

# Ocular counter-rolling during head tilt

Tony Pansell



Stockholm, 2003

**From S:t Eriks Eye Hospital,  
Karolinska Institutet, Stockholm, Sweden.**

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**Whenever a new finding is reported to the world, people say:  
-“It is probably not true”**

**Later on, when the reliability of the new finding has been fully confirmed, people say:  
-“OK, it may be true but it has no real significance”**

**At last, when even the significance of the finding is obvious to everybody, people say:  
-“Well, it might have some significance, but the idea is not new”**

**Michael Montaigne (1533-1592)**

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***To Hanna with love***

## **Abstract**

When tilting the head towards the shoulder there are numerous mechanisms influencing on the generation and maintenance of ocular counter-roll. Each of these mechanisms has its own temporal and spatial characteristics which influences on the counter-rolled eye position.

We described a fast transient anti-compensatory torsion movement (torsion peak) as the first response to the head tilting which most certainly has its origin in the vestibular organ and the utricular maculae. Superimposed on this torsion peak we described nystagmus beats with the fast phase directed in the same direction as the head tilt movement suggesting a paralleled activation of the vertical semicircular canals. Synchronous with the torsion peak a fast vertical vergence eye movement was seen. The vertical vergence was always with left eye over right eye in the rightward head tilt and always with right eye over left eye the leftward head tilts, thus inducing a physiological skew deviation. The aetiology for this fast vertical vergence response is currently unknown but could probably be explained by a similar vestibular mechanism as for the torsion peak.

A substantial amount of ocular counter-rolling (OCR) was a consistent finding in all subjects and test conditions during static head tilt. The OCR increased with head tilt but the relative compensation to the amount of head tilt decreased. For example, a 15° head tilt induced 3° OCR which corresponds to a gain of 0.20. A 30° head tilt induced an even larger OCR (5°) which corresponds to a gain of 0.16.

A consistent finding was an OCR disconjugacy of the right and left eye which increased with head tilt. For instance, a rightward head tilt induced a larger ex-cyclo of the left eye than in-cyclo of the right eye leading to an ex-cyclovergence. The underlying mechanism might be the increased saccular impact in extreme head tilts. Sacculus has been

suggested to induce disconjugate OCR while utricle is thought to induce conjugate OCR.

The static head tilt induced a vertical disconjugacy (i.e. vertical vergence) that increased with the head tilt. The direction of the eye position was however not consistent. Some subjects demonstrated a right eye over left eye position in the rightward head tilts while others demonstrated the opposite outcome. This might be explained by a difference in the ocular visual and torsional axes. To maintain binocularity the eyes are forced into vergence and depending on the position of the axes the direction of the vergence movement will differ.

When holding the head in a tilted position the torsional position is found to drift. Initially this drift was directed away from the reference position thus increasing the amount of OCR. After a minute the drift was found to change direction and heading towards the reference position, thus decreasing the OCR. The OCR increasing drift might be explained by a decline in the leftward utricular discharge, induced by macula inertia during the initial interaural translation, in favour of the rightward utricular gravitational discharge. The OCR decreasing drift might be explained by an adaptation of the utricular maculae. Other possible explanations might be a leaky neural integrator or a vestibular memory loss which could induce the OCR decreasing drift found during a sustained head tilt.

## List of publications

- I. Schworm H.D, Ygge J, Pansell T, Lennerstrand G.  
Assessment of ocular counterroll during head tilt using binocular video oculography. *Invest Ophthalmol Vis Sci.* 2002: 43:662-667.
- II. Pansell T, Ygge J, Schworm H.D.  
Conjugacy of torsional eye movements in response to a head tilt paradigm. *Invest Ophthalmol Vis Sci.* 2003: 44:2557-2564.
- III. Pansell T, Schworm H.D, Ygge J.  
Torsional and Vertical Eye Movements during Head Tilt Dynamic Characteristics. *Invest Ophthalmol Vis Sci.* 2003: 44:2986-2990.
- IV. Pansell T, Tribukait A, Bolzani R, Schworm H.D, Ygge J.  
Drift in Ocular Torsion during Sustained Head Tilt (Submitted)
- V. Pansell T, Tribukait A, Bolzani R, Schworm H.D, Ygge J.  
Ocular Torsion in Response to Head Tilting Velocity (Submitted)

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## List of abbreviations

<b>3D</b>	<b>Three dimensional</b>
<b>BHTT</b>	<b>Bielschowsky head tilt test</b>
<b>CW</b>	<b>Clock-wise</b>
<b>CCW</b>	<b>Counter Clock-wise</b>
<b>CNS</b>	<b>Central nervous system</b>
<b>Deg</b>	<b>Degrees</b>
<b>EOM</b>	<b>Extra ocular muscle</b>
<b>INC</b>	<b>Interstitial nucleus of Cajal</b>
<b>IR</b>	<b>Infra red</b>
<b>LE</b>	<b>Left eye</b>
<b>LED</b>	<b>Light emitting diod</b>
<b>Min</b>	<b>Minutes</b>
<b>MRI</b>	<b>Magnetic resonance imaging</b>
<b>OCR</b>	<b>Ocular counter-rolling</b>
<b>PAL</b>	<b>Phase Alternate Line</b>
<b>PPRF</b>	<b>Paramedian pontine reticular formation</b>
<b>RE</b>	<b>Right eye</b>
<b>riMLF</b>	<b>Rostral interstitial nucleus of the medial longitudinal fasciculus</b>
<b>Sec</b>	<b>Seconds</b>
<b>VOG</b>	<b>Video oculography</b>
<b>°</b>	<b>Degrees</b>

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## Introduction

### Vision and the need for eye movements

The human visual sense is well evolved and extremely complex. The complexity is attributed to the light-sensitive retina in the eye as well as to the highly specialized visual cortex. The largest part of the incoming information in the central nervous system (CNS) evolves from the retina and vision is accordingly very important to gain information about the environment.

For vision to work properly there are at least two requirements that has to be fulfilled. To see clear the retinal image must be centred in the fovea within the central most 1-2 degrees that is specialized on acquiring the high spatial information [38] and the image must also be kept reasonably stable ( $< 4^\circ/\text{sec}$ ) [5], otherwise the interpretation of the image will be blurred which degrades the visual performance.

Eye movements are sub-serving vision and assist in preserving a good visual performance. Eye movements are mainly seen in high developed species where the visual sense plays an important role for survival. Lower species like bugs are not manservant of eye movements because their eyes and visual sense is not as highly evolved like in man and it would therefore not be of advantage for survival.

### Eye Movements

In man there are two general classes of eye movements: those that shift gaze and those that stabilize gaze. We shift gaze with fast eye movements (i.e. *saccades*) to align the visual axis on the object of interest and thereby placing the image of the object onto the retinal fovea. *Smooth pursuits* keep the image of a moving object onto the fovea with a glissade movement while *fixation* eye movements maintain gaze on a stationary targets.

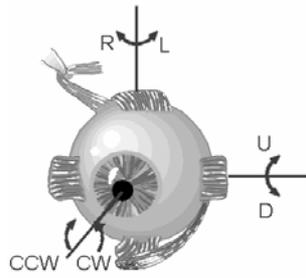
## **Image stabilization**

Since our everyday living consists of continuous movements of the head and body this is in a constant conflict with the requirement of a stable image on the retina [31]. The necessity for stabilizing the retinal image is most likely due to the slow retinal processing and the long projection fibres from the retina via thalamus to the visual cortex. There are two visual stabilization systems that work in parallel in man; the vestibulo-ocular reflex (VOR) and the optokinetic nystagmus (OKN) [44]. The VOR is a short-latency reflex system triggered by head movements (i.e. stimulus). The vestibular apparatus in the inner ear is stimulated by gravitation and accelerations (rotation and translation) of the head [14] and the brain interprets the vestibular stimulation and stabilizes the eye in space and thus both keeping the image on the fovea as well as reducing the image speed on the retina. The OKN is a reflex triggered by a coherent full field image movement (i.e. stimulus) which occur both during head movements as well as when the surrounding is moving [71]. Both systems (i.e. VOR and OKN) require a continuous stimulation to work and the responses ceases when the stimulus has disappeared. The eye movements triggered by these stabilization systems can be in horizontal, vertical and torsional direction.

## **Ocular torsion**

Most people are aware of that the eye can move horizontally and vertically. But not everyone knows that the eye also can rotate around the line of sight. This eye movement is referred to as *ocular torsion* and is defined as the eye rotation around the line of sight, or more correctly, the eye rotation around the ocular anterior-posterior axis

(Fig. 1). Ocular torsion is a non-voluntary eye movement which is induced in response to vestibular, proprioceptive or visual sensory input.



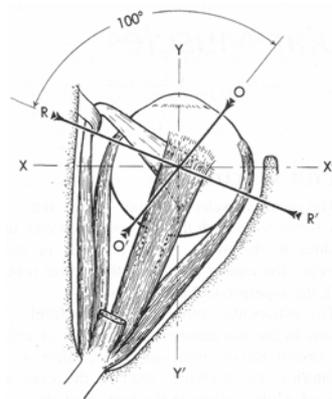
**Figure 1.** Frontal view of the eye with the rotation axes. Right- (R) and leftward (L) movements are rotated around the vertical sagittal axis. Upward (U) and downward (D) movements are rotating around the horizontal coronal axis (D) and counter clock-wise (CCW) and clock wise (CW) movements are rotating around the anterior-posterior axis. With permission from Tutis Vilis.

It has however been shown that torsion can be induced by volitional effort after exercise [3]. The torsional peak velocity is lower compared to horizontal and vertical eye movements and the amplitude range is also limited ( $\pm 25$ ) due to orbital mechanical constraints. Another obvious difference between torsional eye movements compared to horizontal and vertical movements is the relationship between the eye rotation axis and the visual axis. Since ocular torsion rotates around an axis which is close to the visual axis a torsional movement does not displace the point of gaze.

## Anatomical properties of eye movements

### The orbit and eyebulb

The orbital cavity is represented as a pyramid of four walls that converge posteriorly (Fig. 2). The medial and lateral walls form an angle of  $45^\circ$ . The volume of the adult orbit is approximately 30mL and the eyebulb occupies about 20% of the space [81].



**Figure 2.** Sketch of the orbital cavity and the eye bulb with the extra ocular muscles as seen from above. It is worth to note the direction of the visual axis (Y-Y') and the relationship to the pulling direction of the extra ocular muscles (O-O'; R-R'). Used with permission from Elsevier.

The eyeball is a rigid spherical structure which is ~25mm in diameter and the spherical shape is preserved by the intraocular structures and the elevated pressure. The bulb is supported in the orbit by the fascia, orbital fat, soft tissue, the extra ocular muscles (i.e. EOM) and the eye lids. The main component of the fascia is the Tenon's capsule which is continuous with the dural sheet surrounding the optic nerve. The Tenon's capsule attach to the orbital conjunctiva and to the orbital rim. The eye ball is therefore suspended in a "drumhead" which allows the eye to mechanically rotate freely in the orbit. Smooth muscle fibres were recently discovered in this Tenon's capsule which has been shown to have an influence on the effect of the contraction of the EOMs (see below; Muscle pulleys). Due to the support of the surrounding tissues there occur almost no translational movements of the eyeball [78]. The eye movements possible are therefore considered as rotations around three perpendicular axes which share the same point of intersection in the centre of the eye bulb.

### **Extra Ocular Muscles**

The eye bulb is rotated by six EOMs, four rectus muscles (i.e. superior, inferior, lateral and medial) and two oblique muscles (i.e. inferior and superior). The origin of the rectus muscles and the superior oblique are at the apex of the orbital cone [81]. The rectus muscles are inserted anterior to the bulbar equator at different distances from the corneal limbus. The two oblique muscles are approaching the eye bulb from in front at the medial side of the orbit and insert on the eye globe posterior to the equator. The superior oblique is passing the trochlea at the angle of the superior and medial wall in the frontal part of the orbit and turns about 54° laterodorsally.

### **Muscle fibers**

Eye movements are faster and more accurate than limb movements. Both anatomical and physiological differences have been described [65]. The higher accuracy in eye movements are partly accomplished by different types of muscle fibres specialized in different tasks of the contraction. For example, there are twitch-fibres with a fast all-or-

nothing response as well as non-twitch fibres with a graded response. Today there are at least six known fibre types that share some of the described characteristics [64]. Each EOM can be divided in two distinct layers, a central global layer and a peripheral orbital layer. Each layer either contains fibres suited for sustained contraction or brief rapid contraction. In the orbital layer a large part of the fibres has been shown to be of fatigue resistant twitch fibres types. Ocular muscles also differ from skeletal muscles in that there are no stretch reflexes.

### **Muscle pulleys**

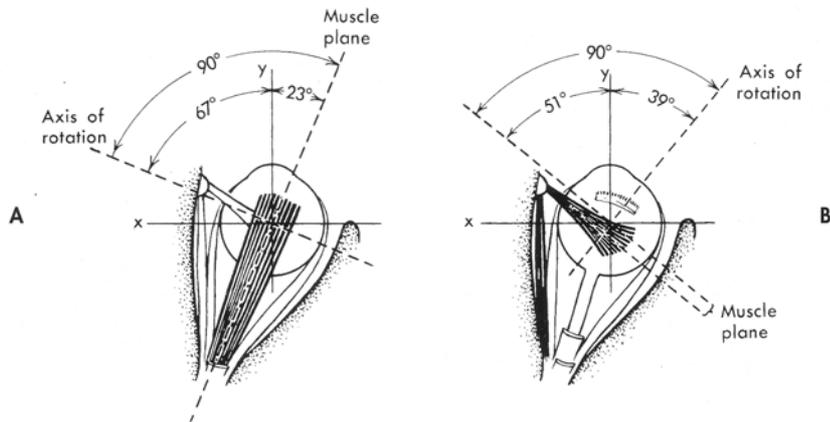
Recently it was found that smooth muscle fibres in the Tenon's capsule, so called fibro muscular pulleys, are present and act on the force direction of the EOMs [19]. In magnetic resonance imaging (MRI) of the orbital area it was shown that the posterior part of the rectus muscles remained fixed in the orbit during large ocular rotations [11]. This finding implies that the rectus muscles pass through pulleys coupled to the orbit and anterior to the muscle bellies. It has been proposed that the pulleys are attached into the orbital layer on the EOM [20]. Since it has also been shown that these pulleys are innervated and consists also of contractile elements, it further implies a far more complex neural control of eye movements than was previously thought [21].

## **Neural properties of eye movements**

### **Muscular action**

The muscle fibres are innervated by axons from motor neurons located in brainstem nucleus (see below). Each neuron innervates only some few muscle fibres each which give the lowest motor unit size known [46]. The muscle tone (tonic contraction) is upheld by a continuous train of action potentials and the isometric contraction (relaxation) of the muscle is achieved by an increased (decrease) frequency of activity [74].

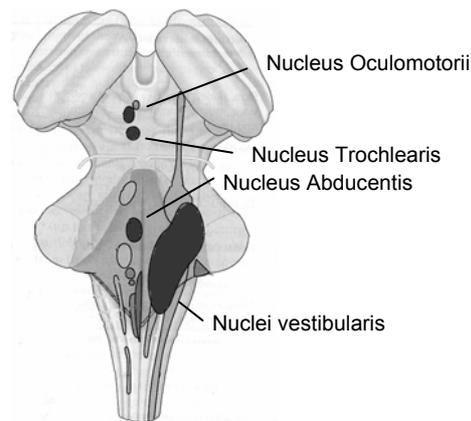
The EOMs are approximately working in pairs. Whenever an agonist receives an impulse to contract, an equivalent inhibitory impulse is sent to its antagonist that relaxes [10]. This is the substrate of Sherrington's law of reciprocal innervations. The medial and lateral rectus muscles are primarily rotating the eye around the vertical sagittal z-axis. The superior and inferior rectus muscles are primarily rotating the eye around the horizontal coronal x-axis and the oblique muscles are primary rotating the eye around the anterior-posterior y-axis. The effect of the medial and lateral recti is approximately constant over the entire field of action due to the insertion of the two muscles on the globe in relation to the visual axis [84]. The effect of the vertical and oblique muscle pairs is more difficult to interpret as the result (i.e. gaze shift) of the muscle action on will differ depending on gaze position. For example, the primary action of the superior oblique muscle is in-cyclo rotation of the eye (i.e. upper pole of the cornea towards the nose). This is true when the eye is looking straight ahead and when the eye is in abduction (temporal). When the eye is adducted (nasal) the superior oblique muscle will become a depressor (secondary action) due to the insertion of the muscle on the eye bulb and its relation to the visual axis (Fig. 3).



**Figure 3.** Sketch of the eye bulb with the extra ocular muscles as seen from above. A) Relationship of muscle plane of vertical rectus muscles to x- and y-axes. B) Relationship of muscle plane of oblique muscles to x- and y-axes. Used with permission from Elsevier.

## Brainstem nucleus and gaze centre

The EOMs' receive the innervations from three nucleuses in the brainstem (Fig. 4). The oculomotor nerve nucleus (nc.III) is situated rostrally to the pons and innervates four EOMs (the *rectus superior*, *medialis*, *inferior* and the *inferior oblique*) as well as the elevator muscle *levator palpebrae superior* of the upper eye lid. The trochlear nerve nucleus (nc.IV) innervates the *superior oblique muscle* and the abducens nerve nucleus (nc.VI) innervates the *rectus lateralis muscle*.



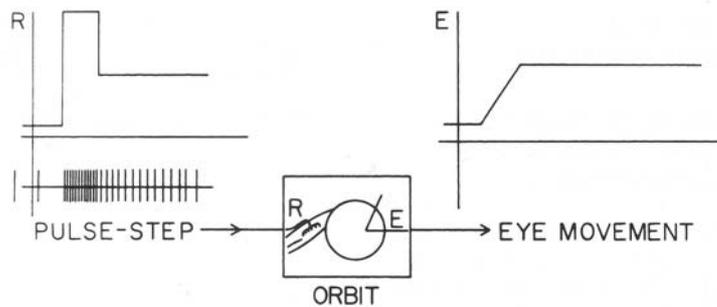
**Figure 4.** Sketch showing the dorsal view of the brain stem and the relative positions of the cranial nerve nuclei involved in the generation of eye movements. Note the close relationship to the vestibular complex.

To perceive a fixated object as single, the eyes have to be rotated in conjugacy, otherwise the image of the object will not fall on corresponding points on the retina [83]. Since a conjugate eye movement requires a balanced contraction of all EOMs depending on the gaze path the components of such a movement has to be organized on a higher level than in the individual ocular motor nuclei, namely the *gaze centres*. There are at least two known gaze centres. The *paramedian pontine reticular formation* (PPRF) is situated caudally in the pons and is closely integrated with the abducens nucleus [36]. The abducens nucleus innervates both the ipsilateral lateral rectus and the contralateral medialis rectus and is thus regarded as a gaze centre for horizontal eye movements [34]. The *rostral interstitial nucleus of the medial longitudinal fasciculus* (riMLF) is the second known gaze centre which is concerned with

vertical and torsional eye movements. The riMLF is situated in the rostral mesencephalon and bursts for upward [58] and downward [59] eye movements but for torsional eye movements only in one direction [79]. Thus the right riMLF discharge for torsional quick phases that are directed clockwise with respect to the subject. Bilateral lesions of the riMLF in monkeys have been shown to abolish vertical and torsional saccades [79]. However, vertical gaze holding, vestibular eye movements and vertical pursuits are preserved.

### Initiation of an eye movement

To rotate the eye bulb the mechanical constraints in the orbit has to be overcome. This requires a burst of neural activity (i.e. pulse) at the initiation of the movement to accelerate the eye bulb (Fig. 5).



**Figure 5.** The neural signal for a saccade. At right is shown the eye movement: E is eye position in the orbit; the abscissa scale represents time. At left is shown the neural signal sent to the extraocular muscles to produce the saccade. The vertical lines indicate the occurrence of action potentials of an ocular motor neuron. The graph above is a plot of the neuron's discharge rate (R) against time (firing frequency histogram). It shows the neurally encoded pulse (velocity command) and step (position command). Used by permission from Oxford University Press, Inc.

The burst is originating from the so called *burst neuron* which lies close to the respective ocular motor nuclei [6]. The burst cells are always in a standing-by mood prepared to full discharge. This is the neural substrate for the extremely short latencies found in eye movements. The burst of neural activity is released by inhibition of the *omnipause neurons* which has been shown to inhibit the burst neurons [7]. The omnipause neurons are located in the *nucleus raphe*

*interpositus* close to the abducens nucleus which send inhibitory projections to pons, medulla and the riMLF. Omnipause neurons discharges continuously except immediately prior to and during saccades [45].

### **Neural integrator and gaze holding**

When the eye has reached an eccentric gaze position, this eye position has to be actively maintained. The eyes will otherwise drift back towards the resting position due to the mechanical constrains in the orbit [72]. This resting position is close to the position when looking straight ahead (reference position). An eccentric gaze holding is possible due to an increased neural activity that increases the muscular tone in the agonist muscle. The accurate amount of neural discharge is planned in the *neural integrator* which generates the eye position command (step) from the eye velocity command (pulse) [27]. Interestingly, previous findings report on different orbital constraints for yoked muscle pairs. For example, when mechanically displacing the eye bulb into ex-torsion the passive return movement (due to orbital constrain) to resting position was found to be significantly faster than a similar displacement into in-torsion. This implies an individual neural integrator for each muscle for yoked muscle pairs to move conjugate [72]. The *interstitial nucleus of Cajal* (INC) is a critical structure for vertical and torsional gaze holding. Pharmacological inactivation of INC causes impaired vertical and torsional gaze holding after a saccade brings the eye to a tertiary eye position [15]. When this integration from pulse to step fails the eye will be carried to its new position by the pulse but drift back to the resting position due to the orbital constrains (i.e. gaze evoked nystagmus).

### **Definition of eye movement / position**

All eye movements in this thesis are described as seen from the subject's point of view [54]. Rightward, downward and clock-wise eye rotations are considered as positive (+) while the leftward, upward and counter-clockwise eye rotations are considered as negative (-).

Version is defined as synchronous and conjugate binocular eye movements and is calculated according to the formula  $(\text{left eye; LE} + \text{right eye; RE})/2$  to describe the mean eye position. *Vergence* is defined as a synchronous and disconjugate (i.e. eye movements in the same direction with different amplitudes) or disjugate (i.e. eye movements in opposite directions) binocular eye movement and is calculated according to the formula  $(\text{LE}-\text{RE})$ .

### **Donders' law and false torsion**

To foveate an object there is only need for an eye rotation around two of three axes. By a horizontal and a vertical eye rotation the object of regard is placed on the fovea. Frans Donders<sup>1</sup> found out that the rotation around the third axis (i.e. torsion) independently of the gaze path always took the same position every time the eye reached a specific position in the orbit. This fundamental decree is called Donders' law [76]. This secondary eye rotation around the ocular anterior-posterior axis due to an oblique eye movement has confusingly been known as false torsion. It is important to state that this so called false torsion is not false; there is a consistent amount of eye rotation around the ocular anterior-posterior axis.

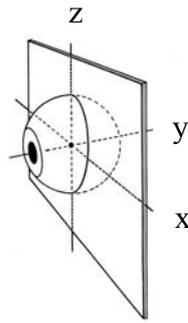
### **Listing's law and the primary position**

Johannes Listing<sup>2</sup> further proposed that an eye movement from the primary position to any other position was equivalent to a single eye rotation around an axis confined with the equatorial plane (Listing plane; Fig. 6). Primary position (pp) is the eye position from where a pure horizontal or vertical eye movement does not elicit any false torsion. The location of the pp varies from person to person and is also dependent on the viewing distance and the convergence of the eyes [42]. There are several descriptions on how to find the pp [26, 86].

---

<sup>1</sup> Frans Cornelis Donders (1818-1889), Netherlands. Ophthalmologist most known for his work on accommodation. Donders did with use of after-image technique determine the three-dimensional eye position and stated the Donders' law (1848).

<sup>2</sup> Johannes Benedict Listing (1808-1882). Mathematician and physicist.



**Figure 6.** Illustration of the eye with the z and x rotation axes confined with the equatorial plane (coronal) called Listing's plane. The y rotation axis is in this setting perpendicular to the plane and thus equal to the primary position.

Due to the inherent problem of defining the real primary position the subjects' position with the head straight and the eyes looking straight ahead was defined as the reference position [33]. This definition has been used in this thesis.

### **Coordinate systems for describing eye position**

The need for describing eye rotations and eye positions has led to development of several coordinate systems. Each system has its advantages and drawbacks. For example, there is a head centred coordinate system that moves with the head but not with the eye. The advantage of using a head centred system for calculation on combined horizontal, vertical and torsional eye rotations is that the calculations becomes relatively easy. The drawback is that there is no correlation between the visual axis and torsional eye movement. In contrary to the head centred system there is also an eye centred coordinate system that moves with the eye. The advantage of using this system for calculation on combined horizontal, vertical and torsional eye rotations is that torsion is directly related to the rotation of the image that we perceive. The drawback is that calculations become more complex.

#### **Fick's coordinate system**

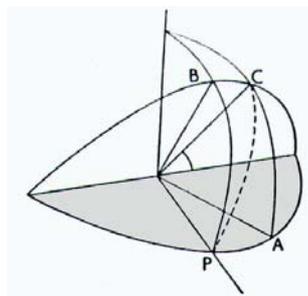
Adolf Fick<sup>3</sup> constructed the so called *Fick coordinate system* which is an eye centred system. The system is built as a gimbal where the eye

<sup>3</sup> Adolf Eugen Fick (1829-1901), German physiologist who made important contributions to the understanding of the mechanical work of the eye muscles and the analytical problems of angular rotations of eye movements.

position is described as a sequence of rotations, first a rotation around a fixed vertical axis and then around a second horizontal axis that moved with the vertical axis and last the third torsional axis (Fig. 7).

### **Helmholtz coordinate system**

Hermann Helmholtz<sup>4</sup> proposed a similar rotation system but where the order of rotation should be the opposite for the horizontal and vertical axes (see Fig. 7). Thus, the first rotation should be around the fixed horizontal axis and then around the vertical that moved with the horizontal axis and last the torsional axis. This system is accordingly called the *Helmholtz coordinate system*.



**Figure 7.** Illustration of the coordinate systems proposed by Helmholtz and Fick. To change gaze from position P to C, Fick proposed the order of rotations PAC while Helmholtz proposed the order PBC. (Modified from a similar sketch from Alpern M. Edited by Davson H. In *The eye*, New York. Academic Press, Inc 1962).

Since none of Fick or Helmholtz coordinate systems behaves like the eye both systems require three coordinates to describe an actual eye position. The same eccentric eye position is thus described differently depending on what system is used. Furthermore, the estimation on the amount of eye rotation around the torsional axis will differ depending on what coordinate system is used.

### **Listing coordinate system**

The *Listing* coordinate system requires only two coordinates to describe the correct 3D eye position since the rotation around the torsional axis is dependent on the rotation around the horizontal and vertical axis only. The drawback of using this system is that the

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<sup>4</sup> Hermann von Helmholtz (1821-1894). German physiologist who made important discoveries in physiology, optics, electrodynamics, mathematics, and meteorology.

Listing system is not valid for vestibular eye movements [55] or for convergence. It has however been shown that the Listing planes rotated temporally during convergence and that each eye position was constrained to a single plane [56].

### **Quaternion**

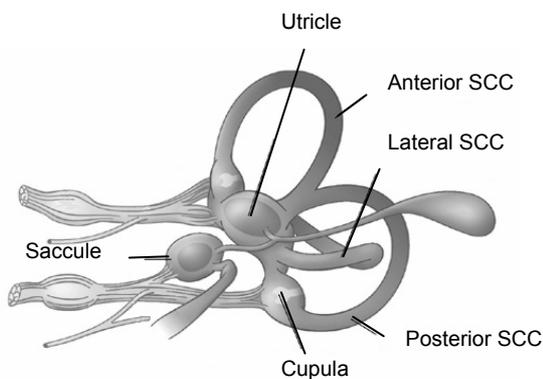
The *quaternion* system converts the eye rotations around the three axes (x, y, and z) into a single rotation which describes the amplitude and direction of the eye rotation (i.e. vector). This system is preferably used when plotting the Listings plane or when investigating patients with vestibular imbalance to find what semicircular canal which gives rise to the pathologic nystagmus [70].

## **Vestibular apparatus – anatomical and physiological properties**

The peripheral vestibular apparatus are located in the inner-ear within the petrous part of the temporal bone cushioned by perilympha [35]. It consists of five receptor organs which can be divided in two anatomical and functional groups, the semicircular canals and the otolith maculae. The semicircular canals detect angular accelerations of the head while the otolith organ detects linear accelerations of the head and earth gravitation.

### **Semicircular canals – head rotation**

The semicircular canals consist of three bow-formed orthogonally arranged tubes, the anterior, posterior and lateral canal (Fig. 8). In each labyrinth the three canals are almost perpendicular to one another. The lateral canals are positioned in a plane that is close to the transverse plan but slightly tilted backward. The lateral canals are accordingly sensitive to horizontal head rotations (i.e. yaw). The anterior vertical canal is positioned in a plane that is slanted approximately  $45^\circ$  with respect to the coronal plane while the posterior canal is positioned  $45^\circ$  in opposite direction to the coronal plane. The vertical canals are thus most sensitive to tilting of the head in the pitch- (back- and forward) and the roll (ear to shoulder) plane [24, 25] (see figure 11 on page 28).

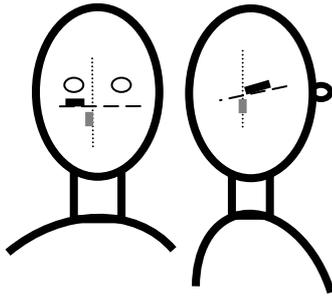


**Figure 8.** Illustration of the peripheral vestibular complex with the three semicircular canals (SCC) and the two otolith maculae. Also marked is the gelatinous cupula in the posterior SCC.

Each canal makes a loop of approximately 8mm in diameter and the canal system is filled with endolymph fluid. As the head rotates it carries the temporal bone and the canals with it. The endolymph fluid will lag behind during head accelerations and as a result rotate in the canals in opposite direction to the head rotation. When the endolymph moves in the canals it will press against the surface of the cupula which is a gelatinous structure that extends across the canal in its widest region, i.e. ampulla. In each cupula there are specialized hair cells that are able to transduce the bending into a change of the neural activity [28, 35]. The hair cells consist of many stereocilia and one kinocilium and are aligned so they respond best to one specific direction of movement. Deflection of the stereocilia towards the kinocilium increase the activity (excitatory) in the vestibular neuron meanwhile deflection of stereocilia away from the kinocilium decreases the activity (inhibitory) in the neuron [50]. For the lateral canal, flow towards the ampulla (ampullopetal) is excitatory. For the vertical canals, flow away from the ampullae's (ampullofugal) is excitatory. Since the flow of endolymph is limited by the canal-wall the brain can not judge the head rotation by stimulation of one canal alone. By a combined stimulation of the three canals in each ear (six in total) the brain can interpret the actual head rotation. Due to the mechanical construction of the canals the head acceleration will immediately be integrated into head velocity [16]. Each canal on one side of the head is approximately paired with a fellow canal on the other side of the head. A stimulation of one canal is always followed by a proportional inhibition of the fellow canal on the opposite side [52, 53].

### **Otolith maculae – head translation**

There are two otolith maculae in each vestibular apparatus, the utricle and the saccule. The utricular maculae are approximately horizontally aligned with a slight backward tilt in the head while the saccular maculae are located vertically on the medial wall [44] (Fig. 9).



**Figure 9.** Illustration of the estimated otolith planes for the utricular macula (slash line) and saccular macula (dotted line) in the head. Left figure illustrates frontal view while the right figure shows the side view.

The maculae of these organs consist of an elliptical shaped structure covered with a gelatinous membrane [16]. Embedded within and lying on the membrane are fine particles, the so called otoconia crystals that consist of calcium carbonate. The otolith maculae have similar specialized hair cells that transform the mechanical force into neural activity in a similar way as described for the semicircular canals. The hair cells extend from the base into the gelatinous membrane and bend in response to movement of the membrane. When the head undergoes linear acceleration the temporal bone with the maculae moves with the head. The membrane with the otoconia is however free to move within the organ and will thus move due to inertia and lag behind the head movement. This movement will deflect the hair cells and thereby exciting a neural response. In contrast to the semicircular canals each otolith macula are able to detect linear acceleration in all three dimensions. This is due to the arrangement of the hair cells as well as to the curved structure of the maculae [17].

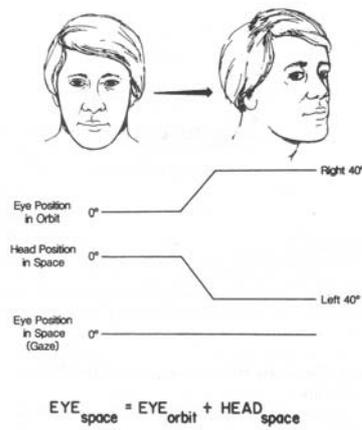
The utricular maculae responds best to side-to-side (interaural translation) and for-and-backward (pitch translation) head movements. The saccular maculae respond best to up and down head movement. Although the two structures seem to have well defined directions of stimulation these directions of stimulation overlap. Thus, utriculus is not stimulated alone by interaural head translation and that sacculus is similarly not stimulated only by up and down movement of the head [1, 17].

## Vestibulo Ocular Reflex; VOR

As mentioned in the introduction, for vision to work properly the image on the retina has to be stable, otherwise the image will be interpreted as blurry. The vestibular organ senses the head movements and induces appropriate compensatory eye movements in opposite direction to the head. This is the substrate for VOR eye movements. The neural connections for the VOR are described as a three neuron arc where the vestibular ganglion, vestibular nuclei and the ocular motor nuclei are relaying the head movement impulse into an eye movement response.

### Rotational VOR

The semicircular canals detect angular accelerations of the head and are responsible for the generation of the slow phase of the rotational VOR (Fig. 10). Both excitatory and inhibitory projections are carried in the same pathways but as a principle excitatory projection from the vestibular nucleus cross the midline while the inhibitory projection does not [44].



**Figure 10.** The angular vestibulo-ocular reflex (VOR). As the head is rapidly turned to the left, the eyes move by a corresponding amount in the orbit to the right. Below, head position in space and the eye position in the orbit are plotted against time. Because the movements of head and eye in orbit are equal and opposite, the sum, eye position in space (the angle of gaze or “gaze”), remains zero (bottom equation). If gaze is held steady, then the images do not slip on the retina and vision remains clear. Used by permission of Oxford University Press, Inc.

Some projections from the lateral semicircular canals overlap with the utricle, presumably reflecting their common roles in detecting horizontal head movements. Similarly some projections from the

vertical semicircular canals overlap with those from the saccule which is involved in detecting vertical head movements [1]. Each semicircular canal directly influences a pair of EOMs that move the eyes approximately in the plane of that canal [24]. The neural connections are however more complex than it might appear at a first glance. The right side anterior semicircular canal will therefore project excitatory on both the ipsilateral superior rectus muscle and on the contralateral inferior oblique muscle. The right side posterior semicircular canal will at the same time project excitatory on the ipsilateral superior oblique muscle and on the contralateral rectus inferior muscle. Simultaneously with the right side excitatory projections the left side anterior canal will project inhibitory on both the contralateral rectus inferior muscle and the ipsilateral superior oblique muscle and the left posterior semicircular canal will similarly project inhibitory on both the contralateral inferior oblique muscle and the ipsilateral rectus superior muscle. For a detailed description of vestibular projections on the EOMs, the readers are referred to table 1.

At very low frequencies, the canal-induced response becomes less effective [8]. While the semicircular canals are clearly involved in the generation of the rotational VOR during head rotation, the role of the otolith organs is more difficult to interpret.

**Table 1.** Direct Vestibulo-Ocular Projections as Determined by Electrophysiologic and Anatomic Studies in Monkey [51, 53], Cat [29, 80] and Rabbit [66, 67]. Used by permission of Oxford University Press, Inc.

Receptor	Effect	Muscle	Relay Nucleus	Pathway	Motor Nucleus
LC	Excitation	c-LR	M/LVN	MLF	c-VI
		i-MR	M/LVN	ATD	i-III
	Inhibition	i-LR	MVN	MLF	i-VI
		c-MR	-	Poly	c-III
AC	Excitation	i-SR	M/LVN*	MLF*	c-III
		c-IO	M/LVN*	MLF*	c-III
	Inhibition	i-IR	SVN	MLF	i-III
		c-SO	SVN	MLF	i-IV
PC	Excitation	c-IR	M/LVN	MLF	c-III
		i-SO	M/LVN	MLF	c-IV
	Inhibition	c-SR	SVN	extra	i-III
		i-IO	SVN	extra	i-III
U	Excitation	i-SO	LVN	MLF	c-IV
		i-SR	LVN	MLF	c-III
		i-MR	LVN	ATD	i-III
		c-IO	LVN	MLF	c-III
		c-IR	LVN	MLF	c-III
S	Excitation		y-group	BC	

**Key.** *Receptors:* LC: lateral SCC, AC: anterior SCC, PC: posterior SCC, U: utriculus, S: sacculus; *Muscles:* LR: lateral rectus; MR: medial rectus; SR: superior rectus; IO: inferior oblique; IR: inferior rectus; SO: superior oblique; *Relay nucleus:* M/LVN: medial and adjacent lateral vestibular nucleus, MVN: medial vestibular nucleus, SVN: superior vestibular nucleus; *Pathway:* MLF: medial longitudinal fasciculus, ATD: ascending tract of Deiters, BC: brachium conjunctivum; *Motor nucleus:* VI: Abducens nucleus; III: oculomotor nucleus; IV: trochlear nucleus. c-: contralateral i-: ipsilateral. (\*= other nuclei and pathways are also probably involved)

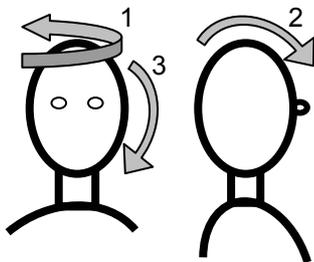
## Translational VOR and OCR

While otolith-induced ocular torsion has been studied during static tilt, its role during dynamic tilt has received little attention. This is due to the simultaneous activation of the semicircular canals, which complicates examination of the otolith component. From studies on a linear track which applied linear accelerations along the interaural axis, it is known that otolith-induced ocular torsion can be characterized as a low-frequency response, being maximal in a frequency range up to about 0.3Hz [32, 87]. Head translational and

head tilt otolith-ocular responses have been identified, each with different spatiotemporal properties. For instance, Paige and Tomko [61, 62] distinguished translational OCR and tilt OCR in squirrel monkeys during horizontal oscillation along various body axes on a linear track. Translational responses included horizontal and vertical eye movements during movement along the interaural axis and the dorso-ventral axis, respectively. Tilt responses included torsional and vertical eye movements during movement along the interaural axis and the naso-occipital axis, respectively. In contrast to the translational responses, the tilt responses were most sensitive to lower stimulus frequencies and were not compensatory to the movement itself. The otoliths have similar projections to the EOMs like the semicircular canals but with an even more complex structure. The exact projections have not yet been discovered. The reader is referred to table 1 for description of the neural pathways known.

## Head movement

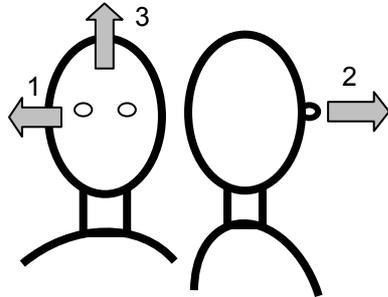
The head both rotates and translates during everyday activities. A head rotation around the horizontal, vertical and naso-occiput axes is described as a yaw, pitch and roll respectively (Fig. 11). A translation of the head in the horizontal, vertical and interaural direction is accordingly described as a surge, bob and heave translation respectively (Fig. 12).



**Figure 11.** Illustration of the head rotations possible. A head rotation around a vertical axis is referred to as a yaw-rotation (1). A head rotation around the interaural and anterior-posterior axis is referred to as pitch- (2) and roll (3) rotation respectively.

When the head rotation axis is not positioned at the level of the head, the movement will always be described as a combination of both a

translation and a rotation. Since the two orbitas with the eyes and the two vestibular apparatus are at a horizontal distance, the effect of translation and rotation will differ between them. A head yaw rotates the head horizontally around a vertical axis which can be described as a prolongation of the vertebral column, thus around an axis which is



**Figure 12.** Illustration of the head translation possible. A head translation towards the side (interaural) is referred to as a surge translation (1). A forward and upward head translation is referred to as heave (2) and bob (3) translation respectively.

positioned between the eyes and the vestibular apparatus in the head. The right eye and right vestibular apparatus will therefore move in opposite translational directions to the left eye and vestibular apparatus. A head pitch rotates the head for- or backward around a horizontal axis parallel with the coronal plane. This axis is not fixed but varies with the neck bending. Nevertheless, it is always positioned below the head and the right and left eyes and vestibular apparatus therefore will move in parallel. A head tilt (roll) rotates the head around a sagittal axis which is positioned in the upper part of the chest which varies with stiffness and length of the neck. The translational effect on the eyes and vestibular apparatus will differ between the right and left side. The ipsilateral eye and vestibular apparatus is moved downward while the contralateral side is moved somewhat upward during head tilt.

### **Head tilt paradigm - stimuli**

In this thesis a tilt of the head towards the shoulder (roll) is described as a *head tilting* while the position obtained after such a head tilting are referred to as *head tilt*. Similarly, the lifting of the head from head tilted position to upright position is referred to as *head straightening*.

## **Bielschowsky head tilt test**

The Bielschowsky head tilt test (BH TT) is an objective clinical test which is performed on subjects suffering of vertical deviation of one eye due to paresis or paralysis. The BH TT is one out of four tests to determine which EOM that is affected. The examiner observes the eyes while performing a cover-uncover test to discover any positional adjustments of the eyes during the test.

The first step in the diagnostic procedure is to determine which eye is hyper-deviated (i.e. the elevated eye). The second step is to determine if the deviation is greater in right or left gaze. The third step is to determine if the angle becomes larger in upward or downward gaze. In the last step the deviation is measured in rightward and leftward head tilt towards the shoulders (i.e. BH TT).

The BH TT will be considered as positive if a positional adjustment of the eyes is observed in head tilt to any shoulder. Accordingly, the BH TT is considered as negative if no adjustments can be observed.

## **Vestibular stimulation during a Bielschowsky head tilt test**

During a Bielschowsky head tilt test the head both rotates as well as translates since the head rotation axis is positioned below the head in the upper part of the chest (Fig. 13). The larger the angles of head tilt from up-straight, the more upwards the centre of rotation will move. The body parts involved or influenced of such a head tilt are numerous. Muscle agonists and antagonists from the lower extremities and upwards are certainly involved as well as numerous segments of the spinal cord and the bones of the passive locomotor system.



**Figure 13.** Photos illustrating a subject in a) upright head position and in b) 30 degrees head tilt towards the right shoulder. A special designed tiltable chinrest with a bite-bar was used to keep the head in the roll plane.

**A rightward head tilt rotates the head clock-wise which will primarily stimulate the vertical semicircular canals. The head tilt induces an ampullofugal endolymph flow in the right side vertical semicircular canals (excitatory). At the same time an ampullopetal endolymph flow will be induced in the contralateral vertical semicircular canals (inhibitory).**

**Simultaneously there is also a rightward interaural head translation (heave). In the accelerating head tilt phase the utricular membrane will thus initially move in the opposite direction to the head movement due to inertia [60]. When the acceleration ceases the inertia will fade out and the membrane will move toward its resting position which is determined by the head position in relation to the gravitation pull. During head tilt the gravitation pull will change the resting position of the membrane with a vector directed toward the gravitational vertical.**

## **Aims of the studies**

### **Paper I**

It has been on debate whether a head tilt towards the shoulder induces ocular counter-roll or remain stationary in relation to the orbit which has previously been proposed [39, 40, 47]. This issue has a profound clinical significance when interpreting the outcome of a BHIT on subjects suffering of disorders of the oblique eye muscles. The purpose was to objectively evaluate ocular counter-rolling in normal subjects with no dysfunction of the EOMs. Furthermore, to investigate the influence by different viewing conditions such as bin-/monocular and fixation with versus without visual spatial cues.

### **Paper II**

The vertical and torsional eye movements are tightly coupled due to the mechanical action of the EOMs as well as the close neural relationship in the rostral brainstem. Since a vertical deviation of the eyes in response to both a static [4] as well as a dynamic [41, 73] head tilt has been shown to exist this necessitates a more detailed investigation of the torsional conjugacy during a head tilt. Furthermore, we sought to find out whether the torsional conjugacy of the eyes is influenced by different viewing conditions such as bin-/monocular and fixation with versus without visual spatial cues.

### **Paper III**

In the above studies (paper I & II) a fast torsional eye movement was found as the initial response to a head tilting. This response was in the same direction as the head, thus in the opposite direction of a presumed compensatory eye movement. This response has been mentioned by some investigators [2, 13] but not elaborated fully. Simultaneously with this torsional eye movement there was a similar vertical vergence eye movement. The purpose of this study was to reinvestigate these findings with the same head tilt paradigm but to supplement the video method (3D-VOG) used in the previous studies

with the Scleral search coil technique to record both the monocular eye position and the head position simultaneously.

#### **Paper IV**

The elastic restoring forces in the orbit tends to pull the eye towards the resting position. An active neural mechanism (integrator) is thus required to maintain the eye in the eccentric eye position. Since ocular torsion rotates the eye around an axis close to the visual axis, the fixated object would not be lost from fovea. For this reason it is uncertain how important the visual feed-back system is for maintaining the eccentric counter-rolled eye position. How the magnitude of ocular counter-rolling is maintained over time is not well known and the reports available are inconsistent. An immediate return of OCR towards reference position has been reported [72] which was suggested to be caused by a deficiency in the neural integrator. The aim of this study was to describe the OCR in humans during a prolonged BHTT and to find out if the OCR is influenced by the appearance of spatial visual cues.

#### **Paper V**

The common theory about the generation of OCR is that the vertical semicircular canals are contributing mostly during high frequent stimulation while the otoliths contribute mostly during low frequent stimulation ( $\leq 0.3$  Hz) [32, 87]. The eye position is maintained in a counter-rolled position during static head tilt by the static otolith ocular reflex [30]. Recently an OCR-decreasing drift during static head tilt was described [63, 85]. The underlying mechanism for this drift has not yet been identified. The purpose of this study was to reinvestigate OCR during different head tilting velocities in order to vary the vestibular (i.e. semicircular canal) input to the origin of OCR. Furthermore, the aim has been to study the drift of OCR to obtain further insight into what mechanisms are critical for OCR maintenance during a static head tilt.

## **Material and methods**

### **Recording techniques**

In the present studies the 3-dimensional Video-Oculography® (3D-VOG; Senso Motoric Instruments, Teltow, Germany) and the Scleral search coil technique (Skalar Medical, Netherlands) were used to record head and/or eye position.

### **3-Dimensional Video Oculography (3D-VOG)**

The 3D-VOG is a fully integrated system for binocular acquisition and analysis of horizontal, vertical and torsional eye movements. The system uses image processing technology where the eyes are filmed by two miniature video cameras. The recordings of right and left eyes are stored time-synchronized on video tape for off-line analysis.

### **Technical specifications**

The 3D-VOG system adheres to the European colour video standard PAL (Phase Alternate Line) as well as the corresponding CCIR monochrome video standard for PAL. The system provides a temporal resolution of 25 frames/second and each frame consists of 768×572 pixels. The relationship of width and height is 4:3. The monochrome image from the video cameras is digitized with 256 grey levels (8 bit).

Infrared light emitting diodes (LED's) which are mounted in the mask illuminates the eyes. The wavelength is 880 to 950nm, thus out of range for the visual spectrum. The instruments are approved and adhere to the following safety standards: IEC 60601-1-1 (Medical electrical equipment: Safety requirement); IEC 60601-1-2 (Medical electrical equipment: Electromagnetic compatibility); EN60825 (Safety of laser products (where applicable)).

### **Image acquisition**

The IR radiation is reflected from the sclera and iris. Almost no IR radiation falling through the cornea is reflected from the cornea or retina. Thus the acquired image shows a black pupil and a bright

sclera and iris ("*black pupil technique*"). The estimation of the pupil centre is performed by identifying the dark pupil and by assuming the borders of the pupil, even when the upper part of the pupil is covered by the eye lid by as much as 50%. This enhances the estimation of the pupil centre which is important for a correct estimation of torsional eye position. The horizontal and vertical eye positions are estimated by the centre coordinates of the pupil (values in pixels) in relation to the frame.

### **Determination of the torsional position**

To determine the torsional position the system need characteristic landmarks on the iris such as pigmentation. The landmarks are easily detected in the monochromatic IR radiation by the camera, therefore the torsional eye movements can be analyzed in most subjects. The rotatory displacement of the iris landmarks around the centre of the pupil is regarded as the shift of torsional position. A radial segment is manually positioned on the part of the iris with the best characteristic landmarks. The centre of the radial segment coincide with the centre of the pupil, therefore the importance of a correct estimation of the pupil centre (see above). The intensity (luminance) of the iris under the radial segment is represented by an iris-profile. The parts of the iris with low intensity are represented by a low value while the parts with high intensity are represented with a high value. When the eye rotates around the centre of the pupil, the iris landmarks shift place on the radial segment since the segment is held in a static position in relation to the pupil. The shift in torsional eye position is directly transferred into degrees.

### **System calibration**

From the cameras point of view a  $5^\circ$  eye movement starting from the primary position will appear larger than a similar eye movement starting from a secondary or tertiary eye position. This is partly a distortion problem which is caused by the optical projection of a three dimensional eye globe onto a 2-dimensional camera CCD-sensor plane. This will have severe implications on the data output if not taken into account.

Since the camera sensor is not at infinity, the distance to the pupil-planes will also vary depending on eye position. When the eye is not in the reference position (i.e. on the optical axis of the camera) this will give optical side effects such as spherical aberrations on the image of the eye.

In the 3D-VOG system there is a calibration program which should be carried out on all subjects. This program takes the distortion- and optical factors into account and converts the acquired coordinates into a correct eye position described in Fick-coordinates. The *linearity error* describes how well a recording system estimates an eccentric eye position. The 3D-VOG system has a linearity error of  $\pm 3.2\%$  for horizontal eye movements ( $\pm 25^\circ$ ),  $\pm 3.8\%$  for vertical eye movements ( $\pm 20^\circ$ ) and  $\pm 1.4\%$  for torsional eye movements. The linearity for the torsional eye position is here calculated in eccentric eye positions since a pure torsional eye movement does not distort the image of the ocular iris.

### **Control experiment**

The 3D-VOG is a head centred recording system and it is important that the head mounted mask with the video cameras is not allowed to move on the head. A mask movement would change the relative position between the eye and the camera and this would be interpreted as an eye movement by the 3D-VOG software. This imaginary eye movement is hereafter referred to as *chimera movements*. Since the action of gravity and inertia during head movements presumably leads to movement of the 3D-VOG head mask, a control experiment has been carried out on three subjects in order to measure the amount of mask movements induced during a Bielschowsky head tilt test. The subjects wore occulopad patches attached to the skin surrounding the eye (Fig. 14). These patches had manually drawn pictures of an eye with iris and a pupil (i.e. phantom eye). The phantom eye was positioned so that the drawn pupil was located in front of the subject's eye. The VOG-mask was worn as in the experiments and the cameras were centred and focused on the phantom eye. Any mask movement would thus change the camera

position relative to the phantom eye and thereby be interpreted as chimera movement.



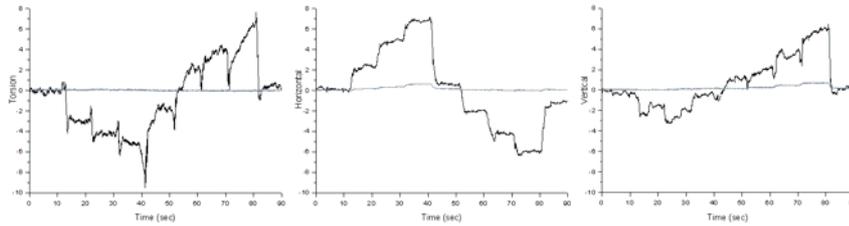
**Figure 14.** Photo of a subject with the phantom eye positioned over the left eye.

Two head tilt tests were performed with head tilts ( $15^\circ$ ,  $30^\circ$  and  $45^\circ$ ) towards both the right and left shoulder. In test 1 the left eye was occluded while in test 2 both eyes were occluded by phantom eyes. The purpose of test 1 was to compare the eye movements of the right eye (not occluded) with that of the left phantom eye. The purpose of test 2 was to quantify the presumed mask rotation. The subjects viewed a stimulus with spatial cues and fixated a centre target. A 9-point calibration was performed prior to the first control experiment on the right eye while the left eye was occluded by the patch. The data acquisition was performed as described above except for the calibration of the left eye. Since no movement of the mask was permitted after the calibration had been performed, the left eye was covered during the calibration and during test 1. The calibration file from the right eye was used to approximate the left phantom eye torsional ( $\omega$ ), horizontal ( $\theta$ ) and vertical ( $\phi$ ) displacement into degrees ( $^\circ$ ). The head mask was removed prior to test 2 to occlude the right eye with the phantom eye. The calibration file from test 1 was imported to test 2.

The control experiments verified that head tilts give rise to a small displacement of the VOG mask which can then be interpreted as eye movements (Fig. 15). In test 1 the amplitude of the chimera movements was always smaller than the amplitude of the eye movements.

## Material and methods

The chimera movements were found to be prompt and synchronous with the right eye movements that were induced by the head tilt. No chimera movement was detected in-between the head tilts, thus no drift of VOG-camera position was seen.

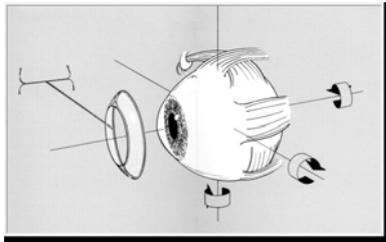


**Figure 15.** An individual recording from the control experiment to interpret VOG mask movements by occluding the left eye with an oculopad patch with a drawn picture of a pupil and iris (phantom eye) while the right eye was fixating. The eye movements of the right eye (*dark trace*) are easily compared with the chimeric movements of the phantom eye (*light trace*). The amplitude of the chimeric movements was always found to be smaller than the amplitude of the eye movements. **(A)** Notice the torsion peaks, OCR, drift of torsion position during static head tilt and incomplete return of torsion position in the second and third head-straight positions, whereas the chimeric movements of the phantom eye were continually close to zero. **(B)** Horizontal eye movement was steady in the static head tilt and similar in the rightward and leftward head tilts, whereas the much smaller horizontal chimeric movements were largest in the 45° rightward head tilt. **(C)** The vertical eye movement and chimeric movements were largest in the leftward head tilt. Note the drift of eye position in the leftward head tilts (60–80 seconds) during the static head position which corresponds very well to the drift of the torsional eye position **(A)** in the same part of the test. Positive (+) corresponds to a clockwise leftward and downward eye movement from the subject's point of view. Note that the chimeric movements have to be inverted to get the actual mask movement (e.g., a rightward chimeric movement corresponds to a leftward movement of the VOG mask).

The disconjugate vertical VOG mask movements ( $\varphi^{\text{diff}}$ ; LE  $\varphi$  – RE  $\varphi$ ) induced chimera torsional movements ( $\omega$ ). In test 2 the vertical chimera movements ( $\varphi$ ) were generally found to be small. However, in one subject the maximum  $\varphi$  corresponded to a 3° vertical eye movement. The largest disconjugate  $\varphi^{\text{diff}}$  was found to be 2° which correspond to a torsional movement ( $\omega$ ) of 0.5°. The chimera torsion ( $\omega$ ) due to the vertical movements ( $\varphi^{\text{diff}}$ ) of the VOG mask was found to be conjugate and range between  $\pm 0.1^\circ$  in the maximum head tilted positions. The largest chimera horizontal displacement ( $\theta$ ) was found to be 0.7°.

## Scleral search coil

The principle of the technique is based upon the magnetic induction of a small coil of insulated copper wire [69]. The induction coil is embedded in a flexible ring of silicone rubber which adheres to the limbus of the eye concentric with the cornea [12] (Fig.16). The concave side (ocular) of the suction ring is slightly more curved than the eyeball. Capillary and suction forces hold the suction ring firmly in its place when the air and fluid between the eye and the suction ring is evacuated by slight pressure. Prior to the insertion of the suction ring, the eye is briefly anaesthetised by one or two drops of a topical ophthalmic anaesthetic (Tetracaine 1.0%). This does not affect pupil size, accommodation or corneal transparency. Some subjects experience a slight irritation of the conjunctiva for a short time after a session with the lens. Occasionally, slight degradation of the visual acuity may occur in the later parts of a long recording session, probably due to drying and/or slight deformation of the cornea. Such effects recover within half an hour and are usually not seen at all with proper insertion and wearing time not exceeding 30 minutes.



**Figure 16.** Illustration of the magnetic induction coil with the thin copper wire and the eye. Used by permission from Skalar medical bv.

### Basic technical principle

Around the head of the subject there is an alternating horizontal and vertical magnetic field generated which induces an alternating voltage in the induction coils. The induced voltage will change depending on the coil orientation in the magnetic field. The two magnetic fields are temporally and spatially separated and the detection part of the system will demodulate the voltage-signal into a horizontal, a vertical

and a torsional part. For a more detailed description of the scleral search coil method the reader is referred to earlier publications [12, 69].

### **Control experiment**

As the head tilt consists of both a rotation as well as a translation of the head in the inter-aural plane the effect of translation of the induction coil was estimated in a control experiment. Three subjects were photographed using a high-resolution digital camera to measure the amount of rotation and translation of the head during a BHIT. The average translation of the orbits from a head straight position to the 45° head tilted position was found to be <9 cm in the horizontal and <7 cm in the vertical direction. The static inter-aural translation artefact within the central 10 cm cube of the magnetic field, in which the subjects' head always remained, was <0.01° for the torsional and horizontal channels and <0,02° for the vertical channel. The torsional deviation from linearity was <2.5% over an operating range of ±30°. When extending the range to 45° the linearity was ≤8.3%.

## **Method for analysing the data**

### **3D-VOG data**

The videotape recordings were digitized and calibrated into ASCII data for the six channels (right and left eye; horizontal, vertical and torsional data) and imported to the Origin® software for evaluation. With the VOG software a torsional quality value (between 0 - 1.0; best) was calculated for each video frame, which gave the concordance between the selected reference of the iris-segment when the eye was in reference position in the beginning of the test and the recorded iris-segment from each evaluated frame of the recording. Only the parts of the recorded file where the torsional quality value were better than 0.3 (0.5 in manuscript I & II) was used and parts containing blinks were identified and manually removed from the data. The signal was smoothed by a boxcar filter (adjacent averaging; 5 samples); the eye position data were then differentiated to obtain the eye movement velocity (°/s). A velocity criterion was used ( $\geq 5^\circ/\text{s}$ )

to define the initiation of the eye movement to each head tilt since no head position signal was available with the 3D-VOG.

### **Search coil data**

The recordings were calibrated and converted into ASCII data for the six channels (right eye horizontal, vertical and torsional data; head yaw, pitch and roll data). The search coil data were then imported into the Origin® software for evaluation. The signal was smoothed by a boxcar filter (adjacent averaging; 50 samples) and differentiated to obtain the eye and head movement velocity ( $^{\circ}/s$ ). A 2-sample differentiation was performed to obtain the eye and head acceleration ( $^{\circ}/s^2$ ). The orientation of the eye and head lens coils before the start of the head tilt was calculated with the use of the average head and eye position during the 100ms prior to the head tilt and used as the reference position.

### **Control experiment**

The data was smoothed by a boxcar filter (adjacent averaging) to reduce signal noise and to allow calculation of torsional velocity and acceleration. A too powerful filtering would interfere on the data by shortening the latencies, reducing the amplitudes of the torsion peak and masking nystagmus beats etc. The influence of the filtering on the data was estimated by regression analysis of the filtered and un-filtered data.

The results demonstrate an interference of the filtering process on the search coil data which depend on the recording frequency used.

- i) At 500Hz (B-value 0.98; coefficient of determination  $>0.99$ ),  
and
- ii) at 200Hz (B-value 0.99; coefficient of determination  $>0.99$ ).

The reason for the larger interference on the 500Hz-data might be due to that the higher recording frequency was always selected during test conditions with fast changes in head position.

The interference on the 3D-VOG data was found to be (B-value 0.95; coefficient of determination  $>0.97$ ). We consider the interference on the data as minor for the aims of our studies.

## **Experiment paradigms**

To record the head and/or eye position, the 3D-VOG technique was used in test 1-4 and the Scleral search coil technique was used in test 3 and 5.

**Test 1-3:** The subjects were seated at a distance of 150 cm from the projection screen. In the beginning of each test the subject viewed the fixation spot for at least 20 seconds before any data was collected. Each test started with the head in upright position and the eyes in the reference position. The head was then tilted 15, 30 and 45 degrees to the right shoulder and then back to the head straight position. After that the head was tilted correspondingly to the left shoulder in three similar steps and then returned to the straight up position. Each paradigm thus resulted in a total of nine head positions. Every single head position was held static for 10 seconds. The shift between the head positions was performed by manually tilting the chin rest (duration 1 sec). Two different viewing conditions (binocular and monocular) and two visual conditions (with and without spatial orientation) were used in three test conditions in test 1 and 2.

- i) binocular viewing without cyclo-spatial orientation (test 1),
- ii) binocular viewing with spatial orientation (test 2), and
- iii) monocular viewing with spatial orientation (test 3).

In test 3 were the stimuli without cyclo-spatial orientation used in two tests during binocular viewing.

- i) recording of right and left eye by the 3D-VOG (test 1), and
- ii) recording of right eye and head position by the Scleral search coil (test 2).

**Test 4:** The subjects were seated at a distance of 150 cm from the projection screen. In the beginning of each test the subject viewed the fixation spot for 40 seconds. Each test started with the head in upright position and the eyes in the reference position. The head was then tilted 30 degrees (duration ~2sec) to the right shoulder and kept in that position for 10 minutes and subsequently raised back to upright head position. Two tests were performed in each subject with the visual target as the only difference.

i) visual target without cyclo-spatial cues, and

ii) visual target with cyclo-spatial cues.

**Test 5:** The subject wore a helmet, which was individually adjusted to attach firmly to the head. On the left parietal part of the helmet one end of an extension cord was fixed and the other end was attached to the wall. A manually controlled winch was coupled by a stiff non-magnetic cord to the opposite side of the helmet (i.e. right parietal). Thus, the head could be pulled by the winch towards the right shoulder with controlled velocity. The extension cord worked as an antagonist during head tilting. When the experimenter slackened the stiff cord the head was pulled back to upright position by the extension cord. The subject was fixating a small laser spot (distance 5 m) with the eyes in the reference position during the entire test. Three tests were then carried out in a complete darkened room. All tests started in upright head position for at least 60 seconds and after that the head was tilted 30° towards the right shoulder. The only parameter changed between the tests was the head tilting velocity.

i) head tilting velocity of  $<0.5^\circ/\text{sec}$  (duration  $>60$  sec),

ii) head tilting velocity of  $\sim 6^\circ/\text{sec}$  (duration  $\sim 5$  sec), and

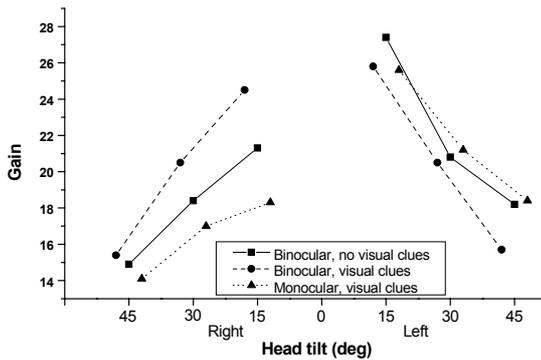
iii) head tilting as fast as possible by pulling the stiff cord manually.

## Results and Discussion

### Paper I

A step-wise tilting of the head induced a consistent amount of OCR in all subjects. The OCR increased with the head tilt and no significant difference was seen between rightward and leftward head tilting. The maximum OCR amplitude during 15° head tilt ranged between 2.3° and 3.6°. The corresponding values at 30° head tilt ranged between 4.7° and 6.4°, and those at 45° head tilt ranged between 5.4° and 7.4°.

The static gain was calculated as the ratio between the amplitude of OCR and the amount of head tilt (°). The gain ranged between 18% and 27% at 15° head tilt, between 17% and 21% at 30° head tilt, and between 14% and 18% at 45° head tilt (Fig. 17). These data illustrate that the relative amount of OCR was higher at a lower amount of head tilt, and that the compensatory response decreased with increasing tilt of the head.



**Figure 17.** Mean static gain of five normal subjects after head tilt towards right and left shoulder.

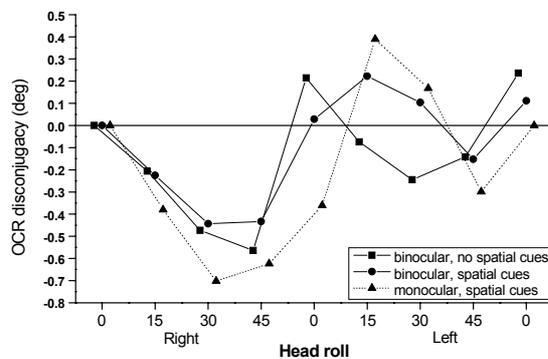
Concerning the question whether the torsional response to head tilt is influenced by visual orientation and binocular input, the low sample size (5 subjects) of this study has to be taken into account. The difference in OCR between the two eyes was less than 1° in all tests, indicating a generally good torsional conjugacy of the eyes during the two different viewing conditions (mon- and binocular) as well as the two different visual conditions (with and without spatial cues).

However, during test 1, where no spatial cues were present, there was a tendency for consistent small disconjugacy during the first part when tilting towards the right shoulder. This disconjugacy corresponded to a larger amplitude of ocular counter-roll of the left eye (excycloduction) than of the right eye (incycloduction), thus inducing an excyclovergence which somewhat increased with the amount of head tilt.

In accordance to a number of previous reports [9, 13, 22, 23, 37, 43, 48, 57, 77, 82], our study results demonstrated that OCR in response to lateral head tilt is a consistent finding in healthy subjects without disturbances of the ocular motor or the central nervous systems. In the light of these studies we feel that the previous reports where no such response could be confirmed must have been based on misinterpreted recording data and can not be maintained any longer [39, 40, 47].

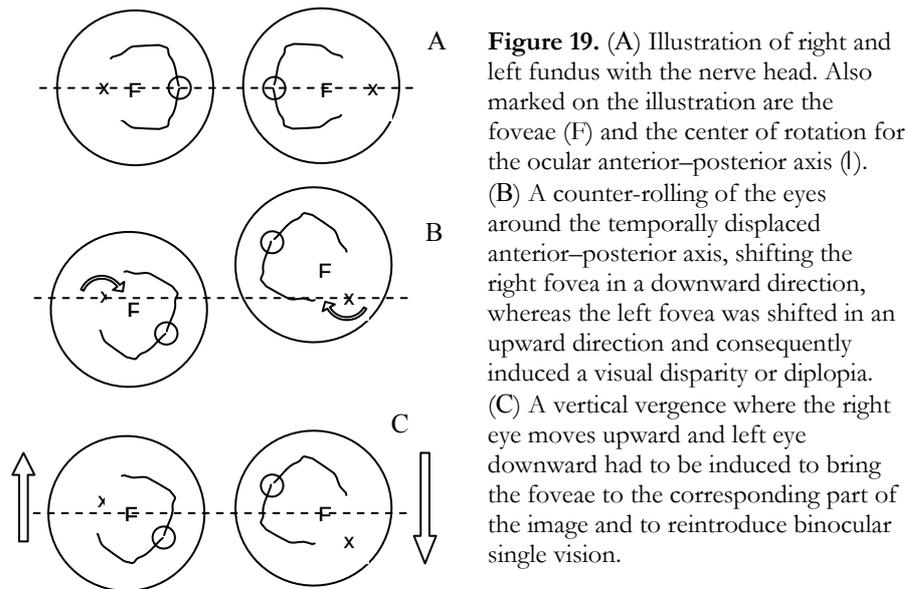
## Paper II

A head tilt induced OCR disconjugacy which increased with head tilt. A consistent finding was a larger OCR ex-cycloduction of the superior eye (i.e. contralateral to the head tilt) than the OCR in-cycloduction of the inferior eye, thus inducing an ex-cyclovergence. This disconjugacy increased with the amount of head tilt and the maximum ex-cyclovergence found was  $4.9^\circ$  (Fig. 18).



**Figure 18.** The average disconjugacy (vergence) of right and left eyes during each head position. Note the negative (-) movement during both the rightward and leftward head tilts, which returned toward reference position ( $0^\circ$ ) when the head was straightened. Negative (-) corresponds to excyclovergence.

The cyclovergence was significantly separated from 0 in the 30° ( $p < 0.01$ ) and 45° ( $p = 0.05$ ) but not in the 15° head tilt when performing a General Linear Model analysis. The ex-cyclovergence found in response to a head tilt has, as far as we know, not been reported previously. An explanation for the disconjugacy in OCR might be that, with increased head tilt there is a decline in utricular input and a rise in saccular input in the brain circuits controlling the OCR [18]. The utricle has been suggested to generate conjugate torsional eye movements and the saccule to generate disconjugate torsional eye movements [18]. The disconjugacy found may also be the result of an unequal OCR of the right and left eye. Each eye is driven by the both utricles but there is no reason to expect that these eye movements are inherently conjugate. All these suggestions might explain the findings of ex-cyclovergence in response to a head tilt. The head tilt also induced conjugate horizontal eye movements in the opposite direction to the head movement and a vertical disconjugacy (i.e. vertical vergence) that increased with the head tilt. In 15 of the subjects the rightward head tilt induced a vertical vergence with the right eye elevating and the left eye depressing. In the remaining 5 subjects the opposite outcome, with the left eye elevating and the right eye depressing, was found. Previous reports have shown similar findings with a vertical skew in response to both a static [4] as well as



dynamic head roll [41, 73]. Jauregui-Renaud [41] suggested that the vertical semicircular canals were responsible for the skewing in response to a dynamic head roll. However, the non-consistent disconjugate response found in the present study might be explained by a difference in the ocular visual and torsional axes (Fig. 19A). The torsional movement might displace the visual axes from the fixation target and induce disparate projections on the two retinas (Fig. 19B). To maintain single binocular vision a vertical vergence movement of the eyes is required (Fig. 19C). Depending on the direction of displacement of the torsional axis (e.g. nasally, temporally) from the visual axis the direction of the vergence movement will differ. We would therefore suggest a visual model to explain our findings of a vertical skew found in the static head tilt.

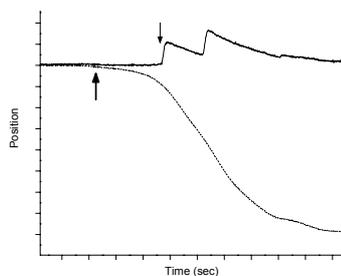
When straightening the head from the 45° right tilt to upright position the torsional return movement of the left eye was larger than the corresponding movement of the right eye inducing an in-cyclovergence. This movement was actually of larger amplitude than the preceding ex-cyclovergence thus inducing an in-cyclovergence position compared to the initial reference position. In the following (15°) leftward head tilts an ex-cyclovergence was again induced.

No difference was found between the two visual conditions when analysing the fluctuation (SD) of cyclo vergence position (test 1 mean SD  $0.71^\circ$  (SD 0.22) and test 2 mean SD  $0.68^\circ$  (SD 0.22)) but a significant difference could be determined between the two viewing conditions (test 2 (binocular) mean SD  $0.68$  (SD 0.22) and test 3 (monocular) mean SD  $1.22^\circ$  (SD 0.51)). The enhanced torsional vergence stability during binocular viewing is probably an effect of visual feedback which presumably corrects for vergence errors induced by the head tilt.

A previous finding of a vertical vergence in a static head tilt [4] was confirmed in this study. Furthermore, a disconjugacy of the torsional eye position in response to a similar head tilt paradigm has been shown to exist. A vestibular origin seems to provide a plausible explanation for the induced torsional disconjugacy.

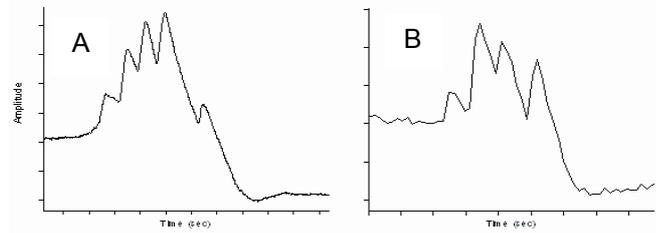
### Paper III

Subsequent to the initiation of the head tilt a fast torsion movement (torsion peak) was seen in the same direction as the head movement (Fig. 20). This rapid torsional response was seen both with the scleral search coil (Fig. 21A) and 3D-VOG recording technique (Fig. 21B). The torsion peak was initiated with a latency of  $\sim 160\text{ms}$  (SD  $\pm 30$ ) with no tendency to a slow phase movement in the opposite direction to the head tilt. The amplitude of the peak had a mean of  $4^\circ$  (range  $2-6^\circ$ ) and the average peak velocity was found to be  $40^\circ/\text{sec}$  (SD  $\pm 6$ ; range  $30-50^\circ/\text{sec}$ ).



**Figure 20.** Graph displaying the simultaneous search coil recordings of the head (*dotted*) and ocular torsion position (inverted for greater clarity). The shift of head position (*bold arrow*) was seen before the shift of eye position (*small arrow*). One step on the axes corresponds to  $2^\circ$  (y-axis) and 0.25 seconds (x-axis).

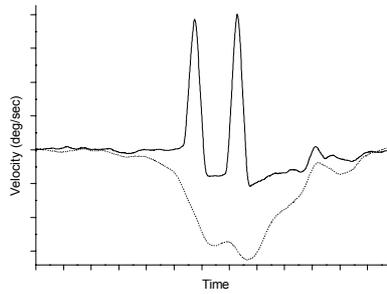
To the best of our knowledge there is no previous description of finding this initial rapid response to the head tilt.



**Figure 21.** (A, B) Graphs displaying the torsion peak from the search coil recording (A) and from the 3D-VOG recording (B). Note the nystagmus beats superimposed on the peaks as well as the similar appearance of the peaks in the two graphs. One step on the axes corresponds to  $1^\circ$  (y-axis) and 0.25 seconds (x-axis).

The finding could be related to the lowered position of the head rotation axis during tilting inducing a rightward inter-aural translation. The utricular mass initially moves in the reverse direction due to inertia and initially bends the direction sensitive receptor cilia in the utricular macula in the opposite direction to the translation [60]. This mechanism could be responsible for the fast transient torsion peak found.

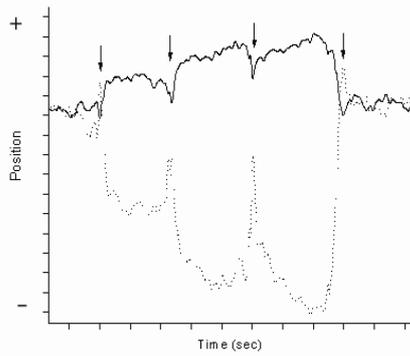
After a time interval of approximately 350ms from the initiation of the head movement, nystagmus beats ( $\sim 3\text{Hz}$ ) were seen superimposed on the torsion peak with the slow phase directed in the opposite direction to the head tilt (Fig. 22). The nystagmus ceased when reaching the tilted head position.



**Figure 22.** Graph displaying the eye and head (*dotted trace*) velocity during head tilt. One step on the axes corresponds to 5 deg/second (*y*-axis) and 0.25 seconds (*x*-axis). This velocity plot corresponds to the position plot in Figure 20. Note there was no tendency for the eye to accelerate in the direction opposite to the head acceleration.

The dynamic gain was calculated from the head tilt and OCR data acquired during the head movement describing how well the OCR compensated for the head tilt movement. A perfect compensatory eye movement gives a dynamic gain value equal to 1.0. The average dynamic gain was found to be 0.51 (SD  $\pm$  0.09).

Similar to the findings of a torsion peak we also found an initial rapid vertical vergence response corresponding to a physiological skew deviation simultaneous in time with the torsion peak (Fig. 23). The direction of this movement was always with left eye over right eye in the rightward head tilt and in the head straightening from the left shoulder. In the left head tilt and in the head straightening from the right shoulder this movement was always with right eye over left eye. The amplitude of the vertical vergence shift had a mean of 3° (range 2-5°). The aetiology for this fast vertical vergence response is currently unknown but could probably be explained by a similar vestibular mechanism as for the torsion peak.

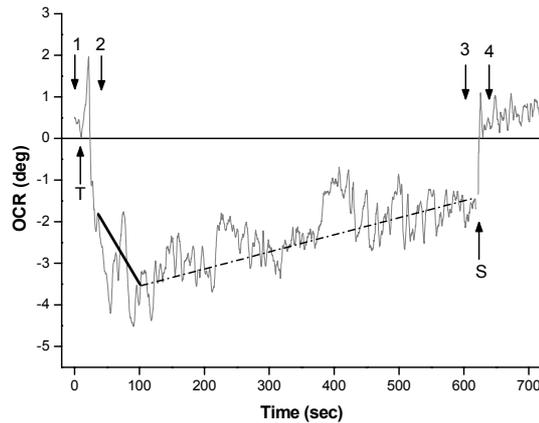


**Figure 23.** Graph displaying vertical vergence (i.e., left eye position - right eye position) and torsion position (*dotted trace*) from one representative subject. Positive (+) corresponds to right eye-over-left eye vergence and clockwise torsion. Observe that the fast vergence movements (*arrows*) were always synchronous with the fast torsion movements. One step on the axes corresponds to  $1^\circ$  ( $y$ -axis) and 5 seconds ( $x$ -axis).

We presume that these rapid changes in torsional and vertical position of the eye are due to a combined stimulation of the vertical semicircular canals and to the inertia of the utricular mass during the acceleration of the head. A stimulation of the canals alone would not elicit a quick phase that we found in the data but rather the slow phase to stabilize the retinal image. The otoliths seem to induce a torsional movement not only during low frequency head roll but also during stepwise high frequency head roll. If the torsion peak found is due to stabilizing the retinal image or if it could be explained by an idiosyncrasy of the vestibulo-ocular system is not known.

## Paper IV

A slow shift of torsion position (drift) was found in the sustained static head tilted position (Fig. 24). This drift was initially directed away from the reference position (CCW) thus increasing the OCR amplitude. After 20 seconds in head tilt position (seq.2) the OCR amplitude was found to range between  $3.0^\circ$  to  $5.1^\circ$  (CCW) in test 1 and between  $1.8^\circ$  to  $6.3^\circ$  (CCW) in test 2. This corresponds to a gain between 0.10 and 0.17 in test 1 and between 0.06 and 0.21 in test 2.

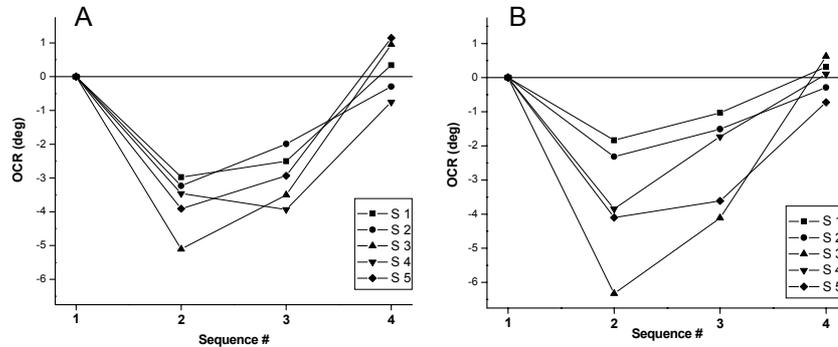


**Figure 24.** Graph displaying the OCR (grey plot) from one representative subject (test 2). The head tilt (black up-arrow: T) and head straightening (black up-arrow: S) is marked for clarification. Note the increasing OCR drift during the period following the head tilt (solid black line) and the imaginary point where the drifting is changing into an OCR decreasing direction. Also note the consistent drift towards the base-line (reference position) during the head tilt (dashed black line). The four time sequences used to calculate the OCR amplitudes (seq. 1-4) are marked with black down-arrows in the upper part of the graph. The y-axis displays the amount of OCR while the x-axis displays the time in seconds. The 0-line corresponds to the reference position.

After the initial drift of the OCR in the CCW direction, the drift was found to change direction from CCW to CW approaching the reference position and thus decreasing the OCR amplitude. The estimated time for the turning-point was analysed by polynomial fitting and by calculation of the mean OCR position every 10 seconds subsequent to the head tilting during 90 seconds. The time for the turning-point was found to be different in the two test conditions, thus estimated to be 30 ( $\pm 5$ ) sec in test 1 and 55 ( $\pm 18$ ) sec in test 2 after the head tilt.

After 9 minutes and 40 seconds in the head tilt position (seq. 3) the OCR was found to range between 2.0° to 3.9° (CCW; gain 0.07-0.13) in test 1 and between 1.0° to 4.1° (CCW; gain 0.03-0.14) in test 2.

As a result of the CW drift towards the reference position all subjects except one in test 1 demonstrated less OCR in seq. 3 compared to seq. 2 (Fig. 25).



**Figure 25 (A, B).** Figures displaying the mean OCR from each subject and test (fig A: test 1, fig B: test 2). The y-axis displays the OCR in degrees ( $^{\circ}$ ). The first column (sequence 1) in each figure represents the reference position obtained prior to the head tilt. The second column (sequence 2) represents the mean position obtained 20 seconds after the head tilt, the third column (sequence 3) prior to the head straightening and the fourth column (sequence 4) in straight up head position. Note the decrease in OCR amplitude between column 2 and 3. The 0-line corresponds to the reference position. The time span between sequence 1 to 2 and 3 to 4 corresponds to 40 seconds each while the time span between sequence 2 and 3 corresponds to 9 minutes and 20 seconds.

An overshoot of the OCR was found when straightening the head to upright position in three of the five subjects (mean  $0.9^{\circ}$ ) whereas the OCR return in the two other subjects did not reach the reference position (mean  $-0.6^{\circ}$ ). After 20 seconds in the head straight position (seq. 4) the OCR was found to be close to the reference position (seq. 1) in all subjects.

The underlying mechanism for the continuous OCR-increasing drift found is unclear but the relatively long duration may talk in favour of a central, rather than a peripheral mechanism. One possible explanation might be a sign of a decline in the leftward utricular discharge, induced by macula inertia during the initial interaural translation, in favour of the rightward utricular gravitational

discharge. The time constants for changes in discharge rate of otolithic afferents may be as large as 10 seconds, as reported by Si et al. [75], which implies a possibility of changes in otolith-dependent phenomena during as much as 30 seconds during static conditions. Another possibility could be that the OCR-increasing drift has something to do with the velocity storage mechanism of the semicircular canal system [68].

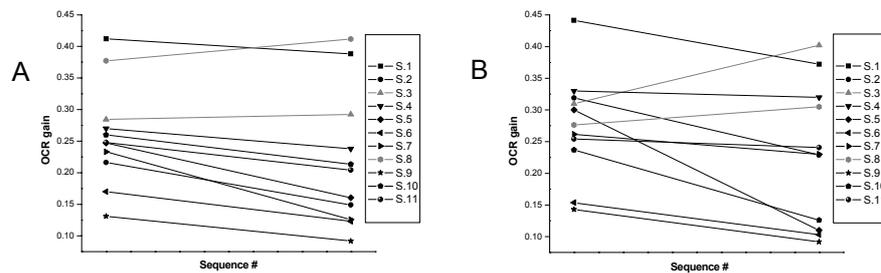
The mechanism for the torsional drift back towards the reference position could be an adaptation of the utricular receptors, which has been studied via recording of the isolated utricle of elasmobranchs [49]. Since OCR is mainly maintained by the Utriculus [30], a receptor adaptation mechanism could explain the decrease in OCR (i.e. drift) in response to a sustained head tilt. A central origin with a leakage of the neural integrator is another potential explanation for the drift of the OCR towards the reference position. Crawford et al. reported that pharmacological inactivation of the interstitial nucleus of Cajal caused impairment of the torsional integrator [15]. An important prerequisite for several spatial orientation tasks is a memory for angular changes in position, detected by the semicircular canals. Such a memory for angular changes in position could possibly also influence the torsional position of the eyes during prolonged static head tilt. If the semicircular canals sense the change in roll head position and contribute to the OCR response, then a “forgetting” of the semicircular canal input would be reflected in a gradual decrease in OCR.

### **Paper V**

Head tilting induced OCR in all test subjects. The analysis of the head position data acquired subsequent to the head tilting revealed mean head tilt amplitude of 33° (SD 5°). Prior to head straightening the head tilt amplitude was found to be smaller in 10 subjects (exception *s.7*). This was caused by a head position drift ( $< 0.2^\circ/\text{sec}$ ) and the average head tilt amplitude was as a consequence lessened by 1.7° (SD 1.7) both in test 1 and 2. The reason for the drifting head position is

not known. One possible explanation might be slippage of the head helmet which thus allowed the head to move slightly. The head silicon annulus was however fixed to the forehead and the true head position was always recorded despite any helmet slippage.

The average OCR and head tilt data was extracted (5 sec samples in test 1 & 2; 1 sec sample in test 3) and divided to describe the OCR gain. The average OCR gain was 0.28 (SD 0.08) subsequent to the head tilting and 0.23 (SD 0.11) prior to head straightening (500 sec after head tilt) in test 1. Similarly the average OCR gain was 0.26 (SD 0.08) subsequent to head tilting and 0.22 (SD 0.11) after 500 sec in head tilted position in test 2 (Fig. 26).

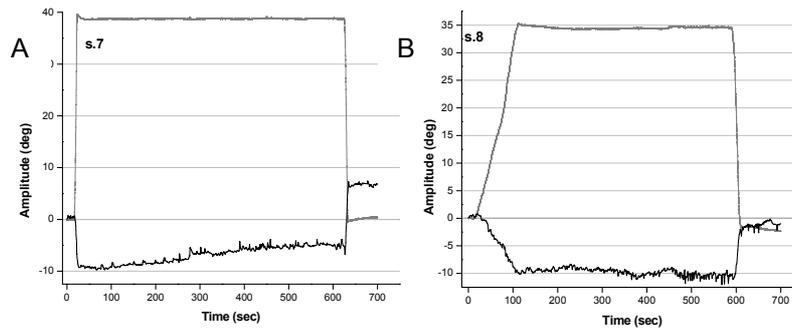


**Figure 26 (A, B).** Change in OCR during head tilt from each subject and test 1 (fig. A) and test 2 (fig. B). The values in seq 2 were calculated 500 seconds after seq 1 in both test conditions. Two subjects demonstrated an increase in OCR in both test conditions.

Test 3 elicited the largest OCR response in 9 subjects and the average OCR gain was found to be 0.39 (SD 0.11) subsequent to the head tilting.

The OCR drift was directed towards reference position (CW) in 9 subjects (Fig. 27 A) and away from reference position (CCW) in 2 subjects (Fig. 27 B) during test 1 and 2.

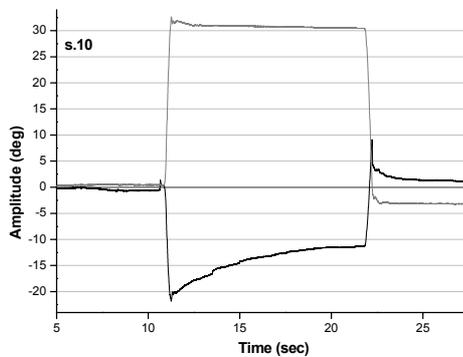
A close to linear relationship could be expected between the head drift and OCR drift in the actual head drift range (between 26° to 40° from upright head position) if the OCR drift was merely caused by the head movement.



**Figure 27 (A, B).** Graphs displaying the OCR (black) and head tilt (grey) during head tilt. **A)** Note the OCR decreasing drift and the stable head tilted position (i.e. no drift) as well as the overshoot of OCR when straightening the head to upright position (subject 7; test 2). **B)** Note the increasing OCR drift which is opposite to the OCR graph seen in figure a (subject 8; test 1).

The results of an analysis revealed a substantial deviation from linearity. Since the OCR decreasing drift was also found in subjects with a stable, or close to stable, head tilted position it is clear that the OCR decreasing drift was not caused by the raised head position only.

All test subjects were demonstrating an immediate OCR return towards reference position subsequent to the head tilting in test 3 (Fig. 28). The OCR drift had a declining velocity and appeared to approach an OCR position close to what was elicited in test 1 and 2.



**Figure 28.** Graph displaying the OCR (black) decreasing drift subsequent to the head tilting (grey) as well as when straightening the head back to upright head position (subject 10 from test 3).

When straightening the head towards upright position, an overshoot of the return torsional movement passing the reference position was

found in 9 subjects. The head straightening movement was always above the detection threshold for the semicircular canals despite test condition. There was a positive correlation between the amount of OCR drift during head tilt and the OCR overshoot reached subsequent to head straightening ( $r^2=0.85$ ). The results revealed a higher amount of overshoot in relation to OCR decreasing drift in test 2 compared to test 1.

It appears like the brain misinterprets the correct torsional position after a period of head tilt and when straightening the head the amplitude of the torsional return movement is solely based on the semicircular canal input acquired during head straightening, independently of the present torsional position.

## **Conclusions**

When tilting the head towards the shoulder there are several mechanisms influencing on the generation and maintenance of ocular counter-roll. Each of these mechanisms has its own temporal and spatial characteristics. Several new characteristics in ocular counter-rolling has been identified, investigated and explained. For instance, a fast short-lasting anti-compensatory torsion movement was found as the initial response to head tilting. Synchronous with the fast torsion movement a vertical vergence shift was detected. Inertia of the utricular otolith seems to provide a reasonable explanation to this response. Furthermore, the binocular torsion position was found to be of different amplitudes during the static head tilted position despite visual or viewing conditions. The disconjugacy was however lessened during binocular viewing of a visual target with spatial cues. A visual feed-back seems to correct for the larger degrees of torsional disconjugacy.

Ocular counter-rolling is an interesting parameter to investigate in patients with eye movement abnormalities. The head tilt test can be considered as an important investigation tool in patients suffering of not only vertical deviations of the eyes but also of torsional misalignments.

## **What can be improved and what might follow?**

The possible future studies on OCR should take some new factors into account to further understand and interpret the relationship between head movement and the eye movement response. For example:

- Vector based analysis of eye and head movements to interpret the real rotation axes
- Integrating measurements of 3D head translation
- Enhanced control of head stimulation

Another field of importance for a deeper understanding of OCR is the pulley mechanism which currently is in focus of many interests.

So, what are we waiting for?

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Figure 4, 9 and table 1 from NEUROLOGY OF EYE MOVEMENTS 3/E by Leigh and Zee, copyright – 1999 by Oxford University Press, Inc. Used by permission of Oxford University Press, Inc. (contract # 11879)

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## Sammanfattning på svenska

För att kunna se klart och tydligt ställs det flera krav på vårt synsinne. Bilden som faller på näthinnan i ögonbotten måste ha en tillräckligt hög optisk skärpa för att stimulera synsinnet. Då enbart den centrala delen av näthinnan, den s.k. fovean, kan urskilja små detaljer i bilden är vi även beroende av att röra på ögat för att bilden av det vi är intresserade av ska förflyttas till eller behållas i fovea. För detta ändamål rör vi ständigt på ögonen. När vi rör oss (går, springer) ställs ytterligare krav på synsystemet eftersom bilden inte bara måste förläggas rätt i ögat utan även hållas tillräckligt stilla för att hjärnan ska hinna tolka bilden.

Utan den koppling som existerar mellan ögonrörelseapparaten och balansorganet hade vi inte kunnat röra oss och se skarpt samtidigt. Balansorganet i innerörat känner av varje liten rotation och förflyttning av huvudet som uppstår när vi rör oss. Genom den mycket snabba vestibulo-okulära reflexen (VOR) kan ögat roteras snabbt och precist i exakt motsatt riktning mot huvudrörelsen. Därigenom kan bilden av omgivningen hållas tillräckligt stilla på näthinnan för att vi ska se klart. Kopplingen mellan balansorganet och ögonmusklerna är således mycket viktig för att vi ska kunna röra oss och se klart samtidigt.

När man lutar huvudet mot axeln, vid s.k. head tilt, roterar ögonen runt synaxeln i motsatt rotationsriktning mot huvudets. Denna ögonrotation benämns vanligen som *torsion* eller *cyklo*, vid huvudlutning dessutom såsom *ocular counter-rolling* (OCR). Torsionen är en icke viljemässig ögonrörelse som framför allt kontrolleras av balansorganet i innerörat. Dessutom kan torsion även initieras av synsinnet och av de sträckkänsliga receptorer som sitter i nackmuskulaturen (proprioception). Balansorganet har dock den starkast bidragande effekten på torsion.

Hos patienter med skelning i vertikalled (ett öga står högre än det andra) gör man ofta en huvudlutningstest (Bielschowsky's huvudlutningstest) för att avgöra om skelningen beror på fel i

ögonmuskulaturen eller i balansorganet. Kunskapen om hur detta huvudlutningstest påverkar ögats torsionsrörelser har i flera avseenden varit bristfällig och i vissa fall saknats. Syftet med de studier jag har genomfört var att kartlägga hur ögats torsion svarar på en huvudlutning mot axel hos den friska människan. Nedan följer en kort sammanfattning av de resultat vi nått genom de fem studier som ingår i denna avhandling.

Som svar på en huvudlutning mot axel fann vi initialt en kortvarig torsionsrörelse i samma riktning som huvudrörelsen vilket tidigare aldrig har beskrivits i detalj (se artikel III). Denna torsionsrörelse som vi nu kallar för *torsionsspiken* induceras efter en reaktionstid av ca 160 msek och har en storlek motsvarande  $\sim 4^\circ$ . Torsionsspiken har troligtvis sitt ursprung i den gelatinösa struktur (utricle) i balansorganet som registrerar linjära huvudförflyttningar och dessutom jordens dragningskraft. När huvudet lutar mot axeln, accelererar huvudet i sidled (translaterar). Utricle släpar då efter p.g.a. accelerationströgheten och denna mekanism är sannolikt vad som skapar den snabbt övergående torsionsspiken. Under huvudlutningen stimuleras dessutom de vätskefyllda bäggångarna i balansorganet och detta skapar den nystagmus (ögonarr) som stabiliserar bilden under huvudrörelsen. Samtidigt med torsionsspiken fann vi dessutom en snabbt övergående vertikal vergens (ett öga rör sig uppåt och det andra ögat nedåt) liknande torsionsspiken. Vid huvudlutning mot höger axel uppvisades alltid en vänster-över-höger ögonposition och vid motsvarande huvudlutning åt vänster axel en höger-över-vänster ögonposition. Denna vertikala ögonposition skapar tillsammans med torsionsspiken en fysiologisk *skew deviation* som normalt ses hos patienter med imbalans mellan höger och vänster balansorgan (yrsel). Här påvisar vi en liknande, snabbt övergående, ögonrörelse hos fullt friska försökspersoner under huvudlutningen.

När huvudet har nått sin lutade position mot axeln drar gravitationskraften tillbaka utricle mot jorden (dvs nedåt) och skapar en ihållande torsion. Vi fann att vid en huvudlutning av 15

grader så inducerades 3° torsion. Vid en ökad huvudlutning till 30 och 45 grader så inducerades 5.5° respektive 6.5° torsion (se artikel I). Ögat kompenserar inte perfekt vid huvudlutning utan svarar endast för ca 10-20% av mängden huvudlutning. Dessutom fann vi att torsionen i höger och vänster öga inte var exakt lika stor vid huvudlutning. Till exempel, vänster öga gjorde en större torsionsrörelse (0.7°) än höger öga vid 45° huvudlutning mot höger axel. Detta skapar en skillnad mellan ögonen som benämns som ex-cyklovergens. Detta fynd har tidigare aldrig beskrivits som svar på en huvudlutning mot axel (se artikel II).

En vertikal diskonjugering (vertikal vergens) uppstod även när huvudet hölls lutat. Denna skiljde sig dock mellan försökspersonerna genom att några uppvisade en höger-över-vänster ögonposition vid höger huvudlutning medan andra uppvisade det motsatta med vänster-över-höger vid samma lutning mot höger. Troligtvis beror denna vertikala vergens på att ögats torsionsaxel och synaxel inte är en och samma. För att bibehålla ett enkelt seende (ej dubbelbild) under huvudlutning krävs en vertikal vergens. Beroende av hur torsionsaxeln och synaxeln förhåller sig till varandra skiljer sig den vertikala inställningsrörelsen mellan försökspersonerna (se artikel II).

Vid en ihållande huvudlutning över 10 minuter visade vi att torsionen inte behåller sin position utan driver tillbaka mot 0-läget som vid upprätt huvudhållning (se artikel IV). Denna drift speglar troligtvis en anpassning i balansorganet vilket ger en avklingande effekt på torsionen. Driften var inte beroende av hur snabbt eller långsamt vi lutade på huvudet (se artikel V). Den fanns både i totalt mörker och i vanlig rumsbelysning.

När huvudet åter restes upp till rak huvudhållning efter huvudlutningen återgick torsionen mot 0-linjen. Oftast passerade torsionen 0-linjen och stannade 2-3° på motstående sida. Efter en kort stund drev torsionen tillbaka mot 0-linjen. Denna s.k. *over-shoot* av torsionen kan även den bero på den adaptation som vi tror existerar i balansorganet.

## Summary in swedish

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Dessa fynd har lett till att vi idag bättre förstår vilka mekanismer som inducerar och kontrollerar torsionen under en huvudlutning. En huvudlutningstest kan med fördel användas inte bara hos patienter med vertikal felställning av ögonposition utan även hos patienter med torsionsfelställningar.

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The foundation started December 18, 1989 by the initiator, Princess Marianne Bernadotte, organizing an auction at Bukowskis Auction House in Stockholm where donated art was sold. Part of the profit from the foundation is annually given out as scholarships and travel grants to applicants. Every other year (starting 1995) the *Princess Marianne Bernadotte prize* has been awarded to a person who has conducted superior paediatric eye research. There is also a Prince Sigvard Bernadotte honorary lecture held at the Nordic Paediatric ophthalmology conference every other year which is sponsored by the foundation.

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## **Appendices**

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