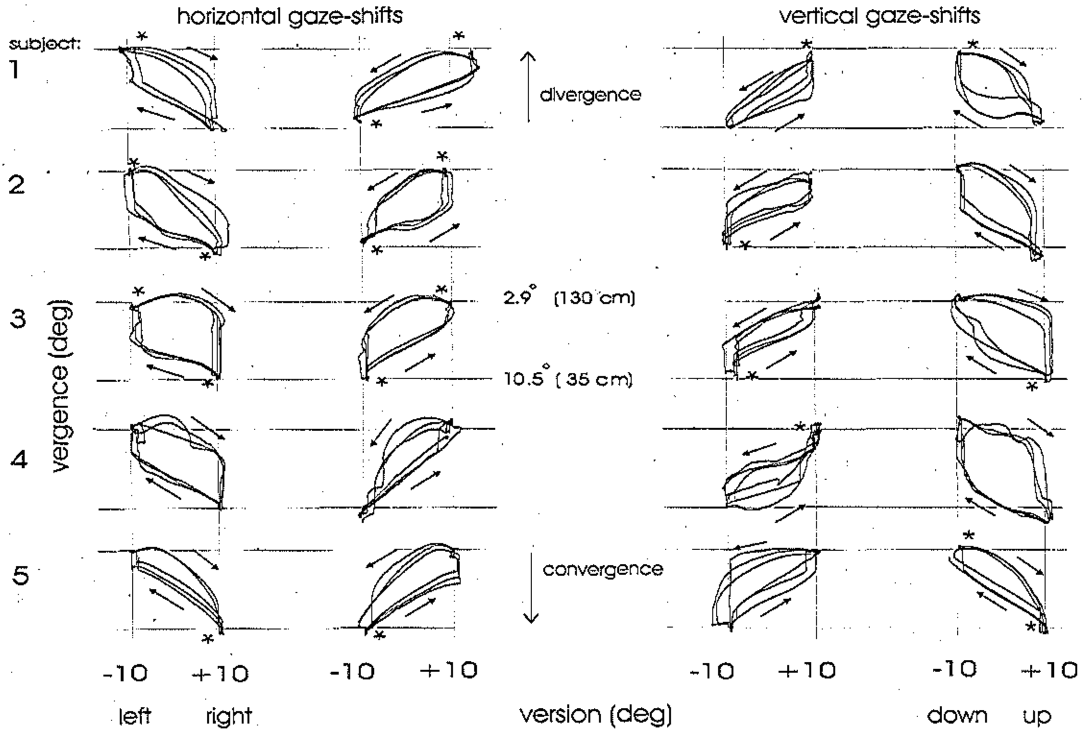


Fig. 2.5
2-D plots of combined version-vergence shifts of all 5 subjects during horizontal and vertical 20° saccades in both directions. The left and right panel show horizontal and vertical saccades at the two distances. In this figure, divergence is depicted positive and convergence negative. Rightward and upward version are depicted positive. The arrows indicate the direction of the gaze-shifts. The asterisks indicate the occasions of consistent pre-saccadic vergence. Especially in subject 3, the pre-saccadic divergence is visible as a small initial non-directional shift at the start of the horizontal version-divergence trace.

combined version-vergence gaze-shifts than during pure vergence shifts of the same magnitude. As can be seen in Fig. 2.8, divergence peak-velocity became at least twice the pure divergence peak-velocity. The difference between pure convergence peak-velocity and convergence peak-velocity during horizontal saccades was smaller. Divergence and convergence peak-velocities were usually around 100°/s during combined gaze-shifts.

Saccadic peak-velocity was smaller in the eye that made the smaller saccade; that is the abducting eye during a convergent shift or the adducting eye during a divergent shift. The fellow eye made slightly larger saccades than during pure version but saccadic peak-velocity remained equal. As a consequence, version peak-velocity during horizontal disjunctive gaze-shifts was lower than during horizontal isovergent gaze-shifts, as described previously by Collewijn and colleagues (1995). Version velocity and duration had a larger variability during combined horizontal gaze-shifts than during isovergent horizontal saccades.

Vertical saccades with horizontal vergence

Fig. 2.6a and 6b show typical traces for two subjects' 20° vertical saccades with the convergence shift with the upward saccade and the divergence shift with the downward saccade (a) and vice versa (b). In this figure vertical eye orientations and horizontal vergence are plotted. As during horizontal gaze-shifts, the vergence velocity often showed a double peak. The version-vergence relations during vertical saccades, some of which are shown in the right panel of Fig. 2.5, were highly idiosyncratic. The asterisks again point out consistent pre-saccadic vergence in the required direction. This pre-saccadic vergence was of comparable magnitude as the pre-saccadic vergence observed preceding horizontal gaze-shifts and consistently present in each subject in at least one direction. The version-convergence traces were not curved consistently more than version-divergence traces. During convergent vertical saccades, initial divergence was absent in subjects 1 and 4 in both directions. Subject 3 showed absence of transient divergence during downward convergent saccades only. When we compare these version-vergence traces with the corresponding traces during version shifts, it seems that the transient vergence during vertical version was incorporated in the gaze-shifts whenever it was in the appropriate direction.

In four subjects (1, 2, 3 and 5) vergence peak-velocity was higher during vertical

Fig. 2.6a

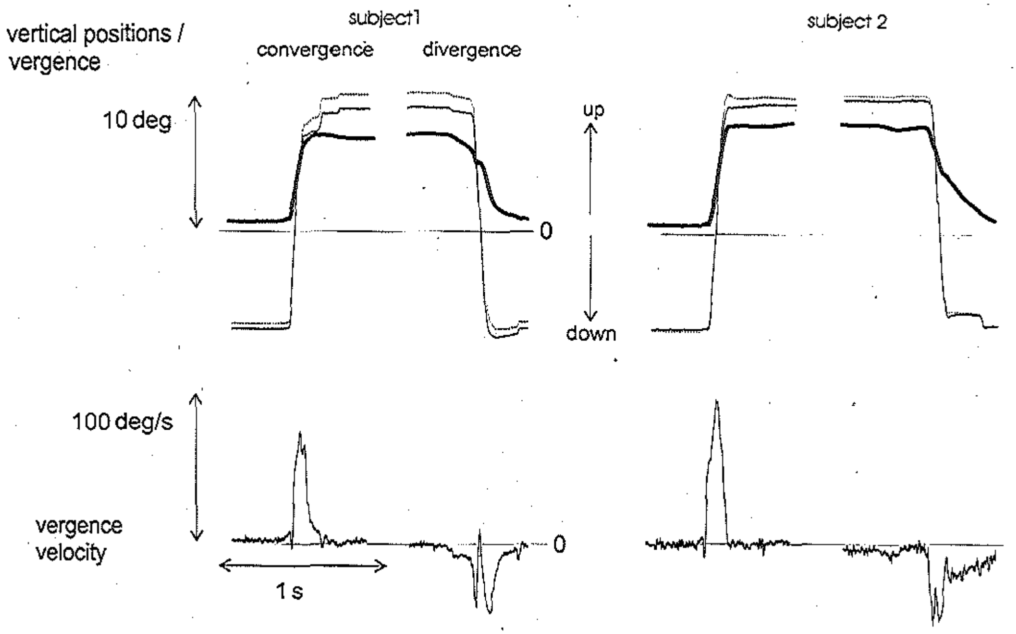


Fig. 2.6b

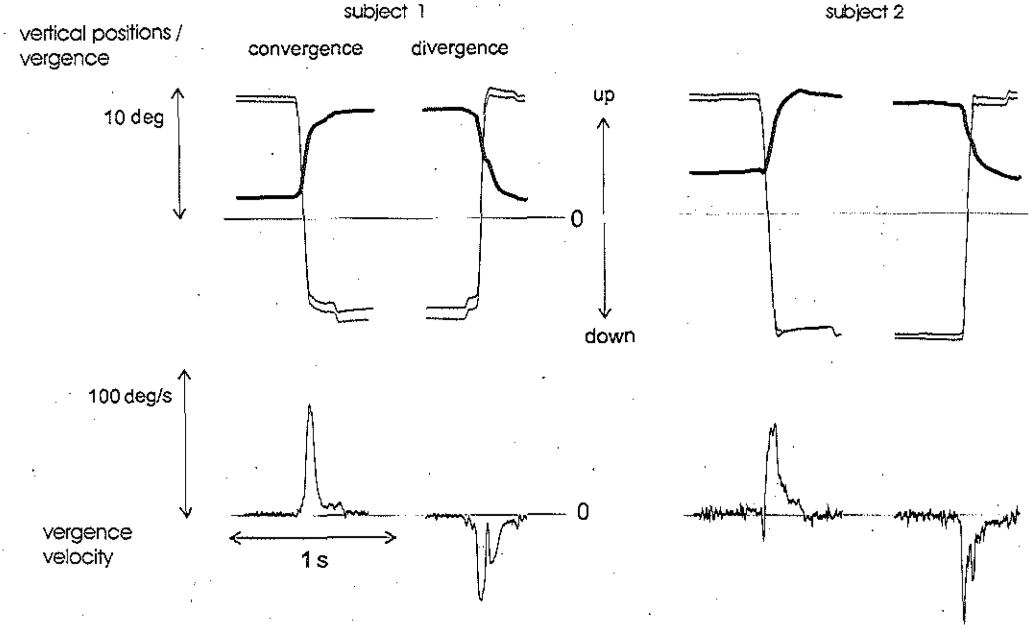


Fig. 2.6
Representative examples of vertical eye orientations of 2 subjects during 20° vertical saccades a): between a near upper target and a far lower target and b): between a far upper target and a near lower target. The thin lines represent the vertical eye positions, the thick line horizontal vergence. Upward going traces represent upward movements or convergence. A small idiosyncratic vertical vergence component is clear from the vertical orientations of both eyes. Pre-saccadic vergence, although present, is difficult to see here. Horizontal version is not plotted but a horizontal component (usually smaller than 3°) was sometimes present. The lower panel shows the vergence velocities.

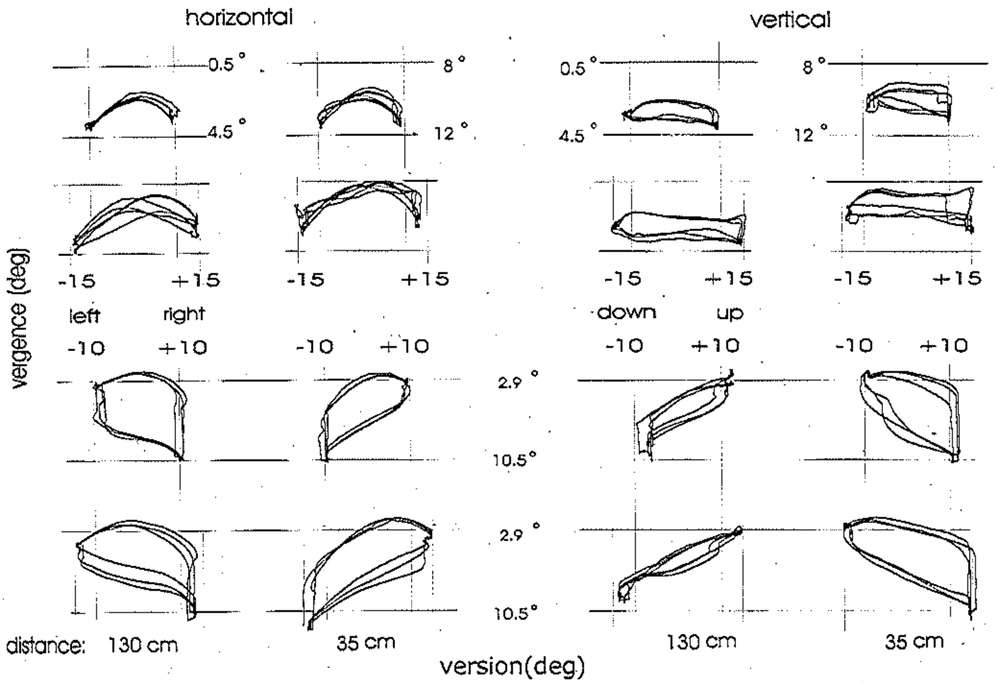


Fig. 2.7
2-D Plots of version-vergence shifts of 1 subject (no. 3) during 20° and 30° horizontal (left panel) and vertical (right panel) saccades between isovergent targets (upper panel) and between the two distances (lower panel). In this figure, divergence is positive and convergence negative. Rightward and upward version are depicted positive. Notice the larger transient divergence during 30° saccades than during 20° saccades.

gaze-shifts than during pure vergence shifts but never as high as during horizontal gaze-shifts (Fig. 2.8). Subject 4 showed almost the same vergence velocities after combination with vertical saccades as during pure vergence tasks. Divergence peak-velocity seemed linearly related to saccadic peak-velocity; convergence peak-velocity seemed independent of saccadic peak-velocity.

Vertical saccadic peak-velocity often stayed the same and sometimes became lower after adding vergence shifts. Upward divergent saccades were usually faster than downward divergent saccades. Downward convergent saccades were usually faster than upward convergent saccades. Only subject 5 had the highest saccadic peak-velocities during downward divergent saccades. Occasionally a vertical combined gaze-shift was faster than an equally sized isovergent vertical saccade and sometimes even the average peak-velocity of vertical combined gaze-shifts became higher. Due to the larger variability of combined vertical gaze-shifts compared to isovergent vertical saccades in all subjects, these differences were not statistically significant.

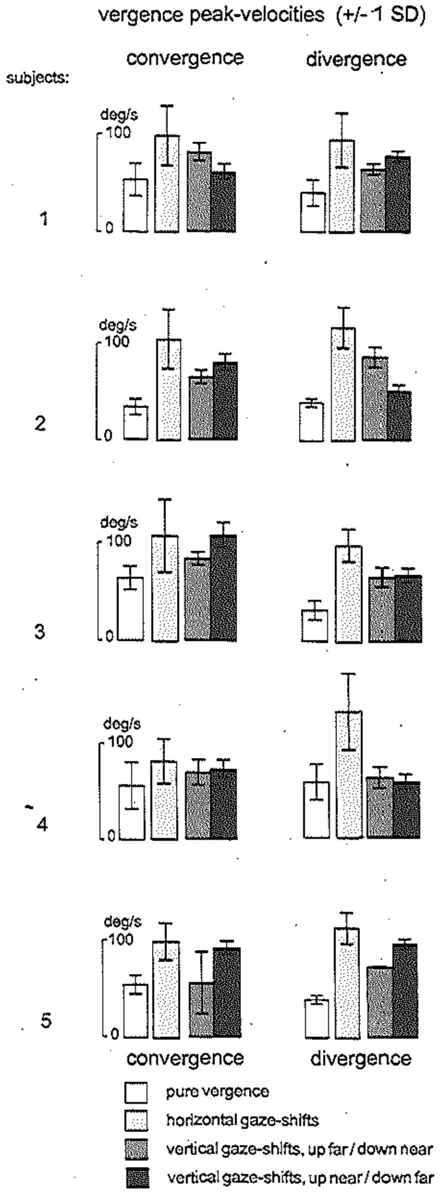


Fig. 2.8
Average horizontal vergence peak-velocities ± 1 SD for each subject. The left panel shows averages for convergence peak-velocities, the right panel for divergence peak-velocities. White bars represent vergence peak-velocity during pure vergence tasks; light grey bars during horizontal gaze-shifts and the other two bars for vertical gaze-shifts. Notice that the vergence velocity is always highest during horizontal gaze-shifts. Vergence velocity averages during vertical gaze-shifts are related to direction in most subjects.

Comparison of vertical and horizontal non-conjugate gaze-shifts

Pre-saccadic vergence was observed more often in combination with vertical saccades than with horizontal saccades. The percentage of total vergence achieved during a saccade was larger during divergent than during convergent horizontal gaze shifts. During vertical saccades, the difference between divergent and convergent gaze-shifts was less clear and sometimes more vergence was achieved during convergent than during divergent shifts. Figure 8 shows the average vergence peak-velocities of each subject during all target combinations that required a vergence shift. From this figure, clearly vergence peak-velocity was consistently higher with horizontal than with vertical saccades. Average vergence velocities during vertical gaze-shifts were related to the direction in most subjects and are, therefore, depicted separately.

The vergence-version plots of convergent horizontal saccades were consistently more curved than those of divergent horizontal saccades. During vertical gaze shifts, differences in version-vergence traces were more idiosyncratic. The more rectilinear traces seemed more efficient in terms of interaction between vergence and version but these traces did not always have the highest peak-velocities for vergence and version.

DISCUSSION

Pure vergence

Our findings suggest that monocular preferences play a role in the oculomotor strategy of subjects during vergence tasks. Barbeito, Tam and Ono (1986) proposed that individual dynamic asymmetries were related to the functional location of the cyclopean eye. Peli et al. (1983) found asymmetrical vergence movements after covering one of the eyes. Uncovering the eye usually led to a saccadic response when the uncovered eye was the preferred eye and to asymmetrical vergence when it was the non-preferred eye. This result can also be explained by the strategy of initial target-fixation with the preferred eye and subsequent correction of the vergence angle. Subjects with this strategy might have a temporary relative suppression of the image of the non-preferred eye. Enright (1996) found that most subjects had more saccade-free trials during a vergence task when targets were aligned in the midline than when targets were aligned with one of the eyes. If monocular preferences are direction-dependent and controlled by a process of local suppression, as suggested by Erkelens et al. (1996), the oculomotor strategy during vergence tasks might also be direction-dependent. Subjects with mild or no monocular preference might not have a consistent relative suppression but a direction-dependent local suppression. The latter would explain the strategy of making pure vergence movements for midline-targets because these targets theoretically give symmetrical input to either eye. We can, however, not confirm this with the present data because we did not present a large array of pure vergence targets in all directions.

Version

Our results confirmed previous saccade studies at most points (Collewijn et al. 1988 a, b). The idiosyncratic up-down velocity differences were not related to the idiosyncratic up-down vergence differences. Mays, Zhang, Thorstad and Gamlin (1991) found that the activity of neurones innervating the superior oblique muscle had a component that related to elevation and to convergence. These findings support the idea of Enright (1989) that transient horizontal vergence during vertical saccades might be related to actions of the superior oblique muscle although convergence is more obvious during downward saccades. We know from Straumann, Zee, Solomon, Lasker and Roberts (1995) that during saccades also cyclovergence occurs. They found that transient torsion was idiosyncratic. Subject-specific up-down differences in (horizontal and torsional) vergence could be explained by a greater variability in oblique eye muscle properties than in the properties of other eye muscles.

Slight back or forward head tilts cause an elevation or a depression of the eyes relative to the head and, therefore, influence the primary muscle orientations with probable effects on the force profiles. This could be the cause of the idiosyncratic up-down differences. Another phenomenon that could be explained by different initial eye orientations (in this case the horizontal orientation) is the slight difference in saccade duration between vertical saccades at 2.9° and 10.5° isovergence angles, that we found.

The difference between version peak-velocity during horizontal and vertical saccades of the same amplitude, that we found, could be the result of separate control systems for horizontal and vertical saccades. On the other hand, they could also be the result of different muscle force profiles of the horizontal and the vertical recti.

Vergence facilitation

During a vertical gaze-shift, different muscles execute version and vergence movements. Nevertheless, vergence is accelerated during these gaze-shifts. This opposes the idea of Kenyon, Ciuffreda and Stark (1980), that vergence acceleration during saccades results from an interaction in the eye muscle system only. Although the facilitation during vertical gaze-shifts is less strong than during horizontal gaze-shifts, we can not conclude that facilitation is caused by separate central mechanisms during horizontal and vertical saccades. If vergence facilitation is caused by one central mechanism during both horizontal and vertical saccades, the resulting vergence peak-velocities do not have to be of the same magnitude. The vergence facilitation during horizontal saccades could be the result of the same central facilitation as during vertical saccades but with an extra facilitation because of activation of the same muscles twice, by two different efferent mechanisms.

The pre-saccadic vergence that we found preceding both horizontal and vertical saccades supports the suggestion of different subsystems for vergence and version. It does not support the gating model by Zee et al. (1992), unless the two movements had different reaction times. Our results strongly support the ideas of Collewijn et al. (1997), that the vergence system and the saccadic system act separately, but interact with each other whenever they occur at the same time. If we assume the existence of a version oculomotor system with subsystems for horizontal and vertical version and a vergence oculomotor system with subsystems for convergence and divergence, we can explain asymmetries within subjects. Variations in subsystem characteristics together with variations in orbital anatomy, muscle insertion and muscle stiffness seem a reasonable explanation for the differences between subjects.

Final conclusions

Our results support the existence of different oculomotor systems for version and vergence with a central interaction between the two when both systems are active at the same time. Furthermore, our results suggest that monocular preferences influence oculomotor strategies during vergence tasks.

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3

Gaze-shift dynamics in subjects with and without symptoms of Convergence Insufficiency: influence of monocular preference and the effect of training.

Anna F. van Leeuwen, Marion J. Westen, Johannes van der Steen
Jan-Tjeerd H. N. de Faber & Han Collewijn

This chapter was published in Vision Research 39(18): 3095-107 (1999)

SUMMARY

We studied gaze-shift dynamics during several gaze-shift tasks and during reading, in 5 subjects with Convergence Insufficiency (C.I., a diminished ability to converge), and in 10 subjects without C.I.. Furthermore, we studied the effect of vergence training in order to verify previous claims that orthoptic exercises can improve vergence performance. We recorded binocular eye movements with the scleral coil technique. Subjects switched fixation between nearby and distant light emitting diodes (LED's) arranged in isovergence arrays (distances 35 and 130 cm) in a dimly lit room. In both the C.I. and non-C.I. group, two classes of subjects occurred: vergence responders and saccadic responders. During pure vergence tasks, saccadic responders made saccades with no or little vergence; vergence responders made vergence movements with no or small saccadic components. In saccadic responders, fixation of nearby targets was monocular. Subjects with a preferred eye, according to our determination, used the preferred eye. The 5 C.I. subjects showed idiosyncratic responses with insufficient vergence during most trials. They all had a tendency to alternate fixation between the left and right eye. Vergence-version tasks always elicited larger vergence components than pure vergence tasks. During a reading task, vergence angles were more accurate than during gaze-shifts between LED's. After the pre-training sessions, 9 subjects (one of which had C.I.) practised a pure vergence task 3 times a day for at least 2 weeks. Vergence amplitudes of 4 of these subjects were larger after training. We conclude that vergence training can change oculomotor performance. Although C.I. is often associated with abnormal vergence dynamics, there are no typical C.I. vergence dynamics. Unstable monocular preferences may play a role in the aetiology of C.I.

INTRODUCTION

Shifts between binocular fixation objects are usually accomplished by a combination of version and vergence eye movements. Particularly during tasks such as reading, working with monitors or manipulating small nearby objects, accurate vergence movements are necessary to maintain binocular fusion. If binocular fusion is lost, diplopia or suppression of one of the visual images occurs.

Vergence movements can be divided arbitrarily into several components (Von Noorden, 1996). Normally, the eyes are in a convergent orientation when we are awake. This basic convergent orientation, not elicited by visual objects, is often called tonic convergence. When the eyes turn towards a nearby target, different components of vergence usually occur simultaneously. Proximal vergence is the vergence evoked by the cognitive notion of the nearness of a target. Nearby visual objects evoke a reflex of accommodation (to focus the object) and convergence (to fuse both images) together with pupillary constriction, called the 'near vision complex'. Accommodation induces convergence whereas fusional convergence, driven by binocular disparity (Stark, Kenyon, Krishnan and Ciuffreda, 1980), enhances accommodation when the eyes move towards a nearby target (Ciuffreda and Kenyon, 1983; Eadie and Carlin, 1995). The AC/A ratio (accommodative convergence / accommodation) expresses the magnitude of convergence (in prism diopters) induced by each unit of accommodation (in spherical diopters). Small residual errors in vergence may occur; these are compensated by sensory fusion (Von Noorden, 1996).

When the AC/A ratio is below or above the normal range, it is difficult to keep an object fused and focused at the same time and complaints may occur. During the process of aging, the ability to accommodate the lens of the eye decreases. Corrective reading glasses virtually eliminate accommodation, with a reducing effect on accommodative vergence. Difficulties in accomplishing vergence can cause many complaints such as painful eyes, headaches, diplopia, blurring of vision and fatigue. These complaints, related to visual tasks with near objects, are called "asthenopia". Convergence Insufficiency (C.I.), a diminished ability to converge, is a relatively common disorder observed in all age groups from the age when reading gets important (Daum, 1988). Patients with C.I. classically close one eye during reading to reduce their complaints. The diagnosis of C.I. is usually based on the existence of asthenopic complaints together with a Near Point of Convergence (N.P.C.) farther than 5 to 10 cm. The N.P.C. is determined by moving a fixation point slowly in a straight line towards the centre between the eyes until fusion breaks down.

Patients with asthenopia and/or C.I. are usually treated with vergence training exercises. Several studies have indicated that patients benefit from these exercises.

Cooper, Selenow, Ciuffreda, Feldman, Feverty, Hokoda and Silver (1983) found that orthoptic training, with real spatial objects, was more effective in increasing the vergence range in patients than was training with random dot stereograms. Nevertheless, random dot stereograms were useful when added to orthoptic training. They concluded that several exercises used at the same time are most effective.

Daum (1982, 1984) found that orthoptic training had an effect on the N.P.C. and the AC/A ratio of normal subjects. Daum, Putstein and Eskridge (1987) found that computerised training could increase the vergence range. Grisham (1988) found that frequent short training sessions were more effective in the treatment of C.I. patients than less frequent, longer sessions. After 4 weeks of training, the performance of most C.I. patients satisfied orthoptic criteria of normality.

Griffin (1987) compared tonic, isometric and phasic training methods and found that all of these increased the vergence range in normal subjects. Grisham and co-workers (1991) evaluated the 'vergence tracking rate', the velocity at which patients could just follow vergence-steps, by measuring eye movements. After training, they found higher tracking rates that correlated with less asthenopic complaints.

In conclusion, all studies indicate that training diminishes complaints and probably increases vergence range. The results of Grisham and co-workers indicate that also vergence velocity might increase through training.

Other research-groups, mainly interested in eye movement dynamics, analysed normal vergence eye movements. They found that vergence movements are faster when combined with horizontal or vertical version movements (Enright, 1986; Erkelens, Steinman, & Collewijn, 1989; Zee, Fitzgibbon and Optican, 1992; Collewijn et al., 1994, 1995 and Van Leeuwen, Collewijn and Erkelens, 1998). Collewijn and co-workers observed that, during pure vergence tasks, most subjects made horizontal small saccades together with vergence movements. A possible function of the occurrence of these small horizontal saccades could be the enhancement of vergence so that a new target is fixated more quickly. Another explanation could be that the small saccades bring one of the eyes close to or even on a target while the fellow eye follows later, as suggested by Van Leeuwen et al. (1998). A closer study of the saccadic behaviour during vergence tasks of subjects with asthenopic complaints could resolve the cause or use of these small saccades.

We hypothesise that vergence dynamics are influenced by asymmetries in visual perception related to eye preferences that have previously been reported (Barbeito, 1981; Peli and McCormack, 1983; Barbeito, Tam and Ono, 1986; Porac and Coren, 1986; Velay, Roll, Lennerstrand and Roll, 1994; Han, Seideman and Lennerstrand, 1995; Erkelens et al., 1996). A preference for one of the eyes can be detected in about 90 per cent of the population (Purves & White, 1994); it differs among individuals and ranges from undetectable to strong. Recently, Rombouts, Barkhof, Sprenger, Valk and Scheltens (1996) found a correlation between eye preference and brain activation. In a functional MRI study, they found that stimulation of the preferred eye activated a larger area of the primary visual cortex than stimulation of the fellow eye.

Eye preference is often called "sighting preference" or "ocular dominance". We use the terms "monocular preference" and "preferred eye" in this paper to avoid confusion with the clinical term "dominant eye", the counterpart of the "amblyopic eye". During problems of fusion, induced by insufficiency of the vergence system or by the difficulty of a binocular task, the visual field of one of the eyes can be completely or partly (Erkelens et al., 1996) suppressed to prevent diplopia or rivalry. When monocular preference is strong, suppression of the non-preferred eye is likely to occur. A subject with no detectable monocular preference, on the other hand, might not suppress one of the visual images during difficult binocular tasks and, therefore, may continue to make fusion efforts. According to this idea, asthenopia would not occur in individuals with a strong monocular preference. In addition, subjects with a strong monocular preference would be more likely to make small saccades during vergence tasks to serve quick monocular fixation with the preferred eye.

The main issues addressed in this paper are: (1) Do monocular preferences play a role in gaze-shift dynamics? (2) Are gaze-shift dynamics different between C.I. and non-C.I. subjects? (3) What is the effect of orthoptic training on gaze-shift dynamics?

Table 3.I
Main subject characteristics. For the 'tube-test', L/R means that there was a symmetrical response and, therefore, no strong monocular preference. For the 'ring-test', L (left eye) or R (right eye) indicates the preferred eye (fixating 6-8 times out of 8), L/R indicates no detected preference. For the C.I. patients, the subjective or clinically detected eye preference is indicated instead of the 'ring-test'. The asthenopia-score had a maximum of 35 for no complaints.
** Right eye acuity of subject 5 was 1.0 at near.*

Subject	Sex	Age (years)	Acuity R/L	Stereopsis (Titmus) (")	NPC (cm)	Asthenopia score	Eye preference	
non-C.I.							tube-test	ring-test
1	M	60	1.0 / 0.9	60	8	35	R	R
2	M	30	1.2 / 1.2	40	6	35	L	L
3	M	27	1.0 / 0.9	40	5	34	R / L	R / L
4	M	28	1.0 / 1.0	40	5	34	R / L	R
5	F	24	0.4*/ 1.0	40	5	33	R / L	R / L
6	M	46	1.0 / 1.0	40	6	32	R	R
7	M	27	1.2 / 1.2	40	5	32	R / L	R
8	M	46	1.0 / 1.0	60	5	32	R / L	R
9	M	31	1.2 / 1.2	400	8	31	R / L	L
10	F	31	1.2 / 1.2	40	5	29	R / L	R / L
C.I.							tube-test	ring-test
11	F	32	1.0/1.0	40	5	28	R/L	R
12	M	37	1.0/1.0	50	6	28	R/L	R
13	F	36	1.0/1.0	60	15	27	R/L	L
14	F	55	1.6/1.25	200	6	22	R/L	L/R
15	F	22	0.7/0.7	40	8	21	R/L	L/R

We found support for a role of eye preference in gaze-shift dynamics and in asthenopia. We found no typical C.I. gaze-shift dynamics but we did find certain fixation strategies in C.I.. Vergence training changed the gaze-shift dynamics in several subjects.

METHODS

Subjects

Ten adult subjects without complaints (1-10: colleagues and students, including 3 of the authors (5, 6 and 10)) and 5 C.I. patients (11-15); diagnosed and recruited in the Rotterdam Eye Hospital, participated in our experiments. All subjects gave their informed consent, according to the rules of the ethics committee. All subjects filled out the asthenopia questionnaire designed by Cooper et al. (1983). From this questionnaire, we computed the asthenopia-score with a maximum of 35 for no symptoms and a minimum score of 7 for extreme asthenopia. All subjects underwent ophthalmologic and orthoptic examinations in the Rotterdam Eye Hospital and additional tests in our department, the main results of which are shown in Table 3.1. All subjects who needed refractive correction wore appropriate glasses or contact lenses during the experiment, except subject 5 who always used one eye for near and the other eye for far fixation. To detect if subjects had a strong monocular preference, we used a 'tube-test', which was comparable to classical preference tests such as described by Barbeito (1981). To detect weak preferences in the non-C.I. subjects, we designed a separate test that we called the 'ring-test'. In this test, subjects had to fixate a self-chosen distant object (>500 m) through a ring (diameter: 3 cm, distance between ring and eyes: ~ 50 cm). If a subject used the same eye to fixate an object through the ring at least six times out of eight, we concluded that there was a mild monocular preference for that eye. The ring-test revealed (weak) monocular preference in several subjects in whom the tube-test failed to detect a preference. Van Leeuwen et al. (1998) have described both the tube-test and the ring-test in detail.

Visual conditions

We used 2 horizontal isovergent arrays of real LED targets. The central targets were straight-ahead at distances of 35 (~ 10.5° vergence) and 130 cm (~ 2.9° vergence) from the eyes. We chose target combinations that elicited pure version horizontal saccades at both distances, version-vergence combinations and pure vergence shifts between the two distances (Van Leeuwen et al., 1998). We always presented saccade targets symmetrically around the centre with 20° or 40° amplitudes. Pure vergence targets were presented in the straight-ahead direction and 10° leftward and rightward. All eye movement tasks were performed with both eyes viewing. In addition, we repeated some trials with monocular viewing. Each target combination consisted of two LED's that switched on alternately at intervals of 2 seconds, in a dimly lit surrounding. The required vergence shift between the two isovergence-arrays was 7.7° for an inter-pupillary distance (I.P.D.) of 6.5 cm (7.1° for I.P.D. 6 cm,

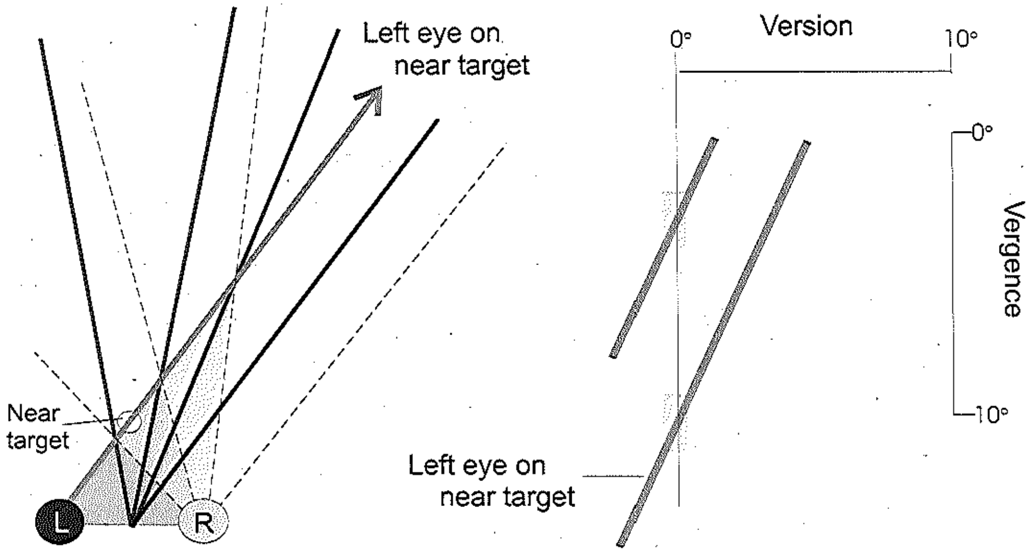


Fig. 3.1
The left part of this figure shows a schematic top view of left eye (L) target fixation with rotation of the non-fixating right eye (R) in four directions (dotted lines). Mean eye rotation (version) is depicted with heavy black lines. When the right eye is rotated, while the left eye orientation remains constant, the vergence angle increases or decreases with the same magnitude while version changes by half of the right eye rotation. For any right eye rotation with a constant left eye orientation, we can determine the version angle and the vergence angle.
The locus of such combinations of version–vergence angles is a straight line (with slope 0.5) when drawn in a version–vergence plot, as drawn in the right half of the figure for left eye fixation of the central nearby target and for the distant target. In the same way, lines can be drawn for rotation of the left eye while the right eye orientation remains constant. The version–vergence lines, during left and right eye target fixation, intersect in the point presenting version and vergence angles of the target in relation to the eyes.
In the right half of the picture, the two gray rectangles depict the binocular fixation range of the two targets, defined as an area within 1° for each eye around the target.

8.2° for I.P.D. 7 cm). The nearby and distant LED's were of such luminance and size that they were perceived equally bright and comparable in angular size. In this way, we minimised convergence-divergence differences due to target inequality. The distant targets were not occluded by the near isovergence array.

For the reading-task, we presented three bodies of text from a Dutch family magazine at 35 cm distance with 4 mm letter-size. We recorded the subjects' binocular eye movements during both binocular reading and monocular reading with either eye.

Data collection and analysis

We recorded the orientation of both eyes with scleral coils (Skalar, Delft) in an a.c. magnetic field (Robinson, 1963). Signals were low-pass filtered with a 250 Hz cut-off frequency, before being sampled at 500 Hz with an A-D converter (CED 1401, Cambridge

Electronic Design, Cambridge) and digitally stored. Search coils were pre-calibrated and, in addition, monocular fixations of the central target and targets 10° out of the centre in each direction at the start and end of the experiment were used for off-line calibration.

We analysed the data off-line with custom software written under PV WAVE (Visual Numerics). All ocular rotation angles were expressed in Helmholtz coordinates (elevation and azimuth; see Carpenter, 1988). We defined 0° eye rotation as both lines of sight straight-ahead and parallel. Because of this definition, binocular fixation of the straight-ahead target at 130 cm distance required a 1.45° rightward rotation of the left eye and a 1.45° leftward rotation of the right eye (for an I.P.D. of 6.5 cm). During optimal binocular fixation of the straight-ahead, nearby target, each eye was rotated 5.3° inward. We signed leftward orientations and velocities as negative. We calculated vergence as left eye orientation minus right eye orientation (vergence angles thus being positive during normal, convergent fixation).

Saccades were detected based on the following criteria in both eyes: velocity exceeding 12°/s, acceleration exceeding $2000°/s^2$, duration between 12 and 200 ms and amplitude exceeding 1°. After this rough detection of saccades, our software (as described earlier by van der Steen and Bruno, 1995) determined the exact starting point and end-point of each real saccade. We detected pure horizontal vergence shifts in a similar way based on the following criteria for rough detection: velocity in each eye exceeding 3°/s, duration between 3 and 800 ms and monocular amplitude exceeding 0.01° (with the left eye moving in the opposite direction of the right eye).

To judge if fixation of a target was monocular or binocular, we used version-vergence plots. In Fig. 3.1, the construction of these plots is explained.

Experimental procedure

To establish correct alignment of the head relative to the targets, we made the subjects aware (if necessary) of the physiological diplopia of non-fixated targets. We positioned them centrally in the magnetic field and made precise position adjustments according to the symmetry of images perceived with either eye of the nearby and distant targets. We adjusted chin and forehead rests to minimise head movements. We instructed the subjects to keep their heads still in the central position, to refrain from blinking during each trial and we asked them particularly not to blink during the gaze-shifts. They initiated each trial themselves by pressing a button when they felt ready.

Recording sessions always began with binocular and monocular fixations. Subsequently the reading task was performed, first binocular, then with the right eye and finally with the left eye. Then binocular vergence- and version-vergence tasks were carried out in a mixed order, followed by pure (binocular) version tasks and monocular gaze-shifts. Finally, we repeated the calibration. In each subject, we recorded the initial calibration, the reading tasks, pure vergence tasks and binocular version-vergence tasks. In order not to exceed the maximum coil wearing time of 30 minutes, some of the other tasks had to be omitted in some subjects.

Training procedure

To standardise the training exercises, we designed a training device consisting of two rods with coloured tops (red and green) that had to be placed on a table at the same distances as in our experimental apparatus. The rods were connected with threads to determine the distances between the rods and between the nearby rod and the nose. We instructed the subjects to switch fixation between both targets, just as they had done in the experimental session, for a period of 15 minutes, three times a day. Subjects received a paper with instructions and a schedule on which they marked each completed training session. After a period of training of at least 2 weeks, we repeated the recording.

RESULTS

Fixation of distant targets

In the binocular viewing condition, twelve of the 15 subjects (3 C.I., 9 non-C.I.) fixated the targets at 130 cm with appropriate vergence angles. The viewing direction of each eye was within 0.5° from the target. This 1° fixation range (target direction ± 0.5°) of each eye corresponds with a 1° version- and a 2° vergence range (target vergence ± 1°) located around the target, which we will call "target range" (See 3.1). The other subjects (no. 6, 11 and 14) fixated the targets with one eye in the target range and the fellow eye outside the target range with vergence angles close to 0°.

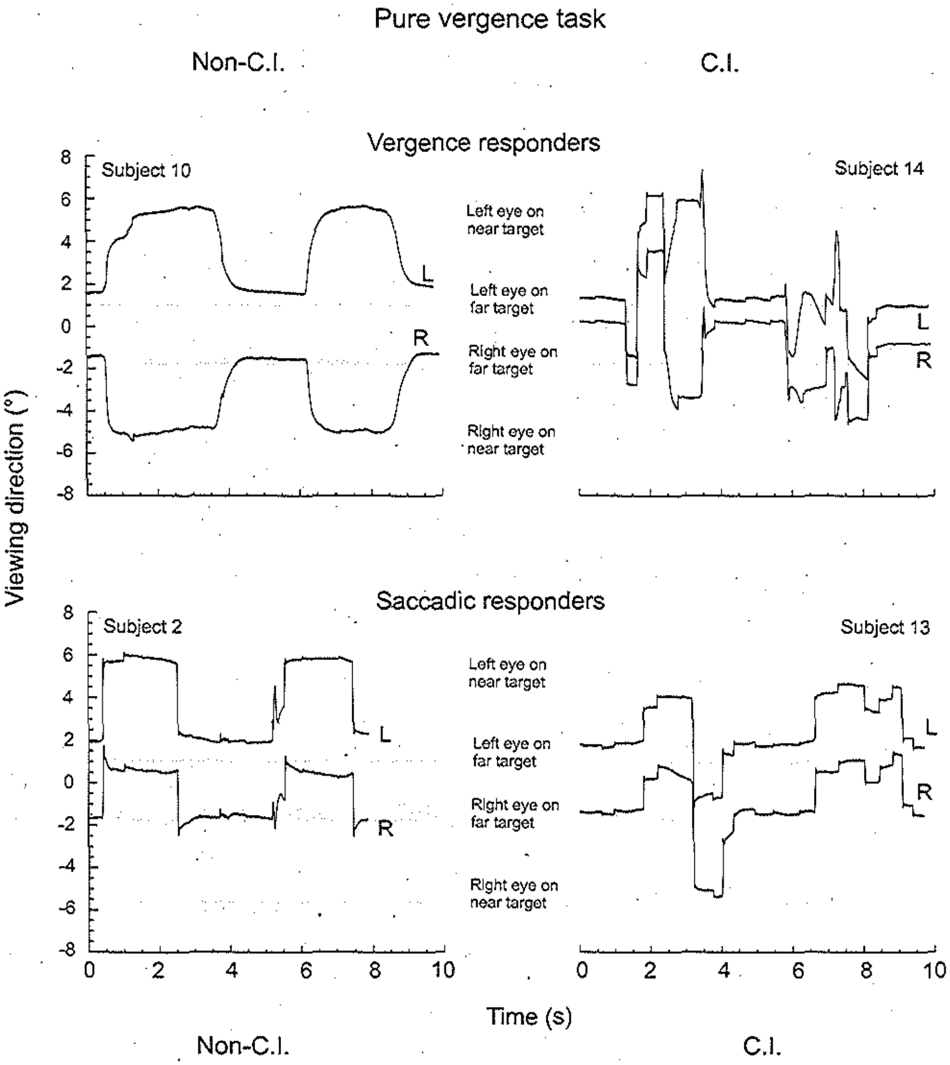


Fig. 3.2
Eye movement traces of four subjects: two typical vergence responders and two saccadic responders (with in each category one C.I. and one non-C.I. subject) during the straight-ahead pure vergence task. The upper right panel shows a C.I. subject with complex mixed responses with episodes of monocular fixation of targets and episodes with binocular fixation efforts. The gray areas indicate the monocular target fixation range for the left and the right eye.

The vergence angles during monocular viewing (with one eye occluded) of distant targets ranged between -0.25° and +5.5° for the asymptomatic subjects and between -3 and +6° for the C.I. patients. Vergence angles during monocular viewing with the left and right eye differed less than 1° for all subjects. Two of the C.I. patients had different vergence angles at the beginning and the end of the experiment. During monocular viewing, subject 12 started with +1° and ended with -5° vergence; subject

13 made monocular fixations with 3° vergence at the start and 6° vergence at the end of the experiment. Vertical vergence was between 0° and 1° for all subjects and was not further analysed.

Pure vergence task

None of the subjects (n=15) consistently made a pure vergence movement during each vergence shift. Small saccades were often associated with vergence shifts. Correctly sized, pure vergence shifts had vergence peak-velocities of -30 to -60 °/s for divergence and 30 to 80°/s for convergence. When small saccades were associated with vergence shifts the vergence peak-velocities were usually higher than during pure vergence shifts. Although the results were idiosyncratic, the (C.I. and non-C.I.) subjects could be divided into two groups: a vergence responder group and a saccadic responder group. Examples of eye movement traces of both groups are shown in Fig. 3.2.

Pure vergence task: Vergence responders

The vergence responders (9 of the 15 subjects) showed substantial episodes of pure vergence during most gaze-shifts in the pure vergence task. If these pure vergence movements occurred just before or after saccadic movements, we still spoke of vergence responders as opposed to subjects with no pure vergence at all. The upper left panel of Fig. 3.2 shows a non-C.I. subject with correct pure vergence responses during most vergence shifts. The upper right panel shows a C.I. subject with complex, mixed responses of saccades and episodes of pure vergence with binocular fixation efforts. Five subjects (all non-C.I.) made smooth pure vergence movements during most gaze-shifts; they sometimes combined the vergence movement with a small saccade. Four subjects (2 non-C.I., 2 C.I) combined virtually all vergence shifts with small saccadic components. During these gaze shifts, one of the eyes was often on the target more quickly. Some subjects (3, 4, 5 and 7) showed pure convergence trajectories while their divergence shifts were combined with saccades.

The vergence responders with a detected eye preference (7, 8, 9 and 11) fixated targets quicker with their preferred eye. Five of the vergence responders with no detected eye preference were quicker on target each time with the same eye during the combined vergence shifts they occasionally made.

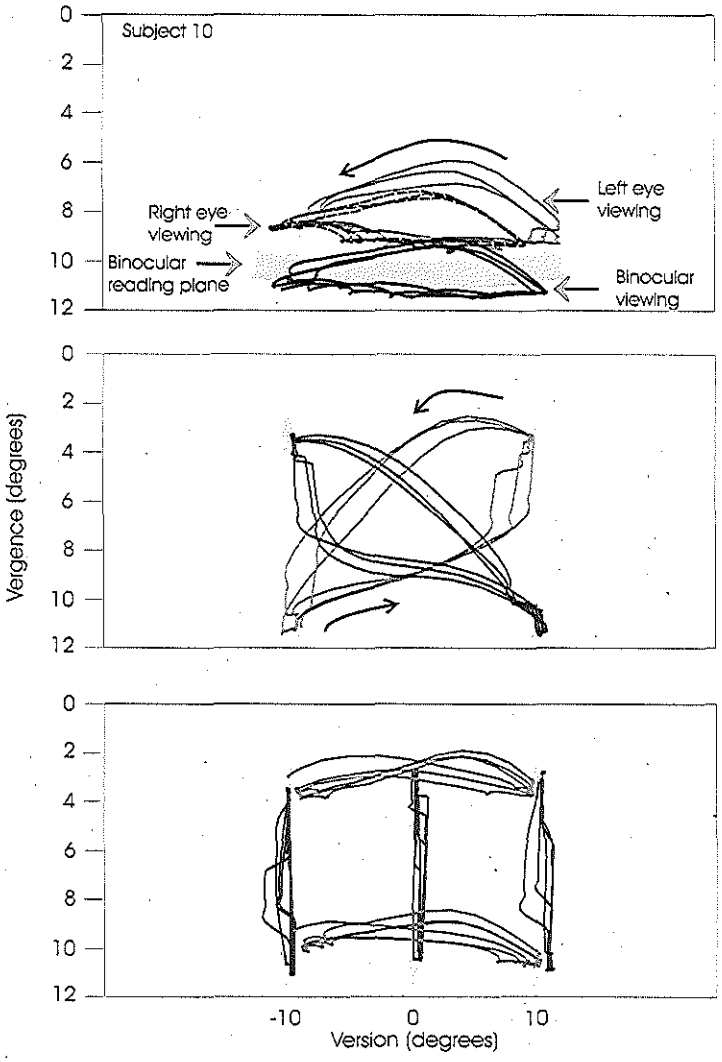
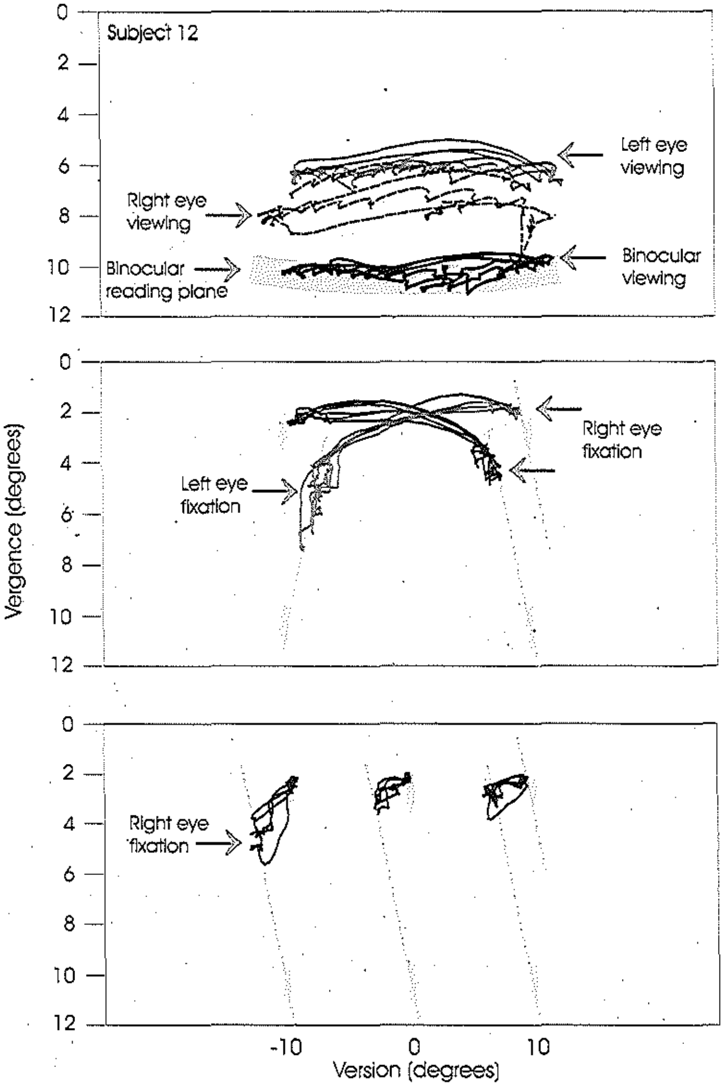


Fig. 3.3
Version–vergence plots for several tasks in one non-C.I. subject with virtually no vergence errors. The target fixation ranges and reading plane range, for correct binocular fixation, are drawn in gray.
The upper panel shows the traces during binocular and monocular reading of text that corresponded with the curved version–vergence plane (gray).
The middle panel shows saccades with vergence between a left nearby target and a right far away target and vice versa. (Target ranges depicted in gray.)
The lower panel shows pure version and pure vergence trials.

Pure vergence task: Saccadic responders with monocular fixation of nearby targets

Six of the 15 subjects (3 non-C.I., 3 C.I.) made saccades instead of vergence movements between the targets during most gaze-shifts in pure vergence tasks. They often fixated the distant targets with both eyes and the nearby targets with one eye. Sometimes small vergence components occurred during or after the saccades. The 3 non-C.I. subjects (1, 2 and 6) always fixated the nearby target monocularly with the preferred eye. The three C.I. subjects fixated with the left or right eye dependent on the task or the target direction. One of the C.I. saccadic responders (subject 15) occasionally reached binocular fixation of the nearby target through combined vergence-version movements, during the central vergence task only.

Fig. 3.4
Version–vergence plots for several tasks in one C.I. subject with insufficient vergence. The target fixation ranges and reading plane range for correct binocular fixation are drawn in gray.
The upper panel again shows reading trials, the middle panel version–vergence trials.
In the middle and lower panel version–vergence lines for left and right eye target fixation are depicted to indicate the monocular fixations of the nearby targets.
The middle and lower panels show the monocular fixation of the nearby targets by this subject.



Pure version task (saccades)

All subjects who performed this task (5 non-C.I. and 3 C.I.) showed normal transient divergence components (Collewijn et al., 1997; Van Leeuwen et al., 1998) during isovergent saccades at both distances. Two of the C.I. subjects fixated nearby targets with one eye. In one of them, the left and right nearby targets were fixated with the same eye; in the other one, the left eye was used for left target fixation and the right eye for right target fixation. Some of the non-C.I. subjects made binocular but imperfect fixations. Subject 2, who showed insufficient vergence during vergence tasks, surprisingly made correct binocular fixations of nearby targets during this task.

Vergence-version task: Binocular viewing condition

During combined gaze shifts, most subjects had greater vergence amplitudes than during pure vergence tasks. All vergence velocities were higher during this task than during pure vergence tasks, as described extensively by Collewijn et al. (1994, 1995 and 1997) and Van Leeuwen et al. (1998).

All vergence responders made combined vergence-version shifts of the required size (e.g. subject 10 in Fig. 3.3). They fixated all targets binocularly. The saccadic responders showed larger vergence components during this task than during the pure vergence task. They often fixated nearby targets monocularly also during this task; the non-C.I. subjects did so with their preferred eye.

Three of the 5 C.I patients showed alternating monocular fixation during this task, fixating the left nearby target with the left eye and the right nearby target with the right eye. Fig. 3.4 shows the monocular fixation of nearby targets with alternating fixation during the version-vergence task in subject 12. Subject 15 made gaze shifts that were correct towards the right nearby target (resulting in binocular fixation), but incorrect toward the left nearby target, which she fixated with the left eye only.

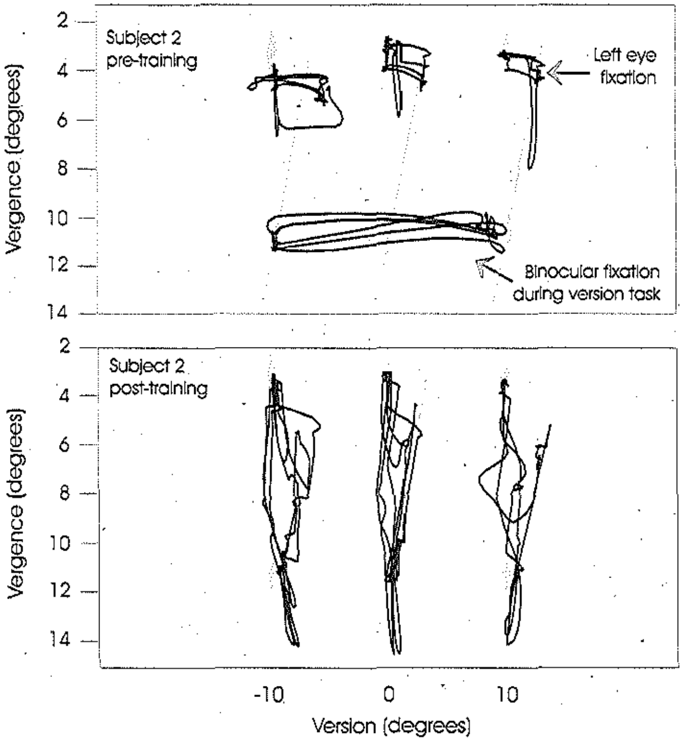
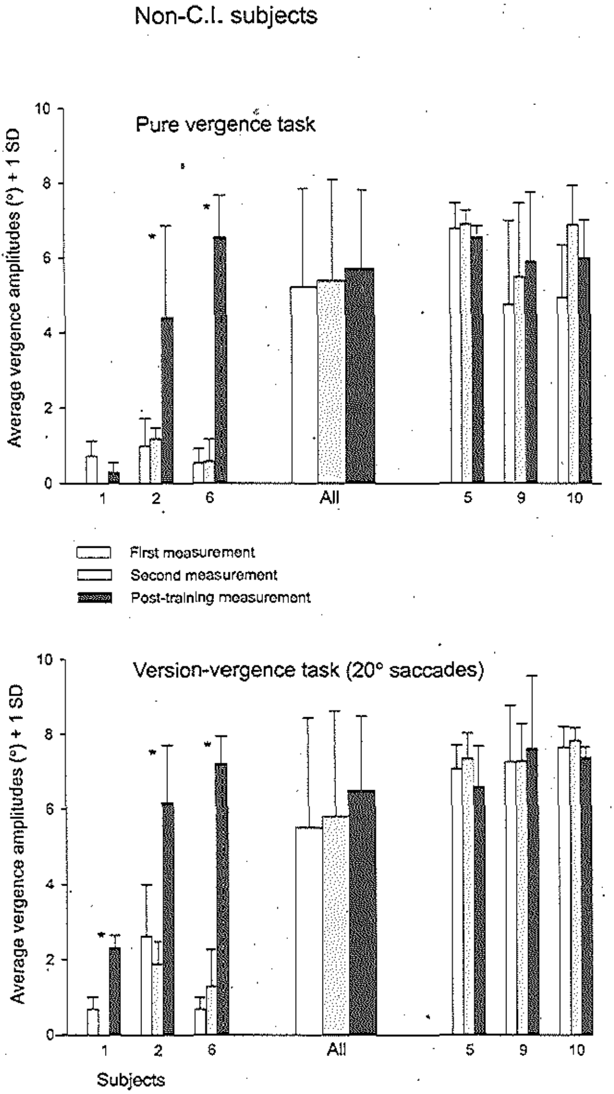


Fig. 3.5
Version–vergence plots of subject 2 during pure vergence tasks in three directions and the nearby pure version saccades task, before (upper panel) and after (lower panel) the training period.
The version–vergence left eye fixation lines are plotted to show that nearby targets were fixated with the (preferred) left eye only before training.
After training, the subject used blinks to initiate the vergence movements. Due to the blink-associated convergence, overshoots are visible in the post-training measurements.

Fig. 3.6
Average vergence amplitudes during vergence and version-vergence tasks in non-C.I. subjects, before (usually twice) and after the training period. On the left the subjects with insufficient vergence, on the right some examples of good responders and in the middle all non-C.I. subjects grouped.



Vergence-version task: Monocular viewing condition

All the subjects who completed the version-vergence task monocularly (5 non-C.I., 3 C.I.) showed saccades accompanied by normal transient divergence and correctly directed vergence components of 1° to 7° amplitudes.

Reading task

All subjects showed transient divergence components during saccades in the reading task as during other saccades. Convergence movements often continued after saccades were finished (consistent with results of Hendriks, 1996) both during monocular and binocular viewing.

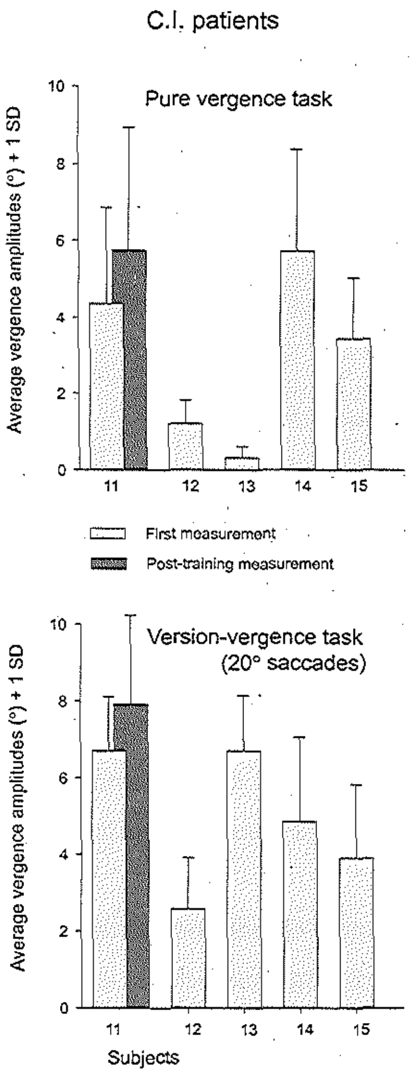


Fig. 3.7
Average vergence amplitudes during vergence and version–vergence tasks in C.I. subjects. All C.I. subjects show insufficient vergence during at least one of the tasks.

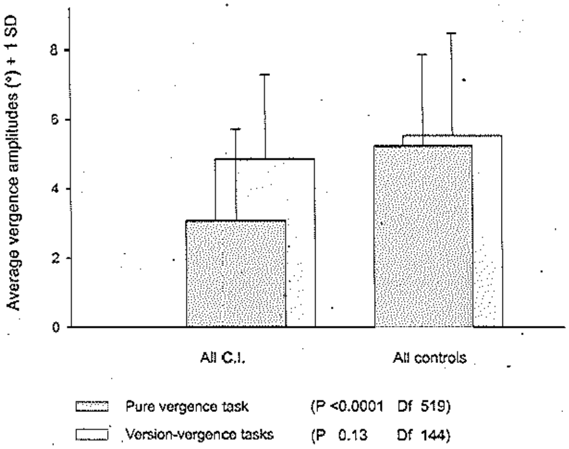
Reading task: Binocular viewing condition

Surprisingly, all subjects fixated the text, at least partly, within a 2° range around the required vergence angle during this task, suggesting binocular fixation of the text. Fig. 3.4 shows an example of the occurrence of monocular fixation of nearby LED's during vergence tasks and binocular reading in the same subject.

Monocular viewing condition

In most subjects, the recordings during monocular viewing showed a somewhat lower vergence angle than during binocular reading. The measurements with the left eye viewing, which were performed after the right eye viewing measurement, usually showed the lowest vergence angles of the reading recordings.

Fig. 3.8
Comparison of vergence amplitudes between the C.I. and the non-C.I. group showing the highly significant difference during the pure vergence task.



Effect of experience and training

Six of the 10 non-C.I. subjects participated in the experimental session a second time without training. Differences between the first and the second measurement were small. Average vergence amplitude during the second measurement was sometimes lower, sometimes higher than the first time (See Fig. 3.6 for details).

Eight of the non-C.I. and one of the C.I. subjects completed the period of training. The other C.I. patients either gave up the training within one week because of the complaints associated with it, or rejected the training due to circumstances. The actual number of training sessions as indicated by the subjects who finished the training period varied between 10 and 35.

After the period of training, vergence amplitude became higher and fixation more accurate in all subjects who performed poorly before training (subjects 1, 2, 6 and 11). In 3 of these subjects, the differences were statistically significant ($p<0.0001$). The other subjects showed small changes in vergence amplitudes, comparable to the changes between the first and second measurement without training. The vergence velocities during version-vergence tasks were significantly higher than before training only in subject 6 ($p<0.01$ for both convergence- and divergence peak-velocity).

Subject 1, who reported that training was difficult, increased his vergence amplitude only during combined version-vergence shifts. Subject 2 usually made *vergence shifts* of the correct size, resulting in binocular fixation, after the training period. At the start of convergence shifts, he used blinks that were associated with fast convergence movements. Peli and McCormack (1986) also found this strategy to facilitate vergence in a subject with convergence difficulties. Fig. 3.5 shows version-vergence plots of his pure vergence performance before and after training, showing the change from saccadic into vergence behaviour. Subject 6 often made pure vergence movements after training as well. Both subjects 2 and 6 were still faster with their preferred eye. Mean vergence amplitudes of the first-, second- and post-training measurements are depicted in Fig. 3.6 and 3.7.

Overall findings

There was a statistically significant difference between the average vergence amplitude in the non-C.I. and the C.I. group (Fig. 3.8). All C.I. patients switched fixation from binocular to monocular and/or from one eye to the other, during at least one of the tasks. Training improved accuracy of binocular fixation in subjects who performed insufficiently before training, even if they had no asthenopia.

DISCUSSION

The role of eye preference

The subjects with the strongest monocular preference according to our testing made saccades and almost no vergence shifts between pure vergence targets and they fixated the nearby targets always with their preferred eye. The fact that none of them had major complaints supports our hypothesis of monocular suppression during these tasks, in subjects with a strong monocular preference. In the subjects who made accurate vergence shifts, often one of the eyes was consistently faster or fixated targets consistently earlier; this was usually the preferred eye. Subjects with this behaviour had minor or no complaints of asthenopia, suggesting a balance between suppression and fusion during binocular gaze-control. Some of the subjects showed an initial saccadic response during divergence only, while convergence was smooth and symmetrical. The more frequent occurrence of small saccades with divergence than with convergence might be an expression of different neural controller pathways for divergence and convergence (Collewijn et al., 1995; Hung, Zhu & Ciuffreda, 1997).

The C.I. subjects showed several binocular and monocular strategies that depended sometimes on the task and sometimes on the target direction. This suggests a less stable monocular preference in the C.I. than the non-C.I. subjects. Dynamic asymmetries have been reported often before (Peli and McCormack , 1983; Enright, 1996; Erkelens et al., 1996) and have been related to monocular preferences by Van Leeuwen et al. in 1998.

Some of the C.I. characteristics that we found resemble features of strabismus. Sireteanu (1982) found that strabismus subjects with alternating fixation had suppressed central regions in the visual field of each eye, while the periphery of both visual fields showed a high degree of binocular cooperation. If the strategy of binocular fixation of distant targets and monocular fixation of nearby targets starts at a very young age, binocular fusion of the central visual field might not develop and strabismus might result. The non-C.I. subjects with this strategy might have become exotropes with a dominant and an amblyopic eye while the C.I. subjects might have become alternating exotropes, if they had developed these strategies at a very young age. Further research in children with C.I. and children with strabismus might be interesting to find support for this hypothesis.

Differences between C.I. and non-C.I. subjects

Differences in asthenopia-score were very small between non-C.I. and C.I. subjects and the N.P.C even proved to be useless in diagnosing C.I. in this group of subjects. Also differences between the eye-movement recordings of C.I. and non-C.I. subjects were sometimes small. Diagnosing C.I. is therefore very difficult. Distinguishing between C.I. and other causes of asthenopic complaints (e.g. psychological reasons or dry eyes) is useful in order to find the right treatment. The combination of complaints and insufficient vergence during eye movement recordings seems the ideal diagnostic criterion. Eye movement measurements in C.I. patients might therefore be *a useful tool* for establishing better C.I. criteria.

Training effect

Practicing 3 times, everyday turned out to be a difficult task, especially because asthenopic complaints were initially evoked by the exercise itself. Although most subjects completed less than 30 training sessions, training of vergence shifts had a positive effect on the size of the vergence shifts in subjects with insufficient vergence shifts before training, even in subjects without complaints. Once a day training sessions might give a better compliance in C.I. subjects. Although the monocular strategy of non-C.I. subjects was satisfactory, vergence training established a binocular behaviour that might be helpful in certain binocular tasks.

Task influence

During (pure version) saccades, binocular fixation was not always perfect, even in the best performing subjects. This could be related to the relatively uninteresting visual task.

The C.I. subjects who fixated nearby targets with one eye during this task did so during vergence tasks as well (saccadic responders). One non-C.I. subject was a saccadic responder in the pure vergence task but made binocular fixations during a near saccade task. This might indicate a difficulty in changing the vergence angle rather than in maintaining the vergence angle. The more accurate vergence during combined version-vergence tasks than during pure vergence tasks are probably due *to the faci*litation of vergence by saccades.

The overall accurate binocular fixation during the reading task can, apart from the facilitation of vergence by saccades, be caused by several mechanisms. Precise accommodation and cognitive attention may play a role. Another factor could be that the virtually constant vergence angle during reading is easy to maintain. Finally the joined contraction of eye muscles during text reading, with slight retraction of the eye into the orbit, as found by Enright and Hendriks in 1994, could be a mechanism for vergence facilitation. Although the asthenopic complaints of C.I. subjects often arise from reading, differences between subjects become clear during vergence-shift tasks.

Conclusions

Binocular motor control is not as binocular as assumed, even in subjects without complaints. The occurrence of small saccades during pure vergence tasks seems a result of quicker target fixation by the preferred eye.

Insufficient vergence shifts do not seem to cause asthenopia in subjects with a strong monocular preference. On the other hand, minor asthenopic complaints can occur in subjects with accurate vergence dynamics. Training of vergence shifts has the potential of changing dynamic strategies during gaze-shift tasks.

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4

Saccadic binocular coordination in alternating exotropia

Anna F. van Leeuwen, Johannes van der Steen, Jan-Tjeerd H. N. de Faber &
Han Collewijn

This chapter was published in Vision Research 2001 Nov;41(25-26):3425-35.

SUMMARY

We studied the coordination of binocular eye movements in human subjects with alternating exotropia (divergent strabismus). Binocular saccades were recorded in 6 subjects during binocular and monocular viewing. Subjects were instructed to make saccades between two continuously lit targets (LED's) presented in an isovergence array (with the straight-ahead target 130 cm from the eyes) in a dimly lit room. For saccades up to 20° amplitude, there were no large differences in the dynamics of the saccades between control and exotropic subjects. However, for larger amplitudes subjects frequently alternated the eye of fixation during saccades. That is, subjects fixated the left target with the left eye and the right target with the right eye. The alternation in eye fixation at the end of the saccade was taken into account in the programming of the saccades. The amplitudes of the alternating saccades were approximately equal to the target amplitude minus the strabismus angle. We conclude that for those saccades where alternation occurs, there is not only a change in the eye of fixation, but also a change in the target representation provided by either eye. Thus, in this group of strabismic patients, saccades may be programmed in a retina-centered coordinate system, if we assume that for making a saccade to a new target in the contralateral visual field its representation on the temporal retinal field of the currently fixating eye is suppressed and the retinotopic target information is derived from the non-fixating eye. In executing the saccade, the non-fixating eye automatically becomes the fixating eye.

INTRODUCTION

Under normal conditions, a target that is being fixated has a foveal representation on the retina of each eye. When a peripherally located target becomes the point of interest, a binocular saccade will be programmed to direct the fovea of both eyes to the new target. In subjects with proper binocular alignment, either eye can theoretically provide the retinotopic reference frame to program the binocular saccades. However, binocular alignment and binocular vision are not innate (Thorn, Gwiazda, Cruz, Bauer and Held, 1994), but develop in early life. This process is disturbed in individuals who develop strabismus. Strabismus can result from disease or trauma (secondary), but often starts during the first 6 months of life (infantile or primary) without known cause (Von Noorden, 1996).

Individuals with manifest strabismus (squint) can not simultaneously direct both eyes towards one single visual target. The non-fixating eye is deviated outward in exodeviations (divergent strabismus) or inward in esodeviations (convergent strabismus) (Von Noorden, 1996). The normal visual target representation, mediated through each eye, is confounded by the presence of a large strabismus angle, which potentially gives rise to multiple internal target representations and thus diplopia. A number of investigators (Steinbach, 1981; Sireteanu, 1982; Travers, 1938; Schor, 1977; Joosse, 1999) have shown that suppression scotomata may play an important role in preventing this from happening.

In this paper, we specifically address the coordination of binocular saccades in subjects with exodeviations who have a tendency to alternate eye fixation. Whereas individuals with micro-strabismus (strabismus of only a few degrees) often have binocular fusion, sometimes even with gross stereopsis, subjects with large angle strabismus have suppression of the fovea of the non-fixating eye to avoid diplopia. This can be achieved by temporary suppression of the fovea of the non-fixating eye (in alternating strabismus patients), or by permanent suppression of one of the eyes. Strabismus patients younger than approximately 7 years of age with permanent suppression of one eye develop (without occlusion therapy) a deep amblyopia in that eye. Strabismus patients who alternate (spontaneously or induced by occlusion therapy) remain capable of using both eyes for (monocular) fixation and have normal visual acuity in each eye.

Some of those patients, like the ones who served as subjects in our study, have a spontaneous tendency to alternate eye fixation during saccade tasks.

A limited number of studies have focussed on the binocular coordination in alternating exotropes. Steinbach (1981) measured alternation (fixation-switching saccades) between the left and right eye in exotropes who fixated a central target with the left eye and the right eye alternatingly. By flashing patterns that were visible to the left or right eye only, he found that the switching of the suppression between the two eyes coincided with the onset of the saccade. Sireteanu (1982) found, in alternating exotropes, that the central visual fields of both eyes were partly suppressed, while the far periphery of the visual fields of both eyes was often combined with some binocularity.

In this paper, we extend the observations made by these investigators to a more complete description of the coordination of horizontal binocular saccades in alternating exotropes. We also provide a possible mechanism by which the brain not only alternates the eye of fixation during saccades, but also uses the retinotopic target representation of each eye alternatingly. We will discuss the consequences of this strategy for the coordination of horizontal saccades.

Table 4.1
Summary of the relevant clinical history of the exotropic subjects used in our study.

Subject	Sex	Age (years)	Visual acuity R/L	Strabismus type	First surgery (years)	Present horizontal strabismus+ angle
1	M	31	1.0/1.0	Infantile Esotropia	<5	Exotropia 8°
2	M	24	1.0/1.0	Infantile Esotropia	1	Exotropia 10°
3	F	17	1.0/1.0	Infantile Esotropia	8	Exotropia 12°
4	M	19	1.0/1.0	Infantile Heterotropia	7	Exotropia 13°
5	F	18	1.0/1.0	Infantile Heterotropia	3	Exotropia 19°
6	M	16	1.0/1.0	Late-onset Intermittent Exotropia	16	Exotropia 20°

METHODS

Subjects

Six adult subjects with exotropia, diagnosed and recruited in the Rotterdam Eye Hospital and 6 controls (colleagues and students), participated in our experiments. All subjects gave their informed consent, according to the rules of the ethics committee of the Erasmus University Rotterdam and of the Rotterdam Eye Hospital. Before the experiments all subjects underwent ophthalmologic and orthoptic examinations in the Rotterdam Eye Hospital. The main results of this examination are shown in Table 4.1. All subjects who needed refractive corrections wore appropriate glasses or contact lenses during the experiment. We selected the strabismus subjects from a larger group of exotropic patients, based on their behaviour of alternating fixation. Five of the 6 exotropic subjects had infantile strabismus and underwent several eye muscle surgeries in childhood, with unsatisfactory long-term results. One subject (# 6) developed normal binocular vision during early childhood. However, he lost binocular fusion when he developed exotropia later on, which he regained after strabismus surgery at age 16 (after our experiments).

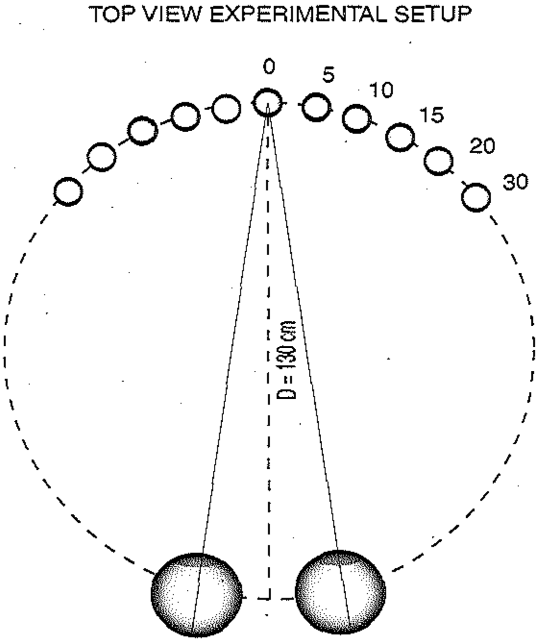

Fig. 4.1
Top view of experimental setup. Visual targets (red LED's) were placed on an isovergence array, thus providing a constant vergence angle. In each trial two targets were lit simultaneously.

Visual conditions

We used a horizontal isovergence array of real LED targets (Figure 4.1). In this array, the central target was straight-ahead at a distance of 130 cm from the eyes (corresponding to approximately 2.9° vergence during binocular fixation, varying with inter-pupillary distance). Pairs of LED's were lit to elicit horizontal saccades ranging in amplitude from 10° to 40°. They were presented symmetrically across the midline or eccentrically. Each target combination of LED's was continuously lit on in a dim background. Saccades were paced by a metronome at 2-second intervals.

Data collection and analysis

We recorded the orientation of both eyes with scleral coils (Skalar, Delft) in an a.c. magnetic field (Robinson, 1963). Signals were low-pass filtered with a 250 Hz cutoff frequency, and sampled at 500 Hz with an AD converter (CED 1401, Cambridge Electronic Design, Cambridge) and digitally stored. We precalibrated search coils and, in addition, monocular fixations were used for off-line calibration.

We analysed the data off-line with custom software written under PV WAVE (Visual Numerics, Houston). We defined the 0° eye angle as the orientation of both lines of sight straight-ahead and parallel. Following from this definition, binocular fixation of the straight-ahead target at 130 cm distance required a 1.45° inward rotation of each eye (with an inter-pupillary distance of 6.5 cm). All ocular rotation angles were expressed in Helmholtz coordinates (see Carpenter, 1988). Leftward and downward orientations and velocities were signed negative. We calculated the vergence- or strabismus angle as left eye orientation minus right eye orientation (strabismus angles in exotropia thus being negative).

Saccades were detected based on the following criteria in both eyes: velocity exceeding 12°/s, acceleration exceeding 2000°/s^2, duration between 12 and 200 ms and amplitude exceeding 1°. After this rough detection of saccades, our software (described before by Van der Steen and Bruno, 1995) determined the exact starting point of each saccade.

Experimental procedure

We positioned the subjects in the center of the magnetic field and made precise adjustments of the head to minimise yaw, roll and pitch offsets. After these adjustments, the head was restrained in this position with chin and forehead rests. We anaesthetised both eyes with drops of oxybuprocaine (0.4 %, Minims, Romford, UK) and inserted the scleral search coils. We instructed the subjects to keep their head stable in the central position against the chin and forehead rest and to refrain from blinking during a trial, particularly during the gaze-shifts. Subjects initiated each trial themselves by pressing a button when they felt ready. Each trial lasted 12 seconds and we obtained at least 4 saccadic gaze shifts per trial.

Target combinations were presented with binocular viewing, monocular right eye viewing and monocular left eye viewing. Recording sessions always started and ended with calibration fixations.

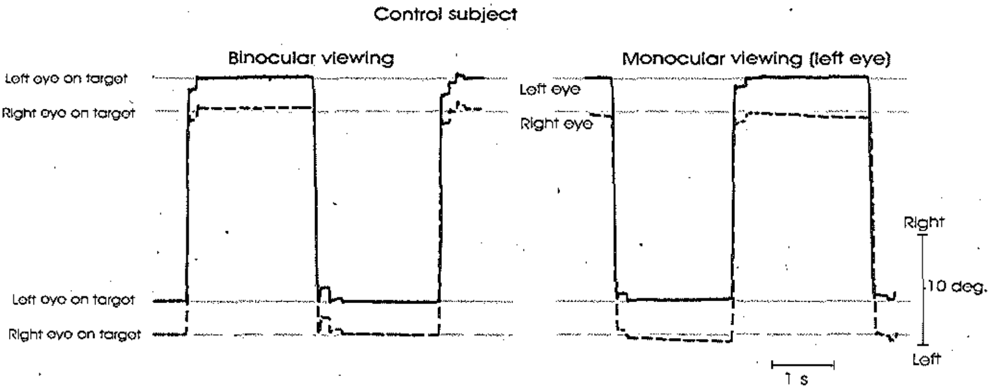

Fig.4.2
Binocular saccades between two targets symmetrically across the midline (A=20°). In this and following figures the Left eye is represented by a solid black line, the right eye by a black dashed line. The grey solid and dashed lines indicate the ideal monocular target fixation for left and rigth eye, respectively. Right- and leftward saccades are upward and downward deflections, respectively.

RESULTS

Alternating versus non-alternating saccades

All control subjects made conjugate saccades under binocular and monocular viewing conditions. The dynamics of the horizontal binocular saccades showed the normal characteristics, including a transient divergence, as described before by Collewijn, Erkelens and Steinman (1988). Typically, under monocular viewing conditions a small drift of the non-viewing eye occurred. The differences in drift velocities between the viewing and non-viewing eye, however, were small (<0.1 °/s and <0.2 °/s, respectively) (See Figure 4.2).

In the exotropic subjects, binocular saccades smaller than 20 degrees were, apart from the presence of a strabismus angle, virtually indistinguishable from saccades made by the control subjects. However, for larger saccades we observed an alternation in eye fixation during horizontal saccades. One of the eyes fixated the first target and, after the saccade, the fellow eye fixated the second target. Figure 4.3 shows an example of binocular saccades made by a control subject (left panel) and alternating saccades made by an exotropic subject (subject #2, right panel) for two targets separated by 20 degrees symmetrically across the midline. The alternating saccades in the exotropic subject can be readily identified: the saccade amplitude of each eye was smaller than the required amplitude between the two targets. When a saccade was made to the left target, the left eye landed on the target (in this case with a small overshoot), and, vice versa, when a rightward saccade was made, the right eye landed on the target. Note that the saccades made by the fixating and non-fixating eye are conjugate, even for the corrective saccades. The subjects were mostly unaware of their spontaneous switching of fixation during saccade tasks.

All 6 exotropic subjects alternated during 40° symmetrical horizontal saccades. During tasks with smaller and/or eccentric saccades, fixation behaviour differed between subjects. Subjects 1, 2, 3 and 4 alternated during saccades larger than 10 degrees to either side, whereas in subjects 5 and 6 alternating saccades occurred only for amplitudes larger than 20 degrees to either side.

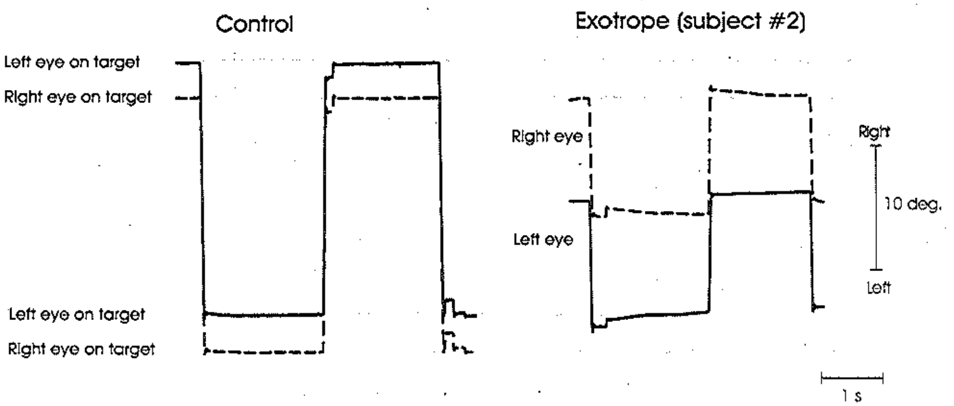

Fig. 4.3
An example of conjugate binocular saccades made by a control subject (left panel) and an example of alternating saccades made by a subject with exotropia (right panel).

A summary of alternating versus non-alternating saccades in relation to target amplitude and position under binocular viewing conditions for each subject is shown in Table 4.2. For each target separation, the occurrence of alternating saccades is indicated by the capital A, whereas situations where the subject preferred to use the left or the right eye only when making saccades, are indicated by L and R, respectively. The combination of L/R indicates that the subject sometimes had a left eye preference, and sometimes a right eye preference, but did not alternate.

Table 4.2
Prevalence of alternating saccades as a function of target amplitude.

a) Symmetrical saccades (across midline)

Subject	10°	20°	30°	40°
1	L	L/A	L/A	A
2	L	A	A	A
3	L/R	A	A	A
4	L	A	A	A
5	L	L	L	A
6	R	R	R	A

b) Eccentric saccades (from midline to periphery and back)

Subject	-30°	-20°	-10°	10°	20°	30°
1	A	A	L	L	L/A	A
2	A	A	L	L/A	A	A
3	A	A	L	L	A	A
4	-	-	-	-	-	-
5	L	L	L/R	L/R	L/R	R
6	A	R	R	R	R	A

A = alternating, L = Left eye fixates, R = Right eye fixating

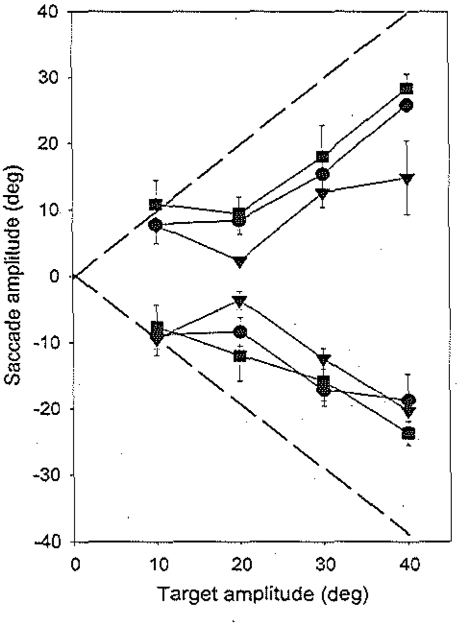

Fig. 4.4
Relationship between target and saccade amplitude in subjects with and without exotropia. Rightward and leftward saccades are plotted separately. The dashed line indicates the linear regression line fitted through the averaged primary saccades of a control subject. The mean saccade amplitude with S.D's for three subjects with exotropia are indicated with solid lines (squares: subject #1, 8° exodeviation; circles: subject #2, 10° exodeviation and inverted triangles: subject #3, 12°exodeviation).
Note the transition in saccade target ratio for saccades larger than 10°. Detailed statistical information is provided in table 4.3.

Table 4.3
Linear fit parameters of saccade/target amplitude relationship in control (averaged over 6 subjects) and three (separately calculated) exotropic subjects. A= slope, R^2=goodness of fit, Y_0= intercept. The far right column shows the variability in primary targeting saccades expressed as the standard deviation of the mean position during the intersaccadic fixation periods.

Subject	Strabismus angle (deg)	A	Direc.	R^2	Y_0	S.D.(Amp.)
Control	-	R	0.98	0.99	-0.3	0.23
		L	0.99	0.98	0.2	0.26
Exotrope # 1	8	R	0.95	0.99	-9.8	1.66
		L	0.59	0.96	4.9	2.29
Exotrope # 2	10	R	0.87	0.99	-9.5	2.28
		L	0.82	0.86	8.2	1.96
Exotrope # 3	12	R	0.63	0.88	-8.8	3.27
		L	0.84	0.99	8.2	3.19

Saccade targeting in exotrope versus control subjects

Alternating the eye of fixation has its consequences for the required saccade amplitude. In computing the correct saccade amplitude, the strabismus angle has to be taken into account. Thus, whereas in normal subjects the ratio between saccade and target amplitude is almost unity, in exotropic subjects this ratio depends on the occurrence of alternating saccades. This is demonstrated in figure 4.4. In this figure the dashed line shows the linear fit (slope=0.99, r^2 =0.98) of saccade versus target amplitude of one control subject. The solid lines show the relation between saccade and target amplitude of 3 exotropic subjects who systematically alternated for saccades larger than 10 degrees. (For each subject the averaged saccade amplitudes at 10, 20, 30 and 40 degree target amplitude are represented with different symbols). Except for 10 degree targets, only those saccades were selected where the subjects alternated, which was the case in 85% of the total number of saccades produced by these 3 subjects. The strabismus angles of the 3 subjects were 8, 10 and 12 degrees, respectively. For target separations larger than 10 degrees, the ratio between target and saccade amplitude in the exotropes deviated from the ratio found in the control subjects. The slopes of the regression lines over the range of 20 to 40 degrees were in most cases close to unity, but the intercepts varied between 5 and 10 degrees. These values approximately correspond to the target amplitudes minus the strabismus angle (see table 4.3). Subjects 4, 5 and 6 were not included in this figure because in those subjects showed alternations only at 40 degree target separation or their data were incomplete, as was the case for subject 4.

The far right column in table 4.3 gives the standard deviations of the averaged targeting saccades at any given amplitude in the control (n=6) and exotropic subjects. These data show that exotropes made less precise primary targeting saccades than the control subjects did. The variability in primary saccade amplitude in the exotropes also explains why the slopes of some of the regression lines plotted in figure 4.4 were considerably less than one. The primary saccade in exotropes frequently undershot the target and had to be corrected by a secondary saccade. These secondary saccades were not taken into consideration in determining the ratio between saccade and target amplitude.

Main sequence characteristics of exotropes versus control subjects

To test for possible differences in the dynamics of saccades, we compared the main sequence characteristics of exotropic versus control subjects. The saccades of both eyes were pooled for binocular and monocular conditions (see figure 4.5, top panel). The eye-switching in the subjects with exotropia causes a limitation to the range of the saccadic amplitudes compared to control subjects. Therefore, we could only compare the amplitudes and peak-velocities of all saccades made during trials with target separations up to 20°.

We used a Monte Carlo bootstrap procedure (n=1000) to test for differences between control and exotropic subjects (Efron and Tibshirani, 1993) The amplitude velocity relationship for the two populations was fitted with the following exponential function:

$$V = S(1-e^{-A/\lambda}) \qquad [1]$$

In this formula V is fitted peak velocity, A is saccade amplitude, and S and λ are the two fit parameters (the saturation level and the length constant, respectively). The amplitude velocity relationship of the exotropic subjects could be described by $S = 427 \pm 9$ °/s and $\lambda = 8.03 \pm 0.3$. The values (n=1000) of S and λ for the control subjects were 490 ±9 °/s and 8.28 ±0.32, respectively (lower panel, figure 4.5, open symbols). Both parameters were significantly different between the two populations (t-test; $p < 0.001$).

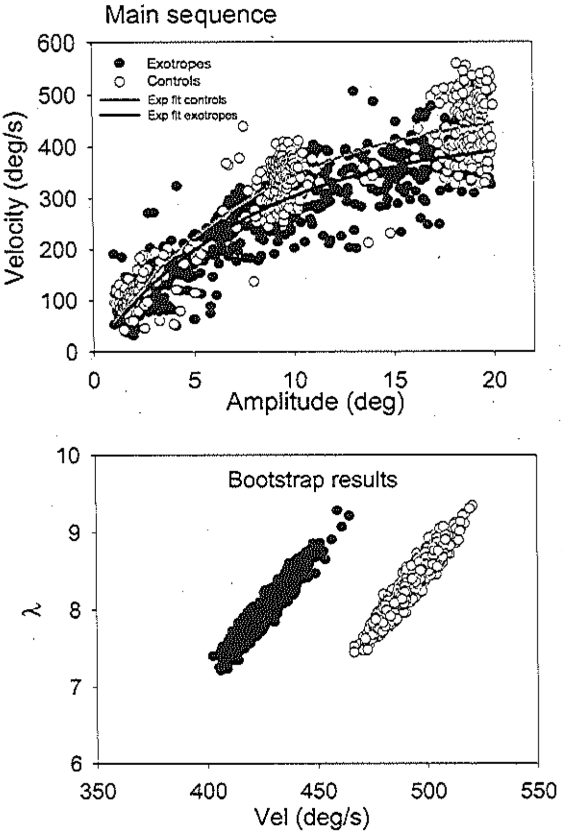

Fig.4.5
A comparison between control (n=6) and exotropic subjects (n=6) in the main sequence of saccades. Top panel: Peak amplitude velocity relationship of the two groups, with the exponential fits through the datapoints.
Lower panel: The relation between λ and S after bootstrapping (n=1000) the main sequences of the two populations in the top panel. Notice the cross-correlation between the λ and P in both populations.

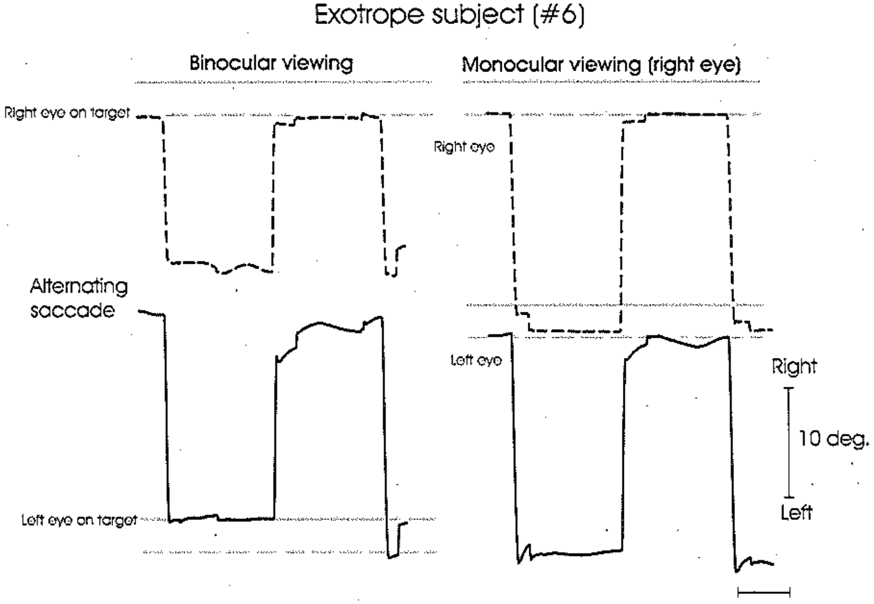

Fig. 4.6
A comparison of saccades made by exotropic subject 6 under binocular (left panel, target amplitude 40°) and monocular conditions (right panel, target amplitude 20°). Notice the fixation of the left target by the left eye and the right target by the right eye in the left panel.

In conclusion, the main sequence for the exotropes was characterised by a lower peak velocity and longer length constant than for the control subjects.

Within the group of exotropes, we also looked for differences in saccade dynamics between alternating and non-alternating saccades. Figure 4.6 depicts a typical example of alternating saccades for subject #6. This subject alternated during 40° symmetrical saccades and 30° eccentric saccades. Alternating saccades during binocular viewing are shown in the left panel of figure 4.6.

During the fixation periods, the non-fixating eye drifted (velocity ~0.2 °/s), while the fixating eye was more steady (drift ~0.1 °/s). The right panel shows non-alternating saccades elicited in the same subject when forced to use his right eye only (left eye occluded), during a 20° saccade task. The alternating saccades during binocular viewing are indistinguishable from non-alternating saccades during monocular viewing. The similarity of saccade dynamics under alternating and non-alternating conditions is more quantitatively demonstrated in the main sequence plots of saccades under the two conditions.

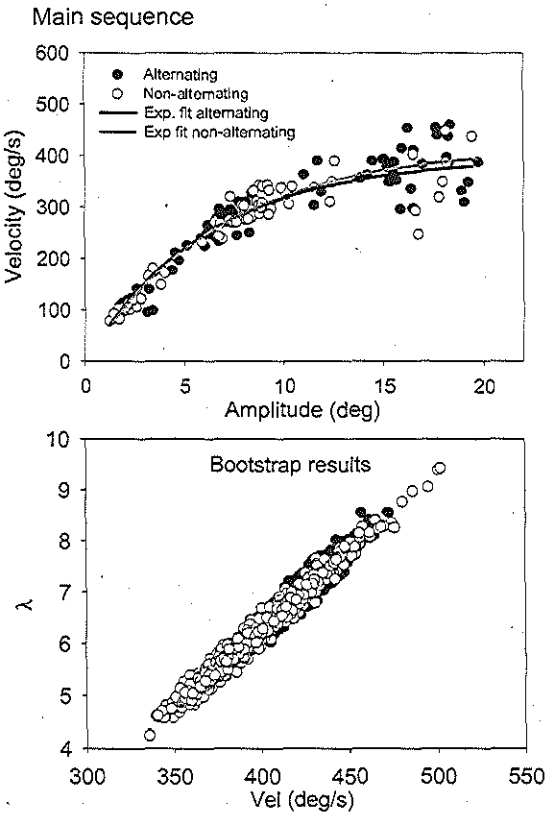

Fig. 4.7
A comparison between main sequence parameters of alternating and non-alternating saccades in subject 6.
Top panel: Peak amplitude velocity relationship of the two groups, with the exponential fits through the datapoints.
Lower panel: The relation between λ and S after bootstrapping (n=1000) the main sequences of the two populations in the top panel.

Figure 4.7 (top panel) shows the amplitude/peak velocity relationship of alternating and non-alternating saccades of subject #6. The bootstrap results are plotted in the lower panel of figure 4.7. The fit parameters (S and λ, the same parameter used to describe exotropes versus controls) were S = 418 ± 15°/s,λ= 6.38 ± 0.48°/s for alternating saccades, and S=398 ± 26°/s, λ = 6.23 ± 0.78°/s for non-alternating saccades. These values were not significantly different. In conclusion, within the exotropes no differences exist between alternating and non-alternating saccades.

Intersaccadic fixation stability in exotropic subjects.

The eye movement traces in figure 4.3 suggest that intrasaccadic fixation stability is less than that of control subjects during intrasaccadic fixation periods. This is further illustrated in figure 4.8. This figure shows XY-plots of left and right eyes of two exotropes and a control subject during + and - 20° saccades from center to periphery and 40° saccades symmetrical across the midline. In these plots, the eye orientation for correct target fixation is depicted for the left (solid traces) and right eye (dotted traces) separately. In the control subject, both the left and the right eye fixate the target. The two exotropes used as examples (Subject 1 and 6, middle and right panel, respectively) fixate with either the left or the right eye. Subject 1 uses his left eye during asymmetrical saccades, whereas subject 6 uses his right eye during the 20 degree saccades. Both subjects alternates during 40 degree saccades. Notice that subject 6 has both a horizontal and a vertical strabismus component. Therefore, during alternation his

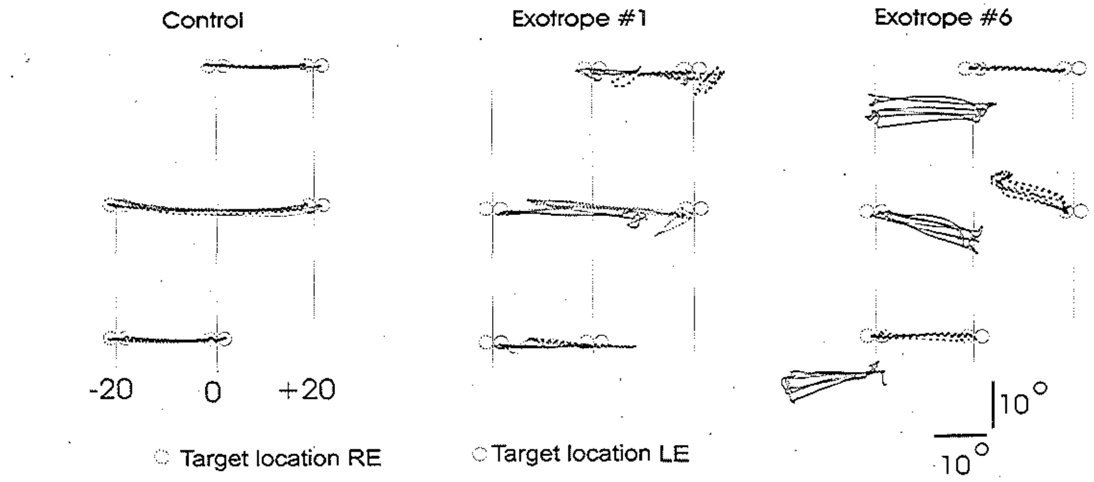

Fig. 4.8
XY plots of a control subject (left panel), and two subjects with exotropia (middle and right panel). For explanation see text.

saccades were oblique.

We quantified the fixation stability in control and exotropic subjects using a peak analysis. We calculated the position distributions (bin width = 0.25°, n =7535) of the right and left eye during the intrasaccadic periods around the mean position during that period. The distributions were fitted with the following Gaussian function:

$$y = y_o + P\, e^{\left[-0.5\left(\frac{x - x_o}{\sigma}\right)^2\right]} \qquad [2]$$

In formula [2] y_0 represents the offset (in percent) of the bins above zero, x the value along the x -axis, and x_0 the value of the central bin. The fit parameters P and σ give an estimate of the height of the peak (in percent) and the width of the distribution (~ standard deviation), respectively. As illustrated in figure 4.9 and table 4 exotropes are less stable during the intrasaccadic periods than the control subjects.

In conclusion, alternating exotropic subjects are not only less precise in saccadic targeting; they are also less stable during fixation, both with the viewing and with the non-viewing eye.

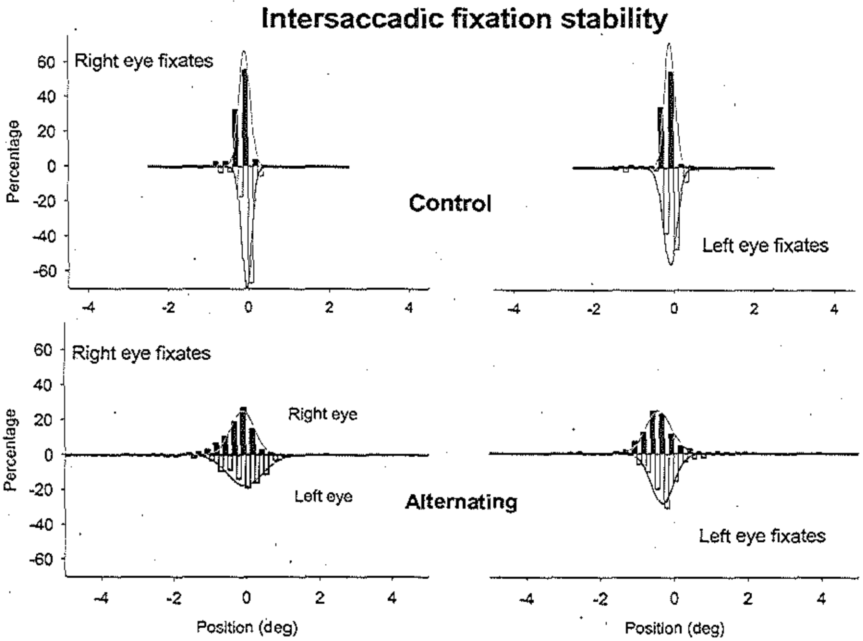

Fig.4.9
Position distributions (bin width = 0.25 deg, n =7535) of the right and left eye during the intrasaccadic periods around the mean position during that period (on average 2 s intervals) in control subjects (top panels) and subjects who made alternating saccades (lower panels). The distributions were fitted with a gaussian function. The formula is shown in the figure. The fit parameters P and σ give an estimate of the heighth of the peak and the width of the Gaussian distribution, respectively.

Table 4.4
Summary of the parameters P (=maximum value in percent) and σ (= standard error) describing the Gaussian fit of the pooled position distribution of control and exotropic subjects Each distribution is based upon 7535 observations. The values for Right (R) and Left (L) eye during Right and Left target fixation are given separately.

		Controls		Exotropes	
	fit	P	σ	P	σ
	Eye				
Right target	R	66	0.14	25	0.32
	L	69	0.13	17	0.48
Left target	R	73	0.13	24	0.34
	L	55	0.17	28	0.3

Surgery outcome

Some of the subjects underwent eye-muscle corrections after our first measurements. Two of them (subjects 2 and 4) participated in our experiment a second time, approximately 6 months after the surgery. Although the strabismus angle had become smaller after surgery, the subjects still alternated, with saccades adapted to the new situation.

DISCUSSION

The alternations observed in exotropic subjects reveal the remarkable capability of the brain to use alternative strategies to overcome the problem of binocular misalignment. In our paradigm, the subjects were instructed to make voluntary saccades between two targets at different locations in visual space. This involves a process where, in order to execute a saccade, a target selection has to take place, based upon which the required saccade amplitude is computed. We will discuss how this process might work in exotropic subjects.

At first sight, binocular saccades in exotropic subjects are, apart from the strabismus angle, remarkably similar to those made by control subjects. Both control and exotropic subjects show a transient divergence typical of binocular saccades (Collewijn et al, 1988). In the exotropic subjects this transient divergence occurs both in alternating and non-alternating saccades. However, a closer analysis reveals that there are a number of quantitative differences in saccade characteristics between control and exotropic subjects. First, binocular saccades made by exotropes are significantly slower than those of control subjects (Figure 4.5). This is true irrespective of the occurrence of alternating or non-alternating saccades. Secondly, in exotropes, the amplitude of the primary saccades (i.e., the initial saccades before correction saccades have occurred) is more variable than in control subjects. The latter group performed similar as the control subjects described by Lemij and Collewijn 1989). Thirdly, fixation during the intersaccadic intervals is less stable in exotropes than in control subjects.

The main question is to find an explanation why these subjects with exotropia make alternating saccades, followed by the question why this strategy might affect fixation stability and saccade dynamics.

The alternating saccades described in our experiments are comparable with the fixation-switch saccades in exotropic subjects as described by Steinbach (1981). However, in contrast to the subjects in the experiment of Steinbach (1981), our subjects were not aware of the changes in eye of fixation. Recent experiments in our department (Van Leeuwen, Westen, Van der Steen and Collewijn, 1999) showed that subjects with insufficient convergence sometimes alternated during saccades, although they had normal stereopsis. The results by Van Leeuwen et al. (1999) suggest that binocular strategies are dependent on the subject's binocular coordination and on the visual task. In these exotropes, the ability to make alternating saccades may have developed as a result of a strategy to avoid large amplitude eye movements. In exotropes, permanent suppression of one eye seems less effective, because mechanical constraints due to the exodeviation complicate large amplitude eye movements.

The strategy to alternate the eye of fixation is the most efficient way for exotropes to use their oculomotor system over its maximum range. This implies that oculomotor mechanisms, and not central cortical mechanisms, are the driving forces behind the strategy of alternating saccades.

This is corroborated by the fact that one of our subjects (subject 6) developed his alternating saccades at the age of 16 (see table 4.1). This suggests that alternating strategies may still develop beyond the age where the visual system has matured.

The ability to make saccades that start with left eye fixation and end with right eye fixation and vice versa, suggests programming of saccades based on retinotopic representation of a target that present alternatingly in one eye and then the other. It has been suggested that normal subjects use this ability when targets are partly occluded (Anderson & Nakayama, 1994), for instance when the nose occludes nearby targets on the left and the right of a subject. Results of Erkelens et al. (1996) and Van Leeuwen et al. (1999) suggest that monocular preferences and oculomotor strategies are correlated. Subjects without a monocular preference (or with an alternating preference) might not have a consistent suppression of one eye, but a direction-dependent or fixation-dependent local suppression. This phenomenon seems comparable between subjects with and without exotropic strabismus.

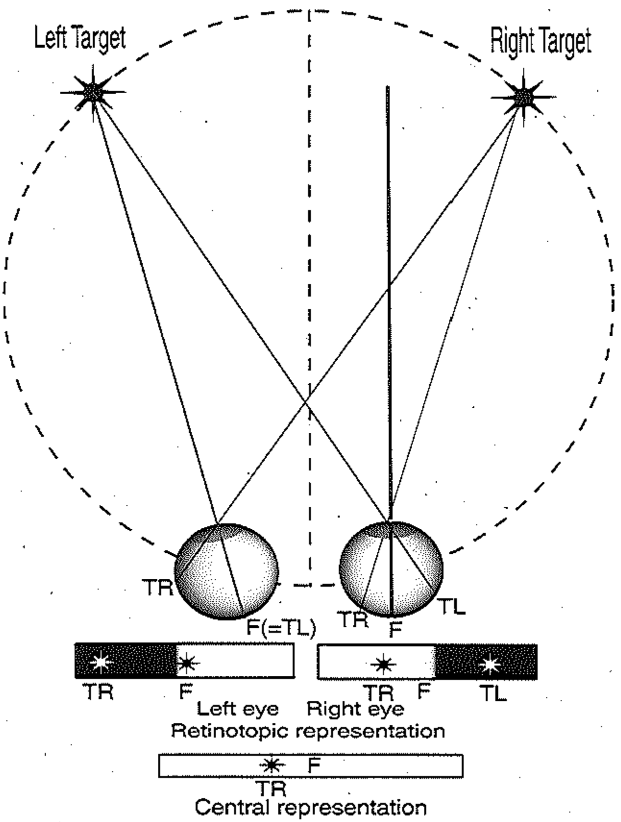

Fig. 4.10
Graphical representation of the role of suppression mechanisms in the generation of alternating saccades. The scheme shows the retinotopic representation of the right and left eye, and at a higher level in the brain the resulting central representation assuming the existence of suppression of parts of the visual field.
TL = left target retinal representation, TR= right target retinal representation, F= fovea. For a more detailed explanation see text.

A number of investigators have reported suppression scotomata in subjects with divergent strabismus. In most studies a scotoma of the nasal visual field in the deviating (=non-fixating) eye was found including or excluding (Travers, 1938; Herzau, 1980) the fovea of the deviating eye. Sireteanu (1982) found that strabismus subjects with alternating fixation had suppressed central regions in the visual field of the non-fixating eye while the periphery of both visual fields showed a high degree of binocular co-operation through anomalous retinal correspondence.

Recently, Joosse (1999) investigated suppression scotomata in 15 subjects with divergent strabismus. Most of these cases (12 out of 15) had under binocular viewing conditions a large area of suppression including the projection of the fixation point as well as that of the fovea in the non-fixating eye. The remaining cases had a nasal hemi-suppression or a small fixation point suppression of the deviating eye. Although these reports on suppression scotomata are highly variable and sometimes controversial, they strongly suggest that suppression mechanisms play an important role in target selection (thereby avoiding diplopia) and in the consecutive step of computing the appropriate saccade motor commands. In addition, in subjects with normal binocular coordination and stereopsis the visual images of both eyes can not always be combined either. During difficult binocular tasks, the visual field of one of the eyes can be completely or partially (Erkelens et al., 1996) suppressed to prevent diplopia or rivalry.

In Figure 4.10, we show a scheme that illustrates a possible mechanism of how saccade programming can be accomplished. In this figure, the left eye fixates the target on the left side. The representation of the left target is on the fovea of the left eye. The left target representation on the retina of the deviating right eye falls on the temporal retina, which according to most investigators is suppressed. In principle, the brain can, in order to program a saccade to the right where the right eye becomes the fixating eye, rely on several mechanisms. One solution is that the brain uses the right target representation in the left eye. This may be the preferred strategy when alternation in exotropes does not occur. However, this implies that when an alternating saccade is made, the brain must also have information about the squint angle to subtract this from the retinotopic coordinates of the left eye. The other more straightforward possibility is that the retinotopic information of the right target in the right eye is used to compute the correct saccade amplitude directly. This strategy, however, has some disadvantages. We showed that the deviated eye is not very stable. Consequently, we expect diminished saccadic accuracy if retinotopic information is used. This is exactly what we find (see table 4.3).

We cannot exclude a third possibility, that is that the system uses, as an extension of retinocentric coding, headcentric information. In strabismic patients headcentric information can be derived from the retinal position information of the eye that perceives the image in combination with the starting eye position of that eye. If the image is perceived in the currently non-fixating eye (the exodeviating eye), the errors due to the strabismus angle in sensed position of target location in headcentric coordinates and information about starting position of that eye, cancel each other. Thus, if this headcentric information is used, the strabismus angle should not affect the accuracy of the saccade. However, an argument against this scenario is the diminished stability of the non-fixation eye. Because in headcentric space, starting eye position is continuously available, fixation instability should not affect saccadic accuracy. This is in contrast to what we find.

A fourth theoretical possibility would be that our subjects had abnormal retinal correspondence (ARC), such that target location could be localized correctly by the fixating and deviating eye. ARC is usually observed in patients with infantile onset of strabismus. However, patients 1 to 5 had a consecutive divergent strabismus following strabismus surgery. Patient 6 developed normal binocular vision during early childhood. However, he lost binocular fusion when he developed exotropia later on, which he regained after strabismus surgery. In none of our subjects ARC could be demonstrated during orthoptic examination. Based upon this we refute ARC as a possibility to explain our findings.

The differences in main sequence parameters between control and exotropic subjects may be related to the presence of suppression scotomata. Zhou and King (1998) have shown that the pontine saccadic excitatory burst neurons (EBN's) projecting to oculomotor neuron pools receive information from both eyes.

It is conceivable that the suppression mechanisms of part of the visual field also have their effect on the amount of input driving these burst neurons. Consequently, both the pulse and step of the saccade will be affected, which is consistent with our findings.

General conclusions

In alternating exotropes, the programming of saccades can be based on information from either eye. If the preference for one eye is relatively strong, the tendency to alternate is small. Alternations during horizontal saccades in exotropic subjects occur more frequently when saccadic amplitudes increase. The presence of suppression scotomata facilitates the programming of alternating saccades, but has its repercussions for saccade dynamics and precision.

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5

Saccadic binocular coordination in strabismus

Johannes van der Steen, Anna F. van Leeuwen, Jan-Tjeerd H. N. de Faber,
Maarten A. Frens & Han Collewijn

This paper was submitted to Vision Research in March, 2002.

Summary

In humans with normal binocular alignment and binocular vision, saccadic eye movements of the two eyes are tightly coupled and have virtually identical dynamic behaviour under binocular and monocular viewing conditions (Collewijn, Erkelens and Steinman, 1988). It is largely unknown if this also holds for humans with strabismus. In these patients the alignment of the two eyes is abnormal and, depending on the age of onset and the strabismus angle, binocular viewing is very often absent or incompletely developed. Oculomotor studies in strabismus have so far focused mostly on ocular misalignment under static conditions. Little is known about the dynamic behaviour of binocular saccadic eye movements in patients with strabismus. In this study we describe the binocular saccade dynamics of 13 subjects with non-alternating strabismus (esotropia or exotropia). All subjects had non-paralytic concomitant forms of strabismus, but were inhomogeneous with respect to type of strabismus (eso- versus exo), visual acuity (amblyopic versus non-amblyopic) and history. We classified our patients in three groups: The first group consisted of six patients with infantile strabismus, but normal visual acuity in each eye. The second group consisted of five patients with infantile strabismus in combination with amblyopia. The third group consisted of two patients with decompensated strabismus, who had normal binocular visual development in early childhood and normal visual acuity in both eyes. From exophoria at young age, they developed exotropia when compensating mechanisms were no longer sufficient. Dynamic properties of binocular saccades in these three groups of patients were assessed from peak velocity versus amplitude relationships and compared with control subjects. Subjects made saccades between two continuously lit targets (LED's) presented in an isovergence array (with the straight-ahead target 130 cm from the eyes) in a dimly lit room under monocular and binocular viewing conditions. We found that patients with infantile strabismus, but normal visual acuity in each eye, had during monocular viewing with either eye, saccadic peak velocities that were lower than during binocular viewing. Saccade dynamics in the group of amblyopic patients were in four out of five cases dictated by the dominant eye (the eye with the highest acuity). That is, no significant differences in the main sequence existed between binocular viewing and monocular viewing with the dominant eye. However, during monocular viewing with the

amblyopic eye saccade velocities were significantly lower than under binocular viewing conditions. In both patients with late-onset exotropia, we found lower peak velocities than in control subjects. In one of these exotropes, we found significantly lower saccade dynamics under monocular viewing conditions compared to binocular viewing conditions. We propose that early onset strabismus affects not only the development of normal binocular vision, but also the development of binocular motor behaviour of saccades. Recent theories on binocular eye movement control postulate the existence of left and right eye burst neuron pools. These burst neuron pools normally receive monocular and binocular input. Apparently, in strabismus patients with normal visual acuity in both eyes, saccade dynamics still depend on the visual input from the two eyes to the burst neuron pools despite the presence of eye dominance. In strabismic patients with amblyopia, saccade dynamics depend more strongly on the dominant eye. The lower saccade dynamics when viewing with the amblyopic eye, in this group, can be explained by the fact that the burst neuron pools are predominantly driven by visual input from the dominant eye. When visual input comes from the amblyopic eye only, this results in significantly impaired saccade dynamics. Therefore, therapy in early childhood to prevent amblyopia does not only have a positive effect on visual function in both eyes, but also on the dynamics of saccadic motor behaviour.

INTRODUCTION

Under normal conditions, binocular saccades are programmed to direct the foveae of both eyes to a new target. Even when one eye is closed the timing and peak velocities of binocular saccades remain virtually identical, reflecting the precise tuning of the brainstem machinery that generates binocular saccades (Collewijn, Erkelens and Steinman, 1988; Lemij and Collewijn, 1992).

Dynamic binocular coordination depends partially on binocular vision. However, binocular alignment and binocular vision are not innate (Thorn, Gwiazda, Cruz, Bauer and Held, 1994), but develop in early life. Impairment of this process can lead to strabismus and/or amblyopia. Also at later stages during life binocular alignment can be disrupted by central or peripheral causes, with (late-onset) strabismus as a result.

In this paper we specifically address the coordination of binocular saccades in subjects with strabismus (eso- or exotropia) with and without amblyopia, who consistently have a dominant eye and who do not alternate. Although the term "preferred eye" is used to indicate eye preference occurring in individuals with normal binocularity, we will use the term "dominant eye" throughout this paper. This to prevent confusion with the terminology used to describe strabismus patients with an amblyopic eye in whom the fellow eye is always called "the dominant eye". Patients with alternating exotropia have been described in a previous paper. (Van Leeuwen et al., 2001). We limited our investigations to the characteristics of saccades in individuals with strabismus who were 15 years of age or older.

A consequence of manifest strabismus (squint) is that subjects can not simultaneously direct both eyes towards a single visual target. The non-fixating eye is deviated outward in exodeviations (divergent strabismus) or inward in esodeviations (convergent strabismus) (Von Noorden, 1996). Thus, the normal binocular correspondence of visual target representation, mediated through each eye, is confounded by the strabismus angle.

We subdivided our patient group in three main categories. The first group consisted of patients who had infantile or primary strabismus with normal visual acuity in both eyes. Infantile or primary strabismus usually starts during the first 6 months of life (Von Noorden, 1996). It coincides with a disturbance of the development of binocular vision. The second group of patients consisted of patients who had infantile or primary strabismus and amblyopia. Amblyopia manifests itself as low visual acuity in one eye. It develops if the image of one of the eyes of an individual is permanently suppressed or blocked at an early age. Although in this patient group amblyopia occurred in combination with strabismus, it must be emphasised that amblyopia is not exclusively linked to strabismus. Other causes are e.g. recurrent eye infections in childhood, occlusion through ptosis and anisometropia as a result of large differences in refractive error. Because these problems can also occur in combination with strabismus, it is difficult to determine the primary cause of amblyopia or strabismus (for more extensive reviews on amblyopia and or strabismus see Leigh and Zee, 1999 and Ciuffreda et al., 1991). Occlusion therapy, periodically patching the dominant eye, can in general prevent or improve amblyopia until the age of 7 years (Van Noorden, 1996). The difference in normal versus low visual acuity in the two groups was partially caused by the fact that most patients in the first group had received occlusion therapy, whereas this was not the case in the second group. The third group of patients consisted of two patients who had late-onset exotropia after having increasing exophoria. We will call this type of strabismus "decompensated exophoria" in this paper. The main difference between this group and the first two groups is that the two subjects in this third group had normal binocular alignment early in life. Therefore, they developed normal binocular vision and normal visual acuity in both eyes during this period. The strabismus developed after the critical period for binocular vision.

In contrast to the extensive knowledge on the abnormalities of oculomotor control during static gaze holding (for reviews see Leigh and Zee, 1999, Ciuffreda et al., 1991), very little is known about the dynamics of saccadic eye movements in patients with amblyopia and/or strabismus. Fast gaze shifts or saccades are important in daily life in a variety of tasks, such as orientation and reading. Ciuffreda et al. (1991) reported increased latencies of saccades in the amblyopic eye in reaction to suddenly appearing targets, but no abnormalities in the main sequence. Kapoula et al. (1997) studied binocular coordination of saccades in patients with esotropia. However, they focused on post-saccadic drift and not on the main sequence. Maxwell et al. (1995) reported nonconjugacies in subjects with deep amblyopia, but they also did not systematically investigate main sequence parameters.

Binocular coordination is achieved by neuronal structures at the motor periphery consisting of motoneurons and specialised interneurons located near or in the cranial nerve nuclei that innervate the extra-ocular muscles. Precise binocular control mechanisms enable healthy subjects to make binocular saccades with great precision and reproducibility (Collewijn et al., 1995). Several investigators have shown that binocular coordination has adaptive properties (Kapoula et al., 1995, Van der Steen and Bruno, 1995). This shows that the neural machinery responsible for binocular coordination is trained and calibrated during infancy and probably throughout life in order to maintain the precise binocular coordination characteristic of primate eye movements despite growth, ageing effects, and injuries to the eye movement neuromuscular system. It has been suggested by King and Zhou (2000) that malfunction of this network or of its ability to adaptively learn may be a contributing cause of strabismus. If this is the case then abnormal binocular development resulting in strabismus and/or amblyopia may also result in abnormal binocular saccade dynamics.

METHODS

Subjects

Thirteen adult subjects with strabismus, diagnosed and recruited in the Rotterdam Eye Hospital and 6 controls (colleagues and students) participated in our measurements. All subjects gave their informed consent, according to the rules of the ethics committee of the Erasmus University Rotterdam and of the Rotterdam Eye Hospital. Prior to the experiments all subjects underwent ophthalmological and orthoptic examinations in the Rotterdam Eye Hospital. The main results of this examination are shown in Table 1.

The first group consisted of six subjects who had infantile strabismus without amblyopia (group 1). Four subjects had infantile esotropia, one had infantile exotropia and one had consecutive exotropia (that is: prior to the exotropia this subject had esotropia). Five subjects of this group had received occlusion therapy. The second group consisted of five subjects who had strabismus in combination with amblyopia (group 2). Two had infantile exotropia, one had infantile esotropia and two had consecutive exotropia. The third group consisted of two subjects who had decompensated exophoria (late-onset exotropia) with normal visual acuity.

All subjects had in common that, at the time of the measurements, they had no stereoscopic vision and they used their dominant eye to fixate objects. It must be noted that the Rotterdam Eye Hospital serves as a centre of expertise to which more difficult strabismus cases from a large part of the Netherlands are referred for second opinions

Table 5.1
Overview of medical history and orthoptic examination results of the studied patient groups.

Subject	Sex	Age at time of experiment	Acuity R/L (correction)	Dominant eye Occlusiontherapy (+or-)	Strabismus type	Age of first surgery, number of operations	Present tropia
Infantile Strabismus with normal visual acuity							
1	f	36y	1.25 / 1.25 (+1.5 / +1)	L +	Infantile esotropia	4y, 1	20° ET
2	m	21y	1.0 / 1.0- (none)	R +	Infantile exotropia	5y, 2	15° XT
3	m	15y	0.8 / 1.2 (+1 / +0.5)	L +	Infantile esotropia	4y, 1	10° ET
4	m	50y	1.0 / 1.0 (none)	L +	Consecutive exotropia	8y, 2	20°XT
5	v	24y	1.0 / 1.0 (+2 / -2.5)	R -	Infantile esotropia	1y, 2	5° ET
6	f	32y	1.0 / 1.0 (none)	R +	Infantile esotropia	7y, 1	15°ET
Strabismus in combination with amblyopia							
7	f	22y	1.0 / 0.25 (-0.25 / +2)	R +	Infantile esotropia	1y, 4	5° XT
8	m	45y	1.0 / 0.7 (0 / -1)	R ?	Infantile exotropia	18y, 3	0-15° XT
9	m	40y	0.15 / 1.25 (+1 / -1)	L ?	Consecutive exotropia	4y, 2	20° XT
10	m	36y	0.1 / 1.0? (?)	L -	Infantile exotropia	none	20-25° XT
11	f	35y	1.0 / 0.1 (+8 / +8)	R -	Consecutive exotropia	8y, 2	25° XT
Late-onset strabismus with normal visual acuity							
12	f	30y	1.0 / 1.0 (none)	R -	Decomp. exophoria	none	0-10° XT
13	f	24y	1.0 / 1.0 (none)	L -	Decomp. exophoria	none	0- 15° XT

or for complex eye muscle surgery. Therefore there may have been some bias in the selection of patients with more complex strabismus.

All subjects who needed refractive corrections wore appropriate glasses or contact lenses during the experiments.

Visual stimuli

We used a horizontal isovergence array of real LED targets (for a detailed description see Chapter 4: Van Leeuwen et al., 2001). In short, the central target was straight-ahead at a distance of 130 cm from the eyes. Pairs of LED's were simultaneously visible against a dim background to elicit horizontal saccades ranging in amplitude from 10° to 40°. The LED pairs were presented symmetrically across the midline or eccentrically, with each LED subtending the same convergence angle. Saccades were paced by a metronome at 2 second intervals.

Data collection and analysis

Binocular eye movements were recorded with scleral coils (Skalar, Delft) in an a.c. magnetic field (Robinson, 1963). Signals were low-pass filtered with a 250 Hz cut-off frequency, sampled at 500 Hz with an AD converter (CED 1401, Cambridge Electronic Design, Cambridge) and digitally stored. Search coils were pre-calibrated and, in addition, monocular fixations were used for off-line calibration.

We analysed the data off-line with custom software written under PV-WAVE (Visual Numerics, Houston). The zero gaze angle was defined as the orientation of both lines of sight straight-ahead and parallel. Following from this definition, binocular fixation of the straight-ahead target at 130 cm distance required a 1.45° inward rotation of each eye (with an inter-pupillary distance of 6.5 cm). The corresponding convergence angle of 2.9° applied similarly to all other targets. All ocular rotation angles were expressed in Helmholtz coordinates (see Carpenter, 1988). Leftward and downward orientations and velocities were signed negative. We calculated the vergence- or strabismus angle as left eye orientation minus right eye orientation (exotropia strabismus angles thus being negative).

Saccades were detected based on the following criteria in both eyes: velocity exceeding 12°/s, acceleration exceeding 2000°/s^2, duration between 12 and 200 ms and amplitude exceeding 1°. After this rough detection of saccades, our software (described before by Van der Steen and Bruno, 1995) determined the exact starting point of each saccade. We calculated amplitude and peak velocity of left and right eye saccades. These two parameters were used to construct a peak velocity versus amplitude plot. This plot typically shows an exponential rise in peak velocity, saturating at higher amplitudes. The amplitude velocity relationship for the two populations was fitted with the following exponential function:

$$V = S\,(1 - e^{-A/\lambda}) \qquad [1]$$

In this formula, V = fitted peak velocity, A = saccade amplitude, and S and λ the two fit parameters (the saturation level and the length constant, respectively). These two fit parameters adequately describe the main sequence plot. The saturation level indicates the maximum speed attained by the eyes, whereas the length constant gives an indication at which amplitude this maximum speed is obtained. We used a Monte Carlo bootstrap procedure to test for differences between saccades under binocular and monocular viewing conditions. (Efron and Tibshirani, 1993). This procedure consists of sub-sampling with replacement (n= 1000) from a set of real-valued observations with an unknown probability distribution. In our experiments this yields two fit parameter populations, one for saccades under monocular viewing and one under binocular viewing conditions. The individual fit parameter populations and their cross-correlation from the bootstrap procedure were compared with a Student t-test. In this way we were able to quantify with a level of significance whether the two populations were identical or not. We used this statistical procedure throughout this paper.

Experimental procedure

Subjects were seated with their head in the centre of the magnetic field with precise adjustments of the position of the head to minimise yaw, roll and pitch offsets. After these adjustments, the head was restrained in this position with chin and forehead rests. We anaesthetised both eyes with drops of oxybuprocaine (0.4 %) and inserted the scleral search coils. Subjects were instructed to keep their head stable in the central position against the chin and forehead rest and to refrain from blinking during a trial, particularly during the gaze-shifts. To initiate a trial subjects pressed a button when they felt ready. Each trial lasted 12 seconds and at least 4 saccadic gaze shifts per trial were obtained.

Target combinations were presented in pseudo-random order under binocular viewing, monocular right eye viewing and monocular left eye viewing conditions. Recording sessions always started and ended with calibration fixations.

We focused on the peak velocity of binocular saccades attained under binocular and monocular viewing conditions. We did not systematically analyse binocular saccade duration because of the large variability in saccade end points, which were due to post-saccadic drifts in one or both eyes in strabismic subjects.

We also compared the horizontal and vertical strabismus angles under binocular and monocular viewing conditions.

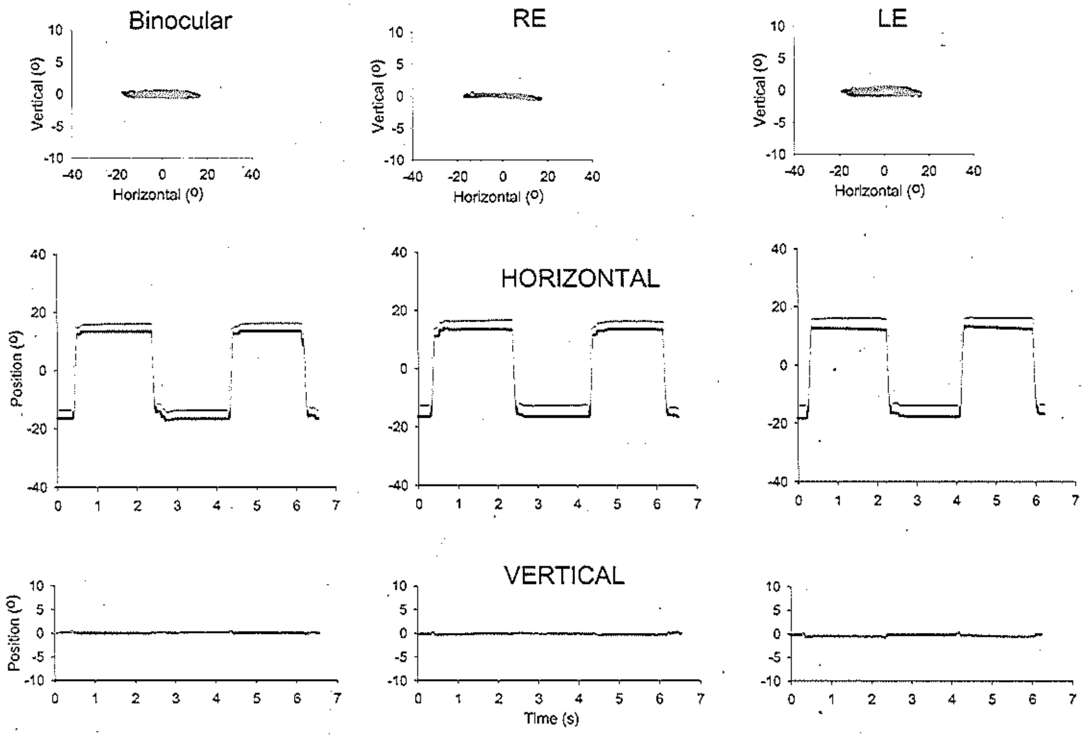

Fig. 5.1
Example of binocular horizontal saccadic eye movements of a control subject under binocular, right eye viewing and left eye viewing conditions. The targets were placed at a distance of 30 degrees symmetrically around the midline. The top panels show x-y plots, the centre and lower panels show time series plots of horizontal and vertical gaze, respectively. Black lines: Right eye, Grey lines: Left eye. Note that the horizontal left and right eye traces in the middle row panels do not overlap during the intersaccadic intervals. The offset of 3 degrees between left and right eye in the horizontal plane corresponds with the vergence angle at this viewing distance (see methods).

RESULTS

Saccade characteristics in control subjects

To allow a direct comparison of saccade dynamics between normal and strabismic subjects, six control subjects underwent the same experimental procedure as our patients. Their saccadic behaviour was in agreement with the literature. That is, all control subjects precisely fixated the targets and made conjugate saccades between the two targets under binocular as well as under monocular viewing conditions (see Fig. 1). Also the dynamics of the horizontal binocular saccades had normal characteristics and were similar to those described before by Collewijn, Erkelens and Steinman (1988).

Typically, under monocular viewing conditions the non-viewing eye had some drift. The differences in drift velocities between the viewing and non-viewing eye, however, were small (<0.1°/s and <0.3°/s respectively; see Fig 1). The x-y plots in the top

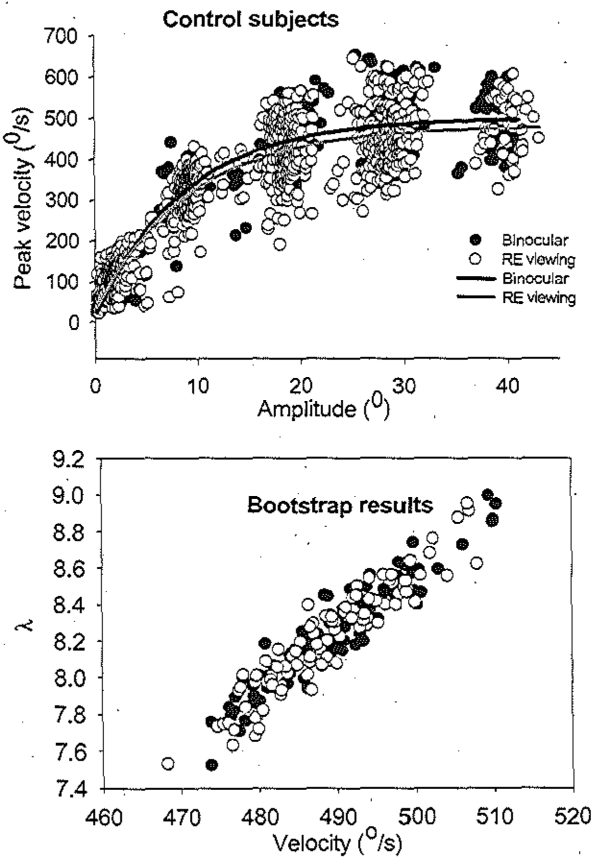

Fig. 5.2
Top panel: Main sequence plot of peak velocity of saccades as a function of saccade amplitude. Black circles: Binocular viewing, Open circles: Monocular viewing (right eye). The Black and grey lines show the fitted exponential regression lines under binocular (grey line) and right eye (black line) viewing conditions.
Bottom panel: Bootstrap results of binocular (black circles) and right eye (open circles) viewing condition in control subjects (N=6).
X-axis: Saturation velocity (deg/s) Y-axis: Lambda, the length constant. This panel demonstrates complete overlap of the distributions of binocular and right eye viewing.

panels of figure 5.1 show the conjugacy of saccades under binocular and monocular conditions. Notice that in this subject the approximately 3° horizontal vergence angle under binocular viewing conditions persisted under monocular viewing conditions. In all six control subjects, the vertical alignment of the eyes was very precise: any vertical vergence angle was less than 0.5 degrees.

Because saccadic behaviour was very similar among the control subjects, we pooled the peak velocities of left and right eye saccades (range: between 1 and 40 degrees) of all six control subjects in order to compare the dynamics of saccadic eye movements under binocular and monocular viewing conditions. Figure 5.2 (top panel) compares the main sequence plots for binocular and right eye viewing conditions. The left eye condition has been left out in this plot for reasons of clarity, as it was similar to the right eye condition.

With the bootstrap procedure, the amplitude velocity relationship of the control group during binocular viewing was described by $S = 489 \pm 8.5°/s$ and $\lambda = 8.23 \pm 0.3$ (lower panel, figure 5.2, closed symbols). The values of S and λ for the monocular right eye viewing condition of our control subjects were $489 \pm 8.1°/s$ and 8.22 ± 0.29 respectively (lower panel, figure 5.2, open symbols). S and λ for the monocular left eye viewing condition were $488 \pm 7.1°/s$ and 8.21 ± 0.31. There was no significant difference (t-test; $p>0.5$) between the values of S and λ during the different viewing conditions

Binocular saccade characteristics in subjects with infantile strabismus and normal visual acuity

All six subjects who had infantile strabismus in combination with good visual acuity in both eyes had a dominant eye (see table 1). Five of these subjects underwent occlusion therapy in their childhood. Normal visual acuity in both eyes allows in theory a functional use of both eyes, although the image of the non-dominant eye might be (partly) suppressed to prevent diplopia. To investigate if this is reflected in the dynamics of binocular saccades, we computed the maximum velocity of saccades of these patients under binocular and monocular conditions and compared the values with those from our control group.

Figure 5.3 and 5.4 show two examples of binocular coordination in patients with

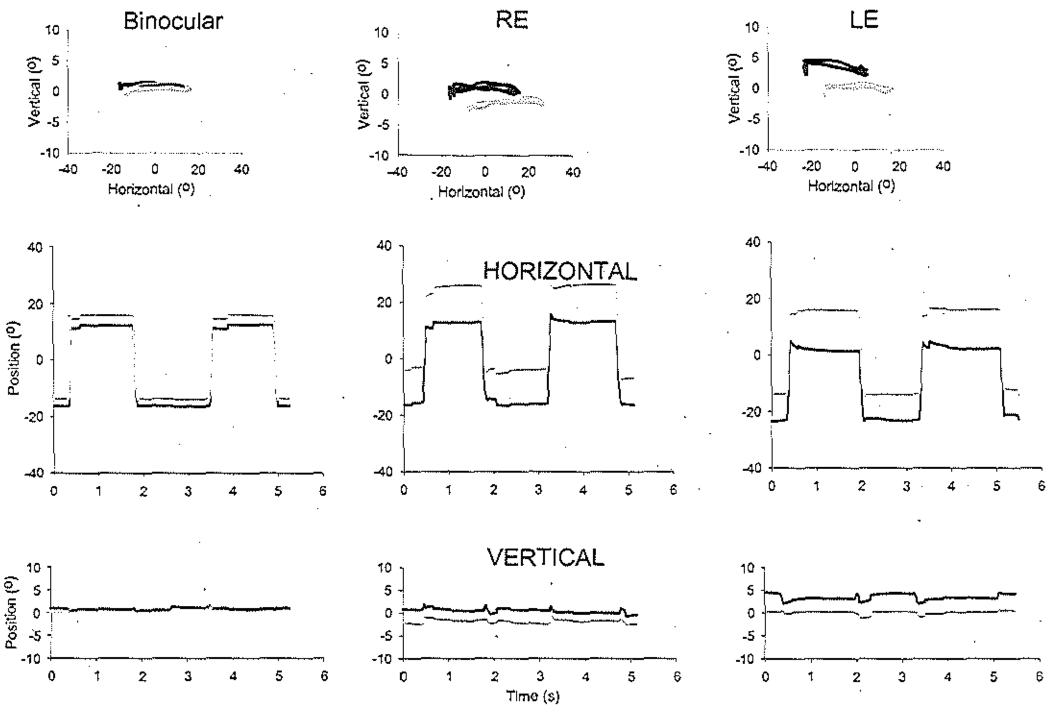

Fig. 5.3
Example of binocular saccadic eye movements of subject 3 with infantile strabismus and normal visual acuity in both eyes. Conventions as in Fig. 5.1.

infantile strabismus (subjects 3 and 2). Both subjects had infantile strabismus with normal visual acuity in both eyes. However, binocular vision was absent. In subject 3 the strabismus angle, as determined during orthoptic examination, was 10° esotropia. The left eye was the dominant eye. Under binocular viewing conditions the saccades were yoked and vertical phoria was absent (see top left panel, figure 5.3). This subject differed from the others in this patient group in the sense that during the measurement the strabismus angle under binocular viewing conditions (3.6 degrees) was considerably smaller than during monocular viewing conditions (compare Figure 5.3, left, middle and right panels). Vertical misalignment occurred only under monocular viewing conditions. When the right eye was viewing, the left eye was depressed (hypotropic), when the left eye was viewing, the right eye was elevated (hypertropic). Figure 5.4 shows another patient who had infantile strabismus (subject 2). This subject had 15 degrees exotropia of the left eye. Note the similarity of the eye movements during binocular and right eye viewing. Despite this similarity in saccade profile and identical strabismus angle under binocular and monocular viewing conditions, the saturation

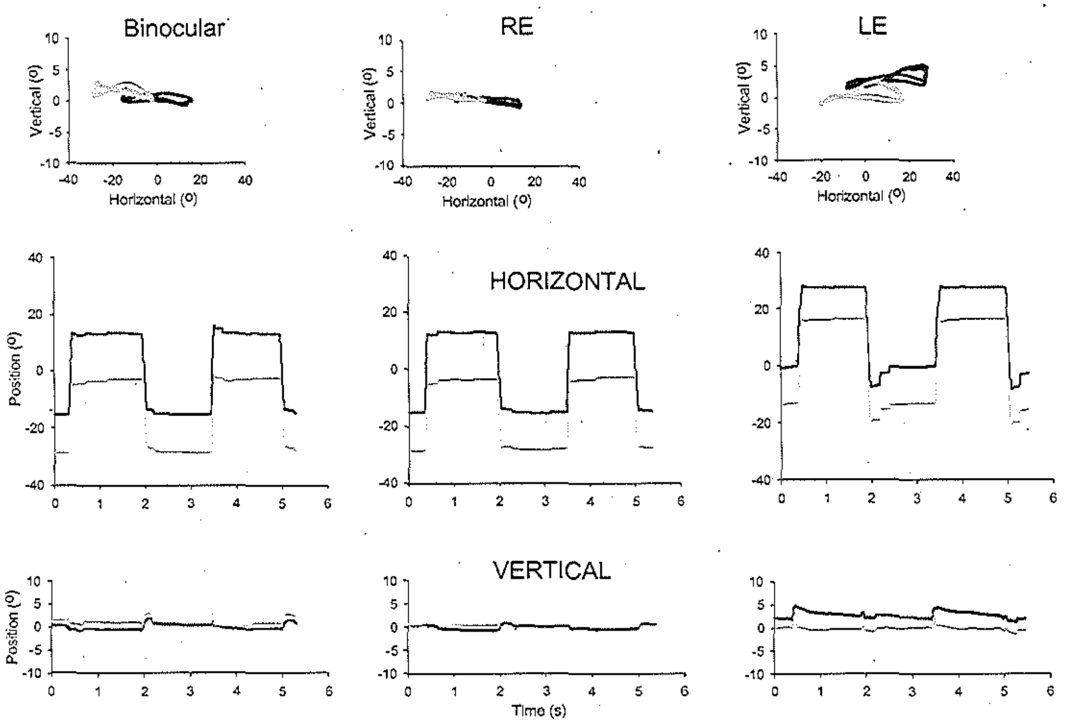

Fig. 5.4
Binocular saccadic eye movements of subject 2 who had 15° exotropia during both binocular and monocular viewing. Conventions as in figure 5.1.

velocities of saccades during monocular viewing were significantly lower during right eye and left eye viewing than during binocular viewing, as is shown in table 5.2.

We compared the main sequence of binocular saccades under binocular and monocular viewing conditions in this group. Figure 5.5 shows the main sequence plot of subject 3. The fit parameters S and λ obtained from the bootstrap analysis (n=1000) were S=563 ± 12.8°/s and λ=10.06 ± 0.62 for the binocular condition (lower panel figure 5.4, circles), S=524 ± 10.7°/s and λ=9.59 ±0.47 for the monocular right eye viewing condition and S=513 ±13.3°/s and λ=9.97 ±0.64 for the monocular left eye viewing condition (see lower panel of figure 5.5, triangles and squares respectively). Both fit parameters were significantly different (P<0.005) between binocular and monocular viewing.

Table 5.2 summarises the saturation velocities (S) for all 6 subjects with infantile strabismus. In four out of six subjects (2, 3, 4 and 6) the peak velocities of saccades under binocular viewing conditions saturated at significantly higher values than under monocular viewing. In these four subjects, the saturation velocity of the dominant eye during binocular viewing was significantly higher than that of the non-dominant eye (t-test, P< 0.05). Also during the dominant eye viewing condition this eye had a significantly higher saturation velocity than the non-dominant eye (t-test, P<0.05). No significant differences were found between the dominant and non-dominant eye when subjects looked with the non-dominant eye only.

In summary, despite the fact that all patients had a dominant eye, in four out of six subjects the saccade dynamics were influenced by the non-dominant eye. In the other two subjects (1 and 5) the differences between monocular and binocular viewing were small or even reversed, implying that during monocular viewing these subjects could generate saccades with identical or even higher peak velocities than during binocular viewing. Notice however, that the peak velocities of these two subjects were significantly lower than those of the other patients in this group (see table 5.2). This suggests that for some unknown reason the main sequence parameters of these two patients were impaired. Table 5.3 summarises the horizontal strabismus and vertical phoria angles of all six subjects in this group under binocular and monocular viewing conditions.

In five out of six subjects, the strabismus angle during binocular viewing was almost identical to the strabismus angle during dominant eye viewing. As shown in figure 5.3, in one patient (3) the strabismus angle during binocular viewing was much smaller than during monocular viewing, which suggests that this patient had some residual mechanism of binocular alignment.

Table 5.2
*Saturation velocities (S) of dominant and non-dominant eye calculated from the main sequence data using the bootstrap procedure during binocular viewing, dominant eye and non-dominant eye viewing conditions. The second column indicates if the right (R) or the left (L) eye was the dominant eye. *:The asterisks mark cases where saturation velocities during binocular viewing were significantly higher than under monocular viewing conditions. The bottom row shows the group means.*

		Saturation velocity (deg/s)					
		binocular viewing		viewing with dominant eye		viewing with non dominant eye	
subject	dom.eye:	dom. eye	non-dom. eye	dom. eye	non-dom. eye	dom. eye	non-dom. eye
1	L	349	338	354	349	354	348
2*	R	471	427	436	426	436	427
3*	L	572	563	529	513	556	526
4*	L	550	553	520	523	480	432
5	R	303	300	351	321	300	327
6*	R	464	424	426	413	420	470
	Mean	452	434	434	411	427	435

Fig. 5.5
Top panel: Main sequence plot of peak velocity of saccades as a function of saccade amplitude.
Bottom panel: Bootstrap results of Right and Left eye saccades of subject 3 under binocular and monocular viewing conditions.
X-axis: Saturation velocity (deg/s).
Y-axis: Lambda, the length constant.

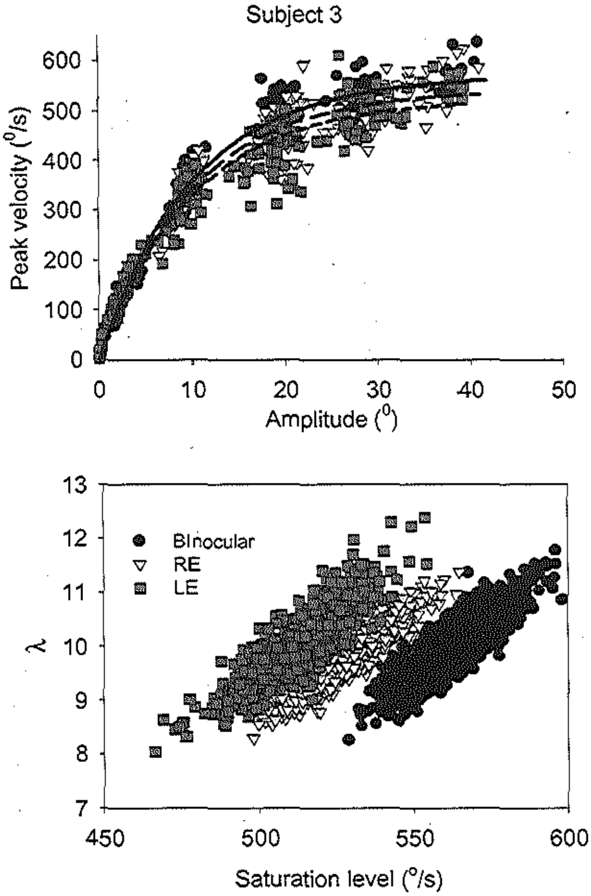

Table 5.3
Summary of horizontal strabismus angle and vertical phoria under binocular, right eye and left eye viewing conditions. Horizontal strabismus angle: Positive values: esotropia, negative values: exotropia. Vertical strabismus angle: Positive values: Right eye elevated with respect to left eye, negative values: right eye depressed with respect to left eye.

		horizontal strabismus angle			vertical strabismus angle		
subject	dom.eye:	binocular viewing	dom. eye	non-dom. eye	binocular viewing	dom. eye	non-dom. eye
1	L	18.00	17.30	30.30	-1.50	-0.60	-3.20
2	R	-15.20	-15.20	-17.20	-1.10	-0.70	2.50
3	L	2.90	11.80	12.00	0.60	3.30	2.30
4	L	-17.50	-18.10	-21.50	0.90	-3.20	-3.40
5	R	7.10	6.00	2.10	6.20	5.00	11.00
6	R	23.30	20.50	28.00	2.00	1.70	3.30

In the majority of cases (4 out of 6) the saturation velocities of binocular saccades were lower than those of the control subjects (average difference: 8%). In these 4 patients, the saturation velocities of binocular saccades were significantly higher than of monocular saccades. In three out of these four patients there were no significant differences in strabismus angle under binocular and monocular conditions. From this we can exclude the possibility that differences in dynamics under binocular and monocular conditions had trivial mechanical causes.

The two patients who had under all viewing conditions considerably lower peak velocities than the control group (difference 40 %) did not have differences in saturation velocity between binocular and monocular viewing conditions.

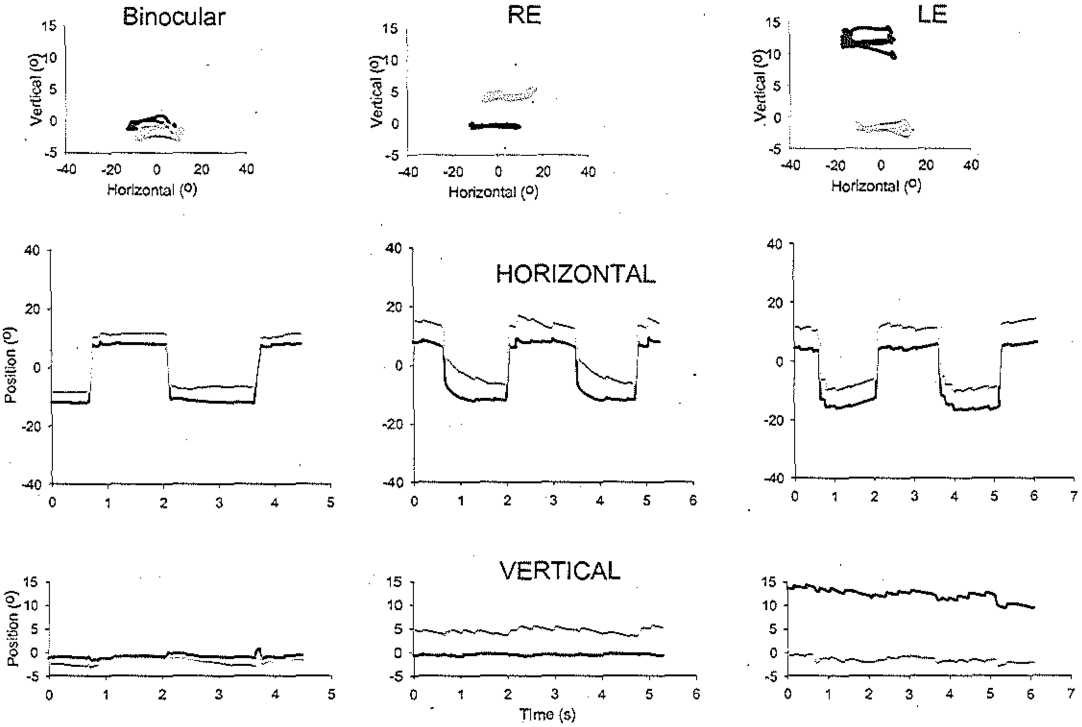

Fig. 5.6
Example of binocular saccadic eye movements of subject 7. The left eye is amblyopic. Left panels: binocular viewing, centre panels: right eye viewing and right panels: left eye viewing conditions. Conventions as in figure 5.1.
Notice the latent nystagmus during monocular viewing.

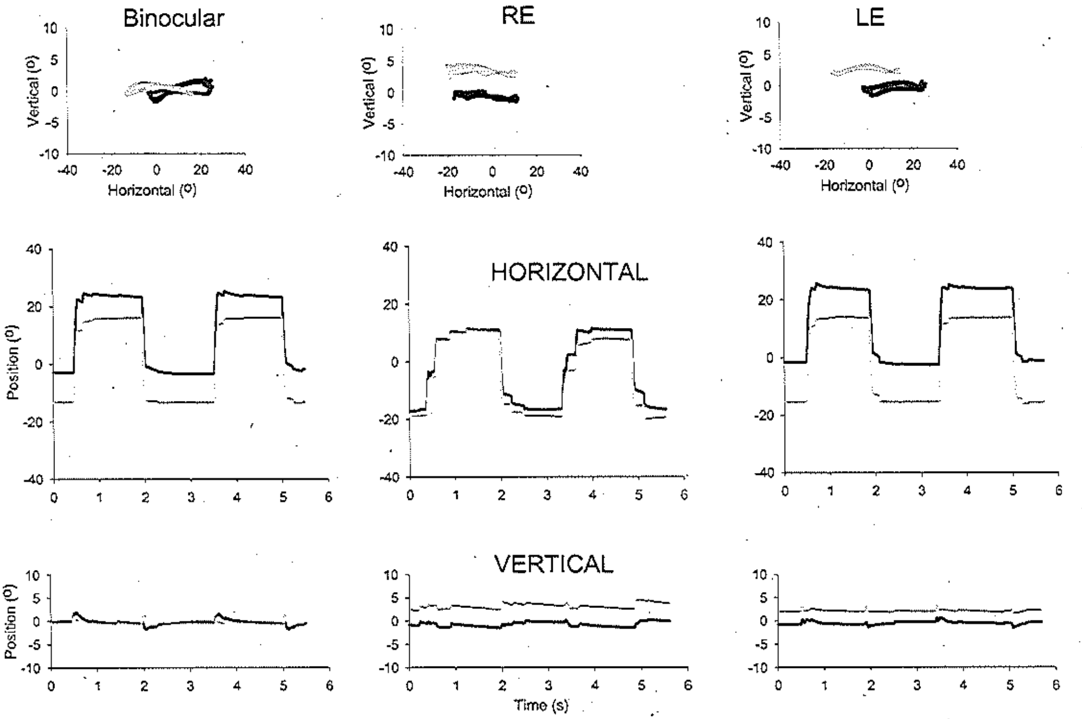

Fig. 5.7
Example of binocular saccadic eye movements of subject 9. The right eye was amblyopic. Left panels: binocular (binocular), centre panels: right eye viewing (right eye) and right panels: left eye viewing conditions. Conventions as in figure 5.1.
Notice the similarities between binocular and left eye viewing, and the inability to generate large rightward saccades during right eye viewing.

Binocular saccade characteristics in strabismus patients with amblyopia

This group consisted of five subjects who had amblyopia in combination with strabismus. Two examples from this group of amblyopic subjects are shown in figures 5.6 and 5.7. In subject 7 (presented in figure 5.6) the left eye was the amblyopic eye (visual acuity right eye: 1.0, left eye: 0.25). Under binocular viewing conditions the saccades were yoked with a small vertical misalignment of the amblyopic eye. This pattern changed under monocular viewing conditions. During right eye viewing there was a latent nystagmus with the slow phase directed leftwards in both the viewing and the occluded eye. Under this condition, the occluded left eye deviated inward resulting in a squint angle of 5°. In addition, there was a 5° upward deviation of gaze in the amblyopic eye. During left eye viewing, the latent nystagmus reversed its direction, direction of gaze in the occluded right eye was 5° inward and 12° upward.

From the observation that occlusion of the amblyopic eye caused impairment of coordinated binocular eye movements, we may conclude that, in this patient, the left amblyopic eye contributed to binocular coordination.

In subject 9 (shown in figure 5.7) the right eye was the amblyopic eye (Visual acuity: RE: 0.15, LE: 1.25). This patient had a convergent strabismus at young age, but later in life this changed into exotropia. According to the orthoptic examination records (static condition) the exotropia angle was 20°. We found slightly different values in our eye movement data. During binocular viewing, when making saccades, the exotropia was 15° with a small transient vertical phoria during the saccade. When saccades to the right were executed, the right (amblyopic) eye also had a transient nasally directed nystagmus. During left eye viewing (rightmost panels, figure 5.7) saccades were almost similar to those in the binocular condition, except that the exotropia increased to 20°, in correspondence with the value assessed during orthoptic examination. There was also a small vertical phoria of 5°. During right eye viewing (the amblyopic eye), the vertical phoria persisted, but the exotropia decreased. Horizontal rightward saccades frequently consisted of multiple steps.

Plots of peak velocity versus amplitude for the two amblyopic subjects shown in figures 5.6 and 5.7 are given in figures 5.8 and 5.9, respectively. The values of S (saturation velocity) of subject 7 (figure 5.8) are similar during binocular and right eye viewing. This is consistent with the fact that the right eye is the dominant eye. In contrast, the saturation velocity during left eye (the amblyopic eye) viewing is significantly lower (squares).

Table 5.4
Saturation velocities (S) of all five amblyopic subjects.

		Saturation velocity (deg/s)					
		binocular viewing		viewing with dominant eye		viewing with non dominant eye	
subject	dom.eye:	dom. eye	ambl. eye	dom. eye	ambl. eye	dom. eye	non-dom. eye
7	R	499	469	492	442	450	429
8	R	380	378	345	350	279	331
9	L	499	524	493	508	492	510
10	L	642	596	570	537	462	570
11	R	390	341	403	347	397	341
	Mean	482	462	461	437	416	436

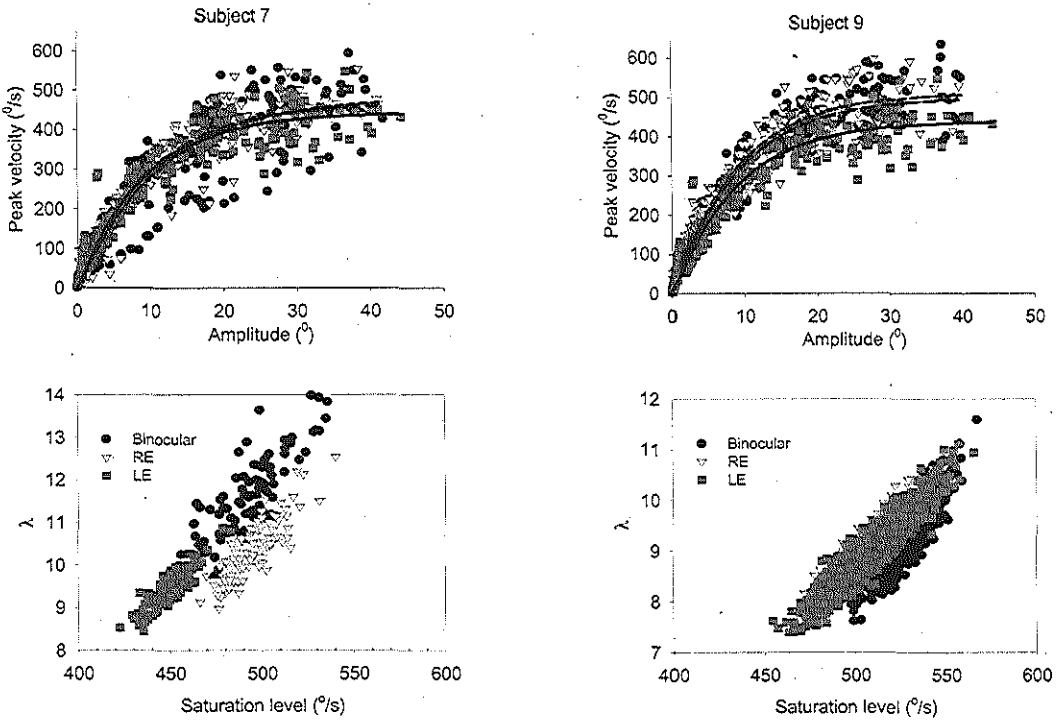

Fig. 5.8
Top panels: Main sequence plot of saccadic peak velocity as a function of saccade amplitude. Bottom panels: Bootstrap results of Right and Left eye saccades under binocular (black circles) and right eye (open circles) viewing conditions.
X-axis: Saturation velocity (deg/s). Y-axis: Lambda, the length constant.

In subject 7, the saturation levels for binocular and right eye viewing were identical, although lambda was lower under right eye viewing conditions. Saturation velocities of saccades during left eye viewing were significantly lower.

The situation is slightly different for subject 9 (figure 5.9). In this patient, the saturation velocity of the amblyopic eye under the binocular viewing condition was 524°/s. This is a small but significant difference ($P<0.005$) compared to the saturation velocity of that eye under the two monocular viewing conditions (see table 5.4). The saturation velocities of the dominant eye were similar under all viewing conditions ($P>0.5$).

Lower saturation velocities under monocular viewing conditions were found in three out five subjects (7, 8 and 10) and were most marked when the amblyopic eye was viewing. The differences in mean saturation velocity values between binocular viewing conditions and viewing with the dominant eye were not significant (t-test, $P>0.05$).

Table 5.5
Horizontal and vertical strabismus angles of amblyopic subjects.

		horizontal strabismus angle			vertical strabismus angle		
subject	dom. eye	binocular viewing	dom. eye	amblyopic eye	binocular viewing	dom. eye	amblyopic eye
7	RE	-3.80	-6.80	-6.70	1.10	-5.10	13.60
8	RE	-9.60	-10.30	-7.60	-5.80	-2.30	-1.90
9	LE	-9.30	-12.20	-2.50	0.20	-2.70	-4.80
10	LE	-25.50	-28.20	-22.80	6.40	-14.80	11.10
11	RE	-23.30	-20.60	-28.80	2.10	1.60	3.30

However, the mean saturation velocities of the dominant and the amblyopic eye when viewing with the amblyopic eye were significantly lower than during binocular viewing ($P<0.05$).

Amblyopic subjects have been investigated before by a number of groups (Maxwell, Lemij and Collewijn, 1995; Ciuffreda, Levi and Selenow, 1991). A common finding in studies on amblyopic subjects are instabilities (drift or latent nystagmus) during intersaccadic intervals. In our study we observed such instabilities under binocular viewing conditions in one out of five amblyopic subjects. These instabilities were augmented under monocular viewing conditions. Two amblyopic subjects had latent nystagmus (present during monocular viewing) during the intersaccadic intervals with the slow phase drift directed nasally and with oppositely directed saccades.

The horizontal strabismus angle amongst subjects was very variable. This is shown in table 5. In four out of five subjects the horizontal strabismus angle increased when viewing with the dominant eye only.

Binocular coordination in decompensated exophoria (late-onset strabismus)

The third group of strabismus patients consisted of two subjects with normal visual acuity in both eyes. In these subjects, strabismus had grown gradually from increasing exophoria. The difference with the group of patients who had infantile strabismus is that these two subjects had experienced in early life a period with binocular vision. Before the onset of exotropia they both had had stereopsis. They both had exotropia with only small vertical phorias. Neither of them had received strabismus surgery before we tested them. Our eye movement records show that the two subjects (12 and 13) had under binocular viewing conditions, despite their present strabismus, very similar binocular saccade dynamics as the control subjects.

Figure 5.10 shows binocular coordination of subject 12. According to the orthoptic examination report, this subject had a variable degree of exotropia from 0 to 15 degrees. The left eye had been determined as the dominant eye. Our eye movement recordings are in correspondence with the orthoptic examination, i.e. they show that the dominant left eye was used to fixate the targets when making saccades back and forth between the left and right target. The saccades were conjugate and the two eyes moved virtually in the same horizontal plane (top panel figure 5.10). Under binocular viewing conditions the strabismus angle was small.

Under monocular viewing conditions there was a moderate increase in the strabismus angle. Also, unlike the situation in the first two groups of strabismus patients, there were only small differences in vertical position of the two eyes (see figure 5.10, top panels and bottom panels). Horizontal and vertical strabismus angles of both patients under binocular and monocular viewing conditions are shown in table 5.6.

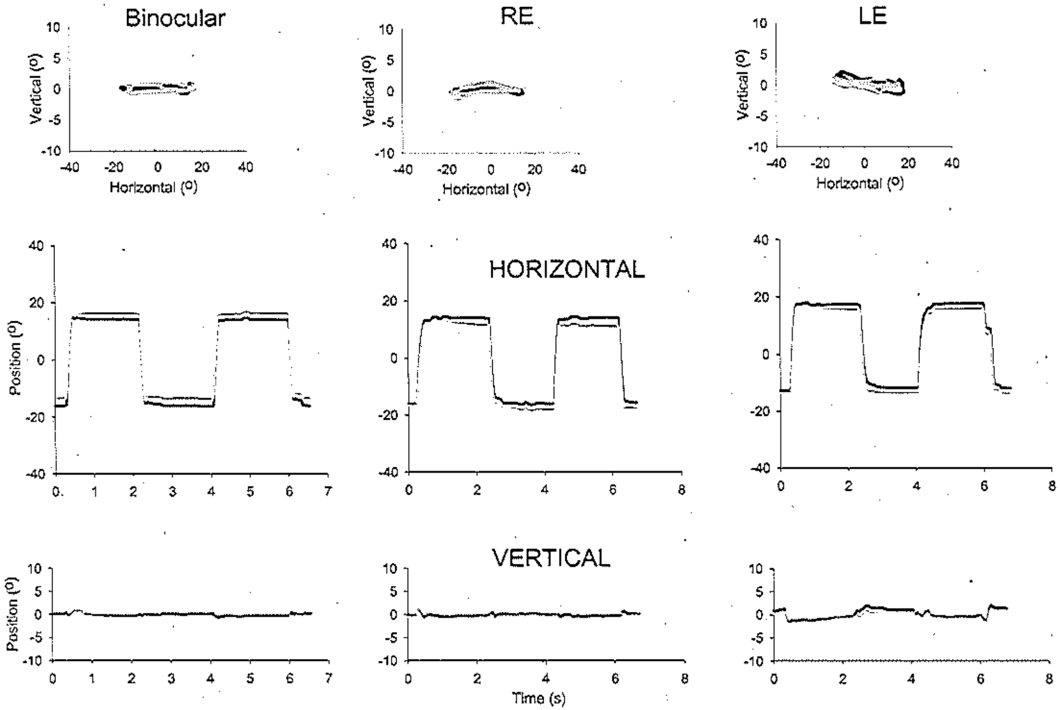

Fig. 5.10
Example of binocular saccadic eye movements of subject 12 who had late-onset strabismus and normal visual acuity in both eyes. Conventions as in figure 5.1.

Table 5.6
Horizontal and vertical strabismus angles of subjects 12 and 13.

		horizontal strabismus angle			vertical strabismus angle		
subject	dom. eye	binocular viewing	dom. eye	non-dom. eye	binocular viewing	dom. eye	non-dom. eye
12	R	1.20	-4.80	-4.80	-0.28	-0.46	-0.10
13	L	-2.20	-1.90	-3.40	-2.50	0.20	-0.10

We evaluated the effects of late-onset strabismus on saccade dynamics by comparing the main sequence of binocular saccades under binocular and monocular viewing conditions. Figure 5.11 shows the main sequence plot of the subject 12. For this subject, the values (n=1000) of S and λ obtained from the bootstrap analysis were 403 ±9.23°/s and 7.04 ± 0.39 for the binocular condition (lower panel figure 5.11, closed symbols). For the monocular right eye viewing condition S and λ were 411 ± 8.37°/s and 7.63 ±0.41 (lower panel, figure 5.8, open symbols: triangles) and 414 ±8.1 °/s and 7.01 ±0.33 for the left eye viewing condition ((lower panel, figure 5.8, open symbols: squares). The differences were not significant (t-test, P>0.5). The values of S for the two subjects are summarised in table 5.7.

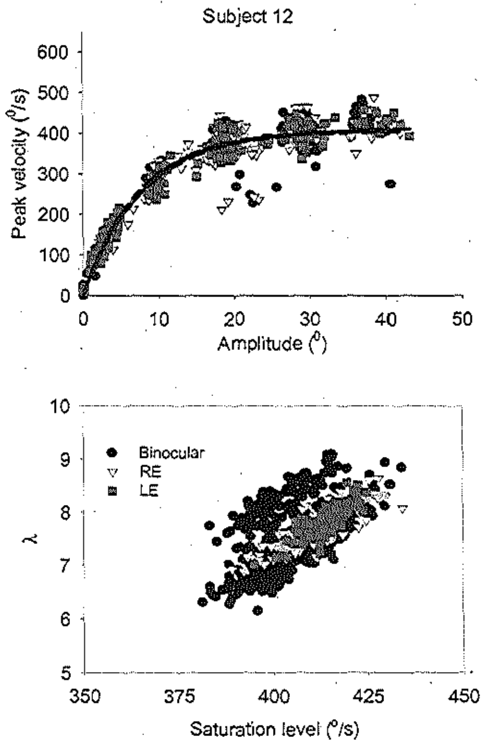

Figure 5.11
Top panel: Main sequence plot of peak velocity of saccades as a function of saccade amplitude.
Bottom panel: Bootstrap results of Right and Left eye saccades of subject 12 under binocular (black circles) and right eye (open circles) viewing conditions.
Notice the overlap of binocular with right and left eye viewing.

Table 5.7
Saturation velocities (S) of dominant and non-dominant eye under binocular, right eye and left eye viewing conditions.

		Saturation velocity (deg/s)					
		binocular viewing		viewing with dominant eye		viewing with non dominant eye	
subject	dom.eye	dom. eye	non-dom. eye	dom. eye	non-dom. eye	dom. eye	non-dom. eye
12	R	403	408	411	401	414	400
13	L	321	324	242	240	279	281

In conclusion, in the two patients with decompensated exophoria, idiosyncratic differences existed in binocular alignment under binocular and monocular conditions. Saturation velocities of both subjects were lower than in the control subjects (20 % in subject 12 and 40% in subject 13). In both patients, occlusion of one eye had only a limited effect on the horizontal and vertical strabismus angle.

DISCUSSION

In this paper we compared the dynamics of saccades and the strabismus angles under binocular and monocular viewing conditions in three different groups of strabismic patients. Patients were subdivided in early onset strabismus with and without amblyopia and late onset strabismus groups. As binocular vision and binocular coordination of eye movements are tightly coupled, this division in three groups of strabismic patients was used to investigate the possible effects of the presence or absence of a period of development of binocular vision on binocular eye movement control. Studies on binocular eye movement control, in patients with amblyopia and/or strabismus, with precise instrumentation such as scleral search coils, are relatively scarce. In addition, so far none of these studies researched the dynamics of binocular saccades but instead focussed on postsaccadic drift (e.g. Kapoula et al., 1997). Our study is, to our knowledge, the first to provide data on binocular saccade dynamics in a variety of forms of manifest strabismus.

Binocular vision is based upon the learned association of the visual inputs from corresponding retinal locations (Howard and Rogers, 1966) that are combined and result in a single perceived object. Under natural conditions not all elements of a visual scene are on corresponding locations. Differences in retinal image positions (disparity) are sensed by disparity-tuned neurons in the visual cortex, which form an important basis for the perception of depth. In addition, to maintain single vision and perception of depth, the oculomotor control system plays an important role by precisely aligning the two eyes to the same object of interest. Although brief periods of monocular deprivation of vision do not impair binocular coordination, long-term periods of disrupted binocular alignment, particularly at young age, such as in patients with congenital strabismus, lead to permanent suppression of one eye (amblyopia) to prevent diplopia. Our findings suggest that the severity of the effect on saccade dynamics and/or on strabismus angle is related to age of onset of strabismus and/or to monocular versus binocular visual acuity.

To explain how saccade dynamics in strabismic patients may be affected, we will first briefly discuss the organisation of the neural network at the motor periphery involved in binocular coordination. Subsequently, we will discuss how changes in the input to this neural network affect saccade dynamics in each of the three groups of strabismic patients.

Organisation of pre-motor and motoneurons involved in binocular coordination

For a long time it was generally accepted that separate pre-motor conjugate and vergence systems control binocular eye movements. The reason that this concept, that had its origin in the so-called Hering's Law (Hering, 1868; for an overview see also Howard and Rogers, 1996), has been so readily accepted by oculomotor physiologists, is that it provides a simple solution to binocular coordination of eye movements. In addition, many researchers provided convincing evidence for the existence of separate version and vergence centres (Rashbass and Westheimer, 1961; Robinson, 1981; Mays, 1984, Mays and Gamlin, 1995). Conjugate commands for horizontal eye movements have been found in the so-called burst neurons located in the paramedian pontine reticular formation (PPRF) (Robinson, 1981, Leigh and Zee, 1999), whereas vergence signals were identified in the so-called near response cells located in the mesencephalon (Mays and Gamlin, 1995). However, it has recently been shown that the neural machinery that generates binocular eye movements is more complicated. It consists of bilaterally as well unilaterally projecting motoneuron pools that receive binocular as well as monocular input (Zhou and King, 1998, for a review see King and Zhou, 2000). In a neuro-anatomical scheme King and Zhou (2000) postulate left and right eye bursters in the PPRF to project to abducens motoneurons and abducens internuclear neurons. This scheme implies that the relative weights of monocular and binocular signals in this neuronal network determine the effective command signals that generate binocular eye movements. King and Zhou incorporated in their model also vergence command centres located in the mesencephalon. Their purpose is to maintain fusional vergence and monocular eye positions.

With this scheme of King and Zhou we can get, at least some understanding how abnormal saccade dynamics can be attributed to particular aspects of abnormal binocular motor control, binocular vision, and/or visual acuity.

Binocular coordination in control subjects

In subjects with normal binocular vision and alignment, binocular eye movements are made with great precision and reproducibility (Collewijn et al., 1988). One of the conspicuous features of binocular coordination in normal subjects is that the change from the binocular to the monocular viewing condition has no significant impact on the accuracy and dynamics of binocular saccades (Lemij and Collewijn, 1989). Our study confirms that monocular visual input does not alter the main sequence of binocular saccades in normal subjects.

Apparently in normal subjects this system is robust enough to operate in conditions where it is temporarily deprived of the input of one eye. On the other hand, long term deprivation, particularly at young age, may have a detrimental effect. E.g. it has been shown that in kittens reared with unilateral strabismus the ability to drive the collicular cells that are important for generating saccades is decreased (Gordon and Presson, 1977).

Binocular coordination in subjects with infantile strabismus

Intuitively it may be expected that subjects with infantile strabismus are the most affected group of patients. These patients never experienced binocular vision in their life, which may have profound effects on the neuronal machinery sub-serving binocular eye movements. In agreement with this, we found that the vertical vergence angles in all patients in this group increased during monocular viewing compared to binocular viewing. This increase was higher when the dominant eye was covered. Changes in horizontal strabismus angle were more variable. We could not correlate this to either dominant or non-dominant eye viewing.

These findings suggest that in most strabismus patients of this group visual input from both eyes is still important. One possible explanation could be that extra-foveal fixation areas in the non-dominant eye play a role in binocular control. Because this group of patients had normal visual acuity in both eyes, a pseudo-fovea may have a supporting role in reducing the vertical phorias via the mesencephalic routes during binocular vision. In particularly when the visual input from the dominant eye is removed, vertical phorias may become evident.

In most patients in this group, the peak velocity of saccades was lower under monocular than under binocular viewing conditions. It is unlikely that mechanical factors play a role, since the amplitude-peak velocity relationship of some of the strabismic subjects was not different from control subjects.

A possible explanation based upon the scheme of King and Zhou (2000) is that the non-dominant eye (having normal visual acuity) under binocular viewing conditions still provides monocular input to the burst neuron pool in the PPRF. Apparently this input is so essential for the generation of binocular saccades that when this eye is covered the burst neuron pool in the PPRF becomes deprived of part of its input and this results in lower peak velocities.

The ability to control the spatial orientation of the non-dominant eye is functionally relevant because this eye can, despite its little use for foveation, still play a role in the processing of visual information. One important function is visual motion detection and object location via extra-foveal areas. Internal spatial representations of fast moving objects via information from extra-foveal areas depend on good retinal image stabilisation.

Binocular coordination in strabismus with amblyopia

In patients who have amblyopia coexisting with strabismus, abnormal properties of eye movements have been reported (for an overview see Leigh and Zee, 1999). In particular, instabilities in the amblyopic eye have been observed during fixations

(Dell'Osso, Leigh, Sheth and Daroff, 1995). Maxwell, Lemij and Collewijn (1995) studied the conjugacy of saccades in amblyopics. In their study, all subjects with amblyopia made non-conjugate saccades during binocular viewing. In addition, they found idiosyncratic differences in size of saccades, drift and the occurrence of latent nystagmus. Although in this study we did not systematically explore differences between left and right eye saccade amplitudes, our eye movement traces showed in agreement with these previous reports considerable variability in left and right saccade amplitude. Two of our subjects (7 and 10) had a latent nystagmus, which became manifest during monocular viewing. Taking all of this together, this could mean that according to the scheme of King and Zhou (2000) the functional loss of visual input from one eye in combination with the absence of normal development of binocular vision, has a detrimental effect on the neural networks in the mesencephalon that are responsible for holding the two eyes in position. Since fusional vergence signals are absent, binocular gaze holding depends more critically on monocular positional commands. However, the increase in drift and phoria under monocular dominant eye viewing conditions compared to binocular viewing condition, shows that the amblyopic eye can still influence binocular gaze stability.

With regard to the dynamics of binocular saccades, we found variable differences in the main sequence of saccades under binocular and monocular viewing conditions. In three out of five cases the saturation velocity of the dominant eye under binocular viewing condition was very similar to the saturation velocity of the dominant eye under the dominant eye viewing condition. Under non-dominant eye viewing conditions the saturation velocity of saccades was significantly lower than under binocular viewing. Our findings are in contradiction with several other investigators, who found the main sequence of saccades in amblyopia and/or strabismus to be in the normal range (Fricker and Sanders, 1975, Ciuffreda et al., 1991). In these other studies, however, the statistical methods that we used to analyse the data were not yet available.

To offer an explanation in the context of the scheme of King and Zhou (2000), we hypothesise that under binocular viewing conditions, as a result of abnormal binocular development, normally only the monocular visual input from the dominant eye is used to drive the burst neuron pools located in the PPRF. This explains why there are no significant differences in peak velocity of saccades under binocular and dominant eye viewing conditions. When the visual input comes only from the amblyopic eye, the burst neuron pools have to rely on monocular information that is normally not used; consequently the peak velocities are reduced.

Binocular coordination in late-onset strabismus (decompensated exophoria)

If development of binocular vision is a critical factor in the effects of strabismus on binocular eye coordination, then the effects on vertical phoria and main sequence should be smaller in patients who develop strabismus after the development of binocular vision than in patients with infantile strabismus. With regard to vertical phoria this was indeed the case. The two patients in the group of decompensated exophoria had only small differences in vertical phoria under binocular and monocular viewing conditions. Before the onset of exotropia they both had had stereopsis. With regard to differences in amplitude-velocity relationship, the results were less clear. Compared to binocular viewing conditions, subject 13 had a significant reduction of saturation velocity under monocular viewing conditions, whereas subject 12 had not. Notice, however, that the overall peak velocities of saccades in subject 13 were much lower than in subject 12. A more extensive study on patients with late-onset strabismus would be necessary to reveal the underlying causes.

General conclusion.

As a general conclusion, the abnormal binocular coordination in strabismus patients has an effect on the static as well as dynamic properties of binocular eye movements. Our data suggest that onset of strabismus before or after the development of binocular vision plays a role in the occurrence of vertical phorias and/or abnormalities in main sequence parameters. In patients with strabismus and normal visual acuity, both the input from the non-dominant and the dominant eye contribute to the dynamics of binocular saccades. Strabismus co-existing with amblyopia increases the dependence of binocular control on the dominant eye. In that sense any therapy that promotes the development of good visual acuity in both eyes is to be recommended. Although it does not re-install binocular vision, it may help to reduce the horizontal and vertical strabismus angle under binocular viewing conditions by establishing normal visual acuity in each eye.

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Summary and conclusions

Samenvatting en conclusies

This thesis is about binocular eye movement control in persons with optimal binocularity, with sub-optimal binocularity and in strabismus patients with abnormal binocular coordination.

Chapter 1 gives a general introduction to normal and abnormal coordination of binocular eye movements and stereovision. This chapter discusses the importance of binocular vision in daily life addressing general principles of binocular sensory and motor coordination. It also discusses general principles of compensation during subnormal binocular coordination (role of eye preference and convergence insufficiency), and during various forms of strabismus.

Chapter 2 describes experiments on version vergence interactions in healthy volunteers with optimal binocular vision. Here we confirm that version eye movements (saccades) facilitate vergence eye movements. Furthermore, we observed that subjects who had a strong monocular preference, always made vergence eye movements in combination with small horizontal saccades. In contrast, subjects who had a weak or no monocular preference were able to make pure vergence movements without saccades. These findings suggest that monocular preferences influence oculomotor strategies during vergence tasks.

Chapter 3 describes experiments in subjects with convergence insufficiency. Based upon the conclusions in chapter 2 we wondered if monocular preferences could explain why some individuals with binocular vision perceive discomfort during vergence tasks (sometimes diagnosed with 'convergence insufficiency'), while others with optimal or sub optimal binocularity do not. Therefore, we invited patients who were diagnosed with convergence insufficiency (C.I.) to participate in our experiments. Again we studied vergence, version and combined eye movements and compared these with those of subjects who had no complaints. To this we added a reading task, as this is the binocular task that usually provokes the complaints of discomfort (asthenopia). In both the C.I. and non-C.I. group, two classes of subjects occurred: vergence responders and saccadic responders. During pure vergence tasks, saccadic responders made saccades with no or little vergence; vergence responders made vergence movements with no or small saccadic components. In saccadic responders, fixation of nearby targets was monocular. During the reading task, vergence angles were more accurate than during gaze-shifts between LED's. In addition, we studied the effect of vergence training and found that training had an effect on vergence performance in 4 out of 9 subjects (one of which had C.I.). The strength of eye preference could not directly be related to the severity of complaints. However, unstableness of monocular preferences may play a role in C.I.. Some of the C.I. subjects had a tendency to alternate their (monocular) fixation from eye tot eye. C.I. might be a problem that falls between optimal binocular coordination and strabismus.

Chapter 4 describes binocular eye movement coordination in a group of patients with alternating exotropia. The phenomenon of eye alternation, which we had observed in some C.I. subjects, was very clear in a group of exotropic strabismus patients in whom we measured saccades. These subjects fixated the left target with the left eye and the right target with the right eye. The alternation in eye fixation at the end of the saccade had to be taken into account in the programming of their saccades. In executing the saccade, the non-fixating eye automatically became the fixating eye. The amplitudes of the alternating saccades were approximately equal to the target amplitude minus the strabismus angle. These subjects with strabismus had an optimal adaptation to their visual situation: They reached a new target as fast as possible with minimum effort. These subjects therefore have adopted an abnormal but effective binocular coordination strategy.

Chapter 5 describes the binocular coordination in a group of patients with various forms of manifest strabismus. This group consisted of 13 individuals with several kinds of complex strabismus, with the exclusion of the alternating exotropes. In these patients, the alignment of the two eyes is abnormal and depending on the age of onset and the strabismus angle, binocular viewing is very often absent or incompletely developed. We distinguished three groups among the subjects. The first group consisted of six patients with infantile strabismus, but normal visual acuity in each eye. The second group consisted of five patients with infantile strabismus in combination with amblyopia. The third group consisted of two patients with late-onset strabismus, who had normal binocular visual development in early childhood and normal visual acuity in both eyes. They developed exotropia when compensating mechanisms were no longer sufficient. We found that patients with infantile strabismus, but normal visual acuity in each eye, had under monocular viewing conditions saccadic peak velocities that were lower compared to binocular viewing. Saccade dynamics in the group of amblyopic patients were dependent on the dominant eye (the eye with the highest acuity). During monocular viewing with the amblyopic eye, saccade velocities were significantly lower than under binocular viewing conditions. In the two patients with late-onset exotropia, we found lower peak velocities than in control subjects. Our conclusion from these experiments is that early onset strabismus affects not only the development of normal binocular vision, but also the development of binocular motor behaviour of saccades. Apparently, in strabismus patients with normal visual acuity in both eyes, saccade dynamics still depend on the visual input from the two eyes, despite the presence of eye dominance. In strabismic patients with amblyopia, saccade dynamics depend more strongly on visual input from the dominant eye. Visual input from the amblyopic eye only, results in significantly impaired saccade dynamics. We suggest that therapy in early childhood to prevent amblyopia, not only has a positive effect on visual function in both eyes, but also on the binocular saccade dynamics.

Acknowledgements:

Overall, the authors would like to thank the control and strabismic subjects for serving in the presented studies. They also thank C. Kingma, R.J. Grootendorst, K. Verhoeff, M.A.Langeslag and C. Wemes for the orthoptic evaluation of our subjects, dr. M. A. Frens for providing the bootstrap procedures used in statistical analyses and dr. J.P. Flipse and dr. D. van 't Ent for their useful suggestions and software-support.

SAMENVATTING EN CONCLUSIES

Dit proefschrift bespreekt de dynamiek en aansturing van menselijke oogbewegingen op basis van experimenten die zijn uitgevoerd bij mensen met optimale, sub-optimale en abnormale oogcoördinatie.

Hoofdstuk 1 geeft een algemene inleiding in de normale en abnormale coördinatie van de bewegingen van de twee ogen en het dieptezien. We gaan in op het belang van het zien met twee ogen in het dagelijks leven. Hierbij komen algemene principes van binoculaire sensorische en motorische coördinatie aan de orde. Verder bespreken we hoe kleine afwijkingen in oogcoördinatie gecompenseerd kunnen worden en wat er met de oogcoördinatie gebeurt bij verschillende vormen van scheelzien. Verder komt aan de orde welke invloed een voorkeur voor één van de ogen kan hebben op oogcoördinatie. In alle experimenten beschreven in hoofdstuk 2 tot en met 5 werden de bewegingen van beide ogen gemeten in een magnetisch veld met behulp van ringvormige contactlenzen waarin zich een koperdraadspoeltje bevond. Via de uiteinden van het koperdraadspoeltje werd gemeten hoeveel stroom er werd opgewekt en dus hoeveel de ogen draaiden. Proefpersonen kregen steeds de opdracht op het ritme van een metronoom met de ogen van het ene naar het andere doel te springen.

Hoofdstuk 2 beschrijft experimenten waarmee wij de interactie tussen versie (oogbewegingen van beide ogen in eenzelfde richting) en vergentie (oogbewegingen waarbij de ogen naar binnen of naar buiten draaien om op verschillende afstanden met twee ogen te kunnen fixeren) onderzochten bij gezonde vrijwilligers met optimale binoculaire coördinatie. De doelen (LED-lampjes) bevonden zich steeds op een horizontale of verticale lijn en konden verschillen in afstand van en richting ten opzichte van de ogen. Op deze manier werd pure vergentie, pure versie of een combinatie van deze oogbewegingen opgeroepen. Onze resultaten bevestigen eerdere experimenten die aantoonden dat snelle versie oogbewegingen (zogenaamde saccades) vergentie oogbewegingen bevorderen. Verder vonden we dat proefpersonen met een sterke voorkeur voor één van beide ogen altijd vergentie oogbewegingen maakten in combinatie met kleine snelle oogbewegingen (micro-saccades) naar links of rechts. Proefpersonen zonder een duidelijke oogvoorkeur of met een zeer lichte voorkeur, waren in staat om pure vergentiebewegingen te maken zonder saccades. Dit resultaat geeft aan dat de mate van voorkeur voor één van beide ogen een invloed kan hebben op oogbewegings stategieën tijdens vergentietaken.

Hoofdstuk 3 beschrijft experimenten bij proefpersonen met convergentie insufficiëntie. Door onze bevindingen bij de eerdere experimenten die in hoofdstuk 2 beschreven staan, vroegen we ons af of de voorkeur voor één van de ogen misschien ook een rol speelt bij mensen met convergentieklachten. Zo zouden we mogelijk kunnen verklaren waarom sommige mensen met sub-optimale binoculaire coördinatie klachten ondervinden en anderen niet. Ook bij deze proefpersonen registreerden we vergentie, versie en gecombineerde oogbewegingen en vergeleken deze met dezelfde oogbewegingen bij controle proefpersonen. Verder voegden we een leestaak toe omdat de klachten bij mensen met convergentie insufficiëntie meestal optreden tijdens lezen. We ontdekten dat zowel in de groep met klachten als in de groep zonder klachten twee soorten proefpersonen te onderscheiden waren: mensen met een vergentie reaktie en mensen met een versiereaktie. Tijdens een pure vergentie taak (het afwisselend fixeren van twee doelen die in afstand verschillen maar niet in richting) maakte de eerste soort proefpersonen saccades met weinig tot geen vergentie terwijl de tweede soort juist vergentiebewegingen maakte met weinig tot geen saccades. De mensen die met voornamelijk saccades reageerden bleken een dichtbij gelegen doel (35 cm van de ogen) maar met één oog te fixeren. Tijdens de leestaak (ook op 35 cm afstand) bleek de fixatie van de doelen (letters) veel preciezer (met de twee ogen)dan tijdens het heen en weer springen tussen LED-lampjes. We herhaalden de experimenten bij een aantal proefpersonen nadat zij een periode vergentie oefeningen hadden gedaan. Bij vier van deze negen proefpersonen (van wie één met convergentie insufficiëntie) had training een gunstig effect op de vergentie. De mate van voorkeur voor één van de ogen konden we niet direkt relateren aan de ernst van de klachten van deze proefpersonen. Het leek er op dat de proefpersonen bij wie minder duidelijk was welk oog het voorkeursoog was, vaker klachten hadden dan proefpersonen met een duidelijk voorkeursoog. Sommige proefpersonen met convergentieproblemen hadden de neiging om afwisselend met het ene en het andere oog te fixeren. De diagnose convergentie insufficiëntie bevindt zich mogelijk in het grijze gebied tussen optimale binoculaire coördinatie en scheelzien.

Hoofdstuk 4 beschrijft de coördinatie van de bewegingen van de twee ogen in een groep patiënten met alternerend scheelzien bij wie de ogen naar buiten staan. Het fenomeen van afwisselend fixeren met het linker en rechteroog, wat we ook bij sommige mensen met convergentieproblemen zagen, was zeer duidelijk aanwezig in deze groep. Deze proefpersonen maakten horizontale saccades tussen doelen op 130 cm afstand van de ogen. Proefpersonen fixeerden het linker doel met het linker oog en het rechter doel met het rechter oog. De saccades waren verder normaal. Bij de aansturing van zo 'n saccade werd dus rekening gehouden met het wisselen van oog. De grootte van de saccades kwam ongeveer overeen met de afstand tussen de doelen minus de scheelzienshoek van een proefpersoon. Deze proefpersonen hadden dus een ideale aanpassing aan hun visuele situatie:een doel werd steeds zo snel mogelijk bereikt met een minimale inspanning. Er kan hier worden gesproken van een abnormale maar effectieve binoculaire strategie.

Hoofdstuk 5 beschrijft de binoculaire coördinatie bij 13 patiënten met verschillende soorten scheelzien met uitzondering van alternerend scheelzien. Of zich een bepaalde vorm van binoculaire coördinatie heeft kunnen onwikkelen hangt af van het soort scheelzien en wanneer het is begonnen. Deze 13 proefpersonen konden we op basis van onze metingen indelen in drie groepen. De eerste groep bestond uit 6 mensen die sinds hun vroege jeugd scheel keken maar die met beide ogen goed konden zien. De tweede groep bestond uit 5 mensen met vroeg begonnen scheelzien in combinatie met een lui oog. Een derde groep werd gevormd door twee mensen met scheelzien dat pas was ontstaan na een normale ontwikkeling van de binoculaire coördinatie. In de eerste groep bleken de pieksnelheden van saccades lager wanneer met één van de ogen gekeken werd dan wanneer met beide ogen samen gekeken werd. In de tweede groep bleken de snelheden van saccades duidelijk lager te zijn tijdens het kijken met het luie oog ten opzichte van het kijken met het andere oog of de beide ogen samen. Bij de twee proefpersonen die pas laat scheelzien hadden gekregen waren de snelheden van saccades lager dan bij controle proefpersonen. Bij mensen met scheelzien en een goede visus in beide ogen zijn saccade kenmerken blijkbaar afhankelijk van de input van de twee ogen, ondanks het bestaan van een voorkeursoog. Bij mensen met scheelzien en een lui oog zijn de saccades meer afhankelijk van de input van het goede (dominante) oog. Wanneer alleen met het luie oog gekeken wordt, raakt de dynamiek van de saccades verstoord. De preventie en behandeling van een lui oog in de vroege kinderjaren heeft waarschijnlijk niet alleen een gunstig effect op de visus van de beide ogen, maar ook op de dynamiek van binoculaire saccades.

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DANKWOORD

Ik wil iedereen bedanken die er op welke manier dan ook toe heeft bijgedragen dat dit proefschrift er is gekomen. Een aantal van deze mensen noem ik hieronder nader.

De proefpersonen, die vrijwillig hun ogen lieten verdoven en beplakken met lenzen om vervolgens uitermate saaie taken uit te voeren, verdienen de grootste dank!

Op de afdeling Fysiologie heerste een creatieve sfeer die ik als erg prettig heb ervaren. Ik ben de mensen die er werkten hiervoor erg dankbaar.
Ik bedank speciaal mijn promotor. Han, jij kon altijd jouw positieve licht op de data laten schijnen wanneer ik door de bomen het bos niet meer zag. Ik heb veel geleerd van jouw pragmatische aanpak en pakkende manier van schrijven.
Ook mijn co-promotor ben ik zeer dankbaar. Hans, jij was ondanks jouw werkdruk op ieder moment bereid om naar de meetapparatuur, de computer of de ruwe data te komen kijken of om jouw nieuwe vondsten toe te lichten. Sinds Santorini kon het niet meer stuk! Heel erg bedankt voor jouw input in de laatste loodjes.
Er was een vruchtbare samenwerking met het Oogziekenhuis. Tjeerd, dankjewel voor alle medische kennis die je me in de praktijk geleerd hebt en voor de steun en gezelligheid op congressen. Alle orthoptisten ben ik erg dankbaar voor het onderzoeken van de controleproefpersonen en het includeren van patiënten.
Van de afdeling Fysiologie dank ik verder Ben en Erik voor de (onder)steun(ing), Dennis voor slimme programmeeradviezen en rust, Jan-Peter voor het part-time opvrolijken, Paolo voor 'stupid questions', Sylvia voor het goede voorbeeld, Wim voor gezellige proeven, Eli voor koekjes en relativering, Jeroen voor instant interpretatie van data, Bert voor (3D-)geduld, Dieke voor begrip, Maarten voor veelzijdigheid, Anil voor mensenkennis, Jan voor leuke werkbesprekingen, Yvonne voor levendigheid, Suzanne voor uitpluizerij, Jaap en Ignace voor mannentaal en leuke discussies, Jos voor geruststelling en alle anderen voor hun interesse.
Speciaal bedank ik Mark de Gids voor gebruikersvriendelijke programmatuur en muziek, aan Marion Westen voor analyse en gezelligheid, aan Koos en Marcel voor een onvergetelijke reis naar de ARVO.

Deelname aan cursussen van het Helmholtz Instituut leverden mij een ruimere kennis op. Vooral Casper wil ik bedanken voor zijn leuke college's en voor nuttige discussies.

Een aantal mensen was reëel of virtueel in de buurt tijdens mijn werk. Bedankt, Joost voor klantvriendelijkheid en vriendschap, Martin 'vandaarboven' voor aktie en complimenten, JW voor prikkeling van verbeelding en smaakpapillen, Martin voor aandacht, inzicht en liefde.

In het Oogziekenhuis heb ik een erg leuke en leerzame tijd gehad. Alle mensen die ik daar heb leren kennen wil ik hiervoor bedanken.
Op het instituut Maatschappelijke Gezondheidszorg is het goed toeven tussen prettige en veelzijdige collega's. Iedereen bedank ik voor het meeleven met de produktie van dit boekje.

Ik bedank alle commissieleden en de paranymfen voor de tijd die zij in mijn promotie hebben gestoken.

Tenslotte bedank ik al mijn familieleden, vrienden, collega's, cursusgenoten, medecongresgangers en kennissen voor hun interesse! In het bijzonder wil ik mijn ouders bedanken omdat ze me alle mogelijkheden hebben gegeven om mijn creativiteit te ontplooien.

Naast dank is hier tevens een excuus op zijn plaats. Sinds 1999 heb ik veel mensen minder vaak gezien en gesproken. Dit heeft niet alleen te maken gehad met het werk aan dit proefschrift naast nieuwe banen, maar ook met een psychologische bijwerking ervan. Ik reserveerde veel tijd voor het proefschrift; tijd die in de praktijk vaak benut werd met moed verzamelen, inspiratie opdoen, goed uitrusten, de juiste bestanden zoeken, openen, bekijken, eerst even ontspannen en inderdaad soms werkte ik daadwerkelijk aan dit boekje. Omdat voor mij het gezegde "uit het oog, uit het hart" niet opgaat, hoop ik dat de promotie ook een reünie zal zijn.

CURRICULUM VITAE

Ik ben geboren op 2 juli 1966 in Rotterdam waar ik ook opgroeide. Na het VWO begon ik in 1985 aan de studie geneeskunde in Rotterdam. In 1986 haalde ik de propedeuse, in 1989 het doctoraal en in 1992 het artsexamen. Tijdens de studie volgde ik keuzecoschappen in neurochirurgie, plastische chirurgie en oogheelkunde. Dit laatste keuzecoschap volgde ik in Israël. Verder deed ik een keuze-onderzoek naar 3-dimensionale beeldvorming bij hemifaciale microsomie. Na het behalen van het artsexamen werkte ik vanaf februari 1992 als keuringsarts bij de Bloedbank Rotterdam. In augustus 1992 werd ik arts-assistent oogheelkunde bij dr. Hagemans in Capelle aan den IJssel. Vervolgens was ik een half jaar arts-assistent neurochirurgie in het Academisch Ziekenhuis Leiden. Van april 1994 tot april 1998 was ik onderzoeker in opleiding op de afdeling Fysiologie van de Erasmus Universiteit Rotterdam. Dit proefschrift is het resultaat van dit vierjarige onderzoeksproject. In 1998 werd ik arts-assistent oogheelkunde in het Oogziekenhuis Rotterdam, vanaf 1999 volgde ik de opleiding tot oogarts. Na een jaar besloot ik met de opleiding te stoppen omdat mijn interesse in andere dan puur medische zaken steeds groter werd. Sinds mei 2000 verricht ik op het instituut Maatschappelijke Gezondheidszorg van de Erasmus Universiteit Rotterdam onderzoek naar de ervaringen van mensen met kanker en naar medische beslissingen bij ernstig zieke patienten.

Anna F. van Leeuwen