Monocular Adaptation of Vestibulo-Ocular Reflex (VOR)

by

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I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT

Purpose: This study asks whether active horizontal angular Vestibulo-Ocular Reflex (VOR) gain is capable of monocular adaptation after 4 hours of wearing 10 dioptres (D) of induced anisometropia in healthy human adults. **Method:** The participants (average age 28 years) wore a contact lenses/spectacles combination for 4 hours. The power of the spectacle was +5.00D (magnified images 8.65%) in front of the right eye and –5.00D (minified images 5.48%) for the left eye, while the power of the contact lenses was equal to the subjects' habitual correction, summed with the opposite power of the spectacle lens. Eye and head position data was collected in complete darkness, in one-minute trials before adaptation and every 30 minutes for 2 hours after adaptation. Eye and head position data obtained using a video-based eye tracking system, was analyzed offline using Fast Fourier Transform in MATHCAD$_{TM}$ 11.1 software to calculate VOR gain. The VOR gain was compared between the right eye and left eyes for the trials before and after adaptation. **Results:** In the first post-adaptation trial, a significant decrease in VOR gain (≈ 6%) occurred in the left eye in response to the miniaturizing lens. The right eye VOR gain did not show a significant change in the first post-adaptation trial (≈2% decrease). During the remaining trials in the 2 hour follow-up time, both eyes showed a significant decrease compared to the baseline trial. This might indicate habituation of the VOR from repeated testing, or fatigue. **Conclusion:** There was monocular adaptation of VOR in response to the combined contact lenses/spectacles, but it was not complete and it was not as we expected. However, trying different amounts of anisometropia in one or two directions, a longer adaptation period (more than 4 hours) or monitoring the gain for more than 2 hours after adaptation with a longer separation between trials, might show different results.

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1 INTRODUCTION

Most animals, when they change their fixation from one target to another, they use a combination of eye and head movements. Since visual acuity can be significantly degraded with retinal slip of only a few degrees per second[1-4], both eye and head movements are used to reflexively stabilize the line of sight as quickly as possible. Therefore, in order to see and move at the same time, the eyes must have the ability to remain stable as the head rotates. When the head begins to move in any direction while viewing a distant object, the vestibular apparatus in the inner ear senses this movement and sends direction and rate information directly to the ocular motor system. The ocular motor system then responds by moving the eyes in an equal but opposite direction, to compensate for the head movement and to keep the visual image stabilized on the retina. This is known as the Vestibulo-Ocular Reflex (VOR). If the VOR fails, then vision during locomotion is damaged and performing even the most basic of tasks, like standing, walking or reading is difficult[5-7]. The VOR is capable of adaptation to visual and vestibular stimuli (e.g., to wearing spectacle correction and constant velocity rotation)[5;6]. The focus of this research is to investigate ocular motor adaptation in the VOR. As such, I will identify how the vestibular system and VOR function and apply them to interpret my results to better understand this system's adaptation.

1.1 Rotational & Linear Vestibulo-Ocular Reflex

In three-dimensional space there are three rotational and three linear degrees of freedom of head movement. Compensatory eye movements respond to both linear and

rotational head movement[5-7]. Rotational VOR, which depends on the semicircular canals, responds to three possible directions of head rotation; Horizontal (around a dorsal-ventral z axis or yaw), Vertical (around inter-aural y axis or pitch), and Torsional (around nasal-occipital x axis or roll). Translational (linear) VOR, which depends on the otolith organs, responds to three possible directions of head translation; Horizontal (heave, along the inter-aural axis), Vertical (bob, along the dorsal-ventral axis), and Vergence (surge, along the naso-occipital axis).

1.2 Anatomy of Vestibular system

The vestibular apparatus is a small structure that exists in the bony labyrinth, in the temporal bone, of the inner ear. The vestibular organ in each inner ear consists of two principle sets of structures, the semicircular canals and the otolith organs, which work together to provide optimum information on head movement, posture and balance, and perception of motion and orientation. The cristae of the semicircular canals sense head rotation while the maculae of the utricle and the saccule in the otolith organ are used to sense linear head motion[5-8].

1.2.1 Semicircular Canals (SCC)

There are three semicircular canals in each ear, which are perpendicular to each other. One is approximately horizontal, whereas the others (anterior and posterior) are vertical. They are filled by endolymphatic fluid. As the head rotates in one direction, the endolymphatic fluid is displaced in the canals that are in the plane of motion, in the opposite

direction. Because of the anatomy and biophysics of the canals, the endolymphatic motion is proportional to head velocity. This movement stimulates the hair cells' sensory endings in the cristae to generate the efferent signal. The signal can be either excitatory or inhibitory, as determined by the directionally sensitive semicircular canal. The processes of each hair cell consist of many stereocilia and one kinocilium. The cilia are aligned so that they react properly to shear the forces applied in a specific orientation. Deflection of the stereocilia toward the kinocilium causes depolarization or excitation of the hair cell; deflection in the opposite direction causes hyperpolarization or inhibition. Semicircular canals work in pairs that occupy the same plane of motion (push-pull pairs). The horizontal canals are paired; the anterior canal on one side is paired with the posterior canal on the contralateral side. Therefore, when one canal is stimulated by a given head rotation, its paired partner on the contralateral side is inhibited[5-9].

1.2.1.1 Matching Canals and Muscles

The three canals are approximately aligned with three conjugate muscle pairs (Figure 1-1)[5-7]. Excitation of the anterior canal results in contraction of the ipsilateral superior rectus (SR) and contralateral inferior oblique (IO) muscles, and relaxation of the ipsilateral inferior rectus (IR) and contralateral superior oblique (SO) muscles, resulting in an upward torsional eye movement. Excitation of the posterior canal results in contraction of the ipsilateral superior oblique (SO) and contralateral inferior rectus (IR) muscles and relaxation of the ipsilateral inferior oblique (IO) and contralateral superior rectus (SR) muscles. This results in a downward torsional eye movement. Excitation of the lateral canal results in contraction of the ipsilateral medial rectus (MR) and contralateral lateral rectus (LR) muscles and

relaxation of the contralateral medial rectus (MR) and ipsilateral lateral rectus (LR) muscles. This results in a horizontal eye movement towards the opposite ear.

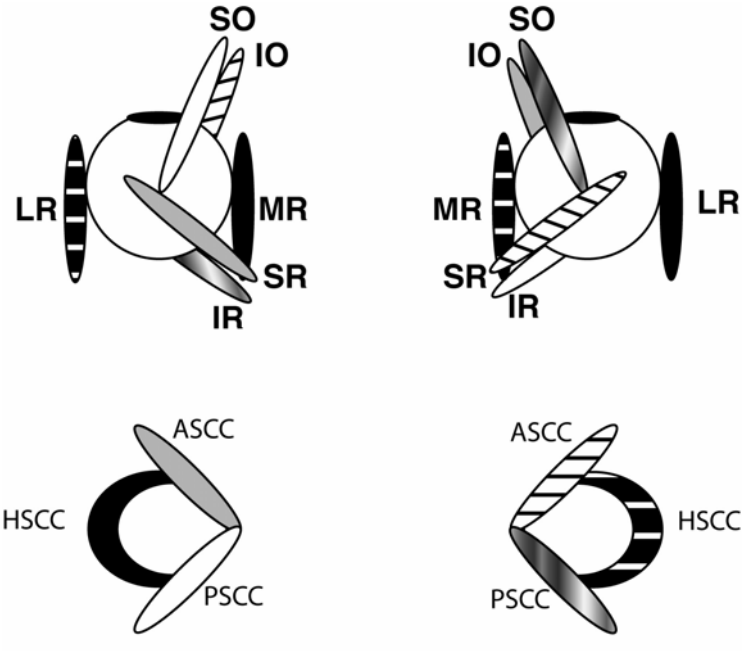

Figure 1-1: Matching canals and muscles. HSCC: Horizontal semicircular canal, ASCC: Anterior semicircular canal, PSCC: Posterior semicircular canal, SO: Superior Oblique, IO: Inferior Oblique, SR: Superior Rectus, IR: Inferior Rectus, LR: Lateral Rectus.
Modified from http://www.med.uwo.ca/physiology/courses/listingweb/matching.htm

1.3 Neural Pathway of Horizontal VOR

There are two neural pathways for VOR, a direct path and an indirect path. During head rotation, there is a phasic afferent response from the vestibular system, which sends a signal to the extra ocular muscles (EOM) to rotate the eyes in an equal but opposite direction

of the head motion. The inhibitory and excitatory signals from appropriate push-pull pairs are sent to the ipsilateral vestibular nucleus (VN) via the VIII nerve. The VN then sends the appropriate eye velocity signal to the oculomotor nuclei (III), trochlear nucleus (IV), and abducens nuclei (VI). Efferent signals from these nuclei then result in contraction and relaxation of the appropriate ocular muscles (Figure 1-2)[5-7].

But, the direct path by itself is not enough. The VOR converts the velocity signal provided by the semicircular canals into the position signals required by the ocular motor neurons and the eye muscles. The ocular motor neurons require more than just an eye velocity command to drive the eye in a certain direction and at a specific speed. They also need an eye position command to hold the eye at the new position so the elasticity of the eye does not cause the eye to pull back toward the primary position after the head movement ends. This tonic command originates via the indirect path through the medial vestibular nucleus and the nucleus prepositus hypoglossi (NPH) for horizontal eye movement commands. A neural integrator exists in the system. This central neural integrator (NI) transforms the vestibular afferent signal into the signal required by the ocular motor neurons and eye muscles. The contribution of velocity-to-position conversion is most important in the 0.1-1 Hz frequency range[6;7;10-12].

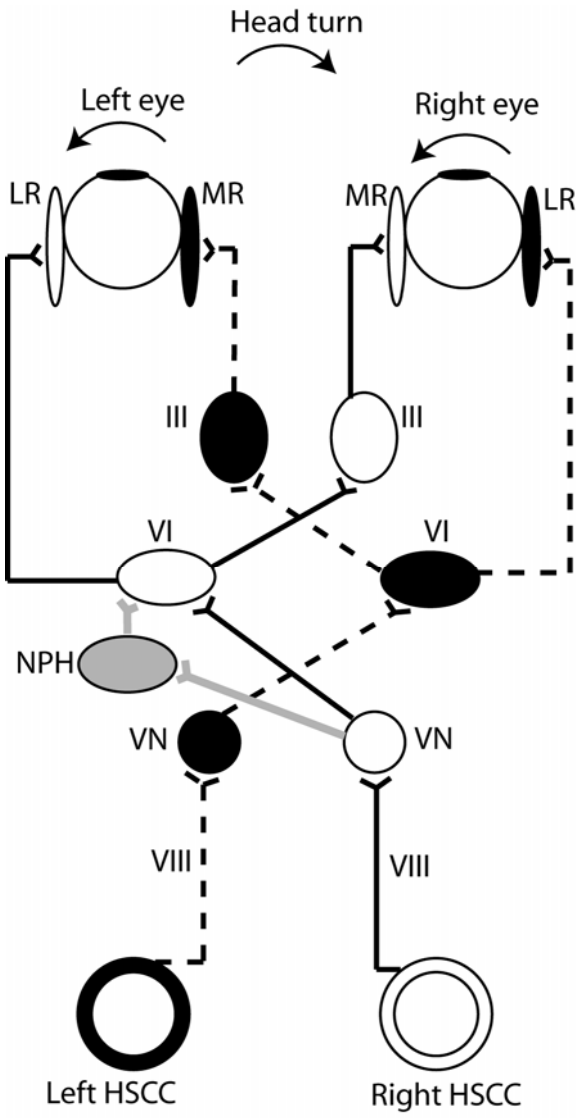

Figure 1-2: Schema of direct and indirect horizontal VOR pathway when the head turns to the right. Solid line and open symbol: Excitatory signal and neuron; Dashed line and filled symbol: Inhibitory signal and neuron; Grey line: Indirect path.
Based on references[5;6]

1.4 VOR Gain

One metric of VOR performance is its gain. The gain is given by the ratio of eye rotation amplitude to head rotation amplitude[5]. It can also be calculated from peak slow-

phase eye velocity divided by peak head velocity. Ideal VOR gain is unity[5;6]. Severe deficits in VOR gain can result in oscillopsia, perceptually noticeable instability of vision, as well as vertigo and imbalance[13;14]. Therefore, laboratory evaluation of the VOR is important in the diagnosis of the patients with dizziness, ataxia, oscillopsia, nystagmus and vertigo.

Research has shown that the VOR acts similar to a band-pass filter. At very low frequency head movements, approximately 0.05 Hz or lower, VOR gain is low[15-17]. At head movement frequencies, between 0.5-5 Hz, the VOR is more responsive. VOR gain reaches its maximum value of unity at about 1 Hz, remains stable until the high frequency limit (5 Hz) is reached. This is the frequency range of every day activity and it seems sensible that the VOR would operate well at these frequencies[5;6;18;19]. However, in a recent study[20] it was shown that in monkeys, VOR gain was close to unity for frequencies ≤20Hz and increased as a function of frequency up to 50Hz.

1.4.1 VOR gain in Light and Dark

VOR gain measurements that take place in complete darkness allow for isolation of the vestibular system. However, VOR gain is affected by the visual environment. If the rotation is in the light, there is an interaction of vestibular and visual compensatory reflexes called visual-vestibular interaction (VVI). The combined action of the VOR and VVI produces the visual-vestibulo-ocular reflex (VVOR)[21]. VVOR measures the VOR in a lit environment and includes the influence of optokinetic stimulation and fixation. Therefore, the central nervous system computes head velocity based on vestibular and retinal inputs (in the light). The result is that VOR gain is greater in the light than in the dark[22-28].

1.4.2 VOR Gain in Active and Passive Head Movements

VOR gain is also affected by the type of head movement. Passive head movements are externally imposed head rotations[29]. Walking, running, whole-body rotation (e.g., on merry-go-round) are some examples of passive head movements in real life. Self generated or voluntary head movements used to stabilize or redirect the visual axis of gaze are in the category of active head movements, for example, shaking the head, as in signifying "yes" or "no". Basically, health, occupation and culture might determine which kind of head movement is more relevant to each individual's every day life.

In the vestibular system, the distinction between sensory events that are related to active head movements and passive head movements are important for perception of spatial orientation and for postural control. Sensory signals are processed in different ways during active and passive head movements. Therefore, VOR function is different during these two kinds of head movements[30]. VOR gain during active head rotation is higher than VOR gain during passive whole-body rotation in normal subjects[24-26;31]. Collewijn et. al. demonstrated that during passive head movements in the dark, the VOR gain is about 13% lower than during active head movements[22].

Higher VOR gain during active head movements can be attributed to several mechanisms. Neck and vestibular velocity signals are summed in the vestibular nuclei. Therefore, the response of ocular motor nerve fibers to vestibular stimulation is modulated by the stimulation of neck proprioceptors during active head movements. This is referred to as the cervico-ocular reflex (COR)[32-34]. During passive whole-body rotation, the rotational axis is more head-centred. But during active head movement, the rotational axis of the head is displaced backward toward the vertebral column. The radius of rotation is larger and the

VOR gain increases[35;36]. It is also believed that an efferent copy of head motor commands during active head rotation contributes to the higher gain[29;37;38]. Therefore, semicircular canal vestibular signals are modified by efferent copy and/or proprioceptive signals related to active head movements resulting in higher VOR gain.

1.4.3 Horizontal & Vertical VOR Gain

It has been shown that the compensatory eye movements are better for horizontal than for vertical head movements[5]. Several studies have demonstrated that horizontal VOR gains during-active head rotation in darkness are close to unity, whereas vertical VOR gains in darkness are approximately 0.9 in normal subjects. During passive whole-body rotation, horizontal VOR gains are less than unity, with typical gains ranging from 0.7 at 0.5 Hz to 0.95 at 1Hz and vertical VOR gains are lower[24;25;27;29;39;40].

1.4.4 Fixation Distance and VOR Gain

VOR gain varies as a function of the distance of the seen object. It is greater for head movements with near viewing distances compared with far viewing distance. Several studies have shown that for near targets, the VOR gain increase is inversely proportional to the target distance during body translation or rotation about a vertical axis. This is because the eye rotation axis is located in front of the head rotation axis, and therefore changes in eye position must be larger than changes in head position for a perfect compensatory response at nearer distances[6;35;41-43].

During active head movements, mental set and motor efferent copy play a large role in VOR responses [37;44]. VOR gain can be enhanced by imagining an earth-fixed visual target. Based on this logic, Clement et. al.[45] showed that VOR is affected by how far away a target is perceived to be by the subject. They found that changes in gain with viewing distance are more closely related to perceived target distance than to actual target distance or fixation distance (as derived from vergence measurements). Their results suggested that the VOR gain can be modulated according to the subject's conscious choice of intended visual goal based on target distance estimates.

1.4.5 Difference Between the VOR Gains of the Two Eyes

Several experiments have compared the gain of the ipsilateral with the gain of the contralateral eye in normal subjects. The eye on the side to which the head is rotating is considered the ipsilateral eye. It is hypothesized that the differences in gain between the two eyes could result from the difference in the distance of the two individual eyes to the target as a function of head position[46]. In this regard, to interpret the inter-ocular gain difference, the initial head position has to be known. Therefore, if the initial head position is to the left of the middle and the head starts rotating toward the right, the ipsilateral eye, which is the right eye, should have a higher initial VOR gain, since it is closer to the target than the left eye. For near targets, the mean ipsilateral gain is significantly higher than the contralateral gain. However, the difference in gain between the two eyes disappears with far targets and in darkness[35;42;46].

1.5 VOR Phase

The temporal difference between head velocity and eye velocity is described by phase. The phase shift is expressed in degrees. If the reflex eye movement leads the head movement, a phase lead is present. Likewise, if the compensatory eye movement trails the head movement, a phase lag is present. By convention, the phase that perfectly compensates for head rotations is assigned a value of 0°, despite the fact that it is really 180°. For head rotation frequencies between 0.5 to 5.0 cycles/sec which correspond to most natural head rotations, the phase shift is close to zero[6;25]. At low frequencies, there is a small phase lead, approximately 6° to 8°, which changes to a small phase lag of about the same magnitude at higher frequencies[18;47]. These findings reflect the inability of the VOR to compensate for high and low frequency head rotations.

1.6 VOR Latency

Latency is the time required for the eyes to initiate a response to the motion of the head. Vestibular eye movements are generated with shorter latencies than visually mediated eye movements. Visually mediated eye movements have latencies >70 msec, compared with ~13 msec for angular VOR[6]. The reason for this is that the elaboration of visual motion signals requires more processing than the VOR. The labyrinth's sensors can detect the motion of the head much sooner than the visual system can detect motion of images on the retina[6;35;46]. Collewijn & Smeets report VOR latencies of 8-9 ms[46], while Crane & Demer find 7-10 ms[43], Johnston & Sharpe find 4-13 ms[48], and Tabak & Collewijn find 8-9 ms[49]. In summary, the range of VOR latencies in humans is 3-13 ms[43;46;48;49].

1.6.1 VOR Latency in Contra-lateral and Ipsilateral Eye

Statistical analysis has shown a significant difference in VOR latency between the eyes. Relative to the direction of head rotation, the contralateral eye has a shorter delay and is ~1 ms faster than the ipsilateral eye[46]. This is in agreement with the disynaptic pathway for the abducting eye and a trisynaptic pathway for the adducting eye (Figure 1-2). Therefore, the latency corresponds to a difference of one synaptic delay between the pathways to the lateral rectus muscle of the contralateral eye and the medial rectus muscle of the ipsilateral eye[6].

1.7 VOR Adaptation

The VOR is a fast open-loop system. In other words, the receptors in the inner ear that provide the input of the reflex receive no information about eye movements, the output of the reflex. Thus, there is no direct feedback to the ears to tell them if the eyes are moving correctly[50].

In order to achieve clear, stable, single vision, VOR must be accurate. Persistent slip of the retinal image during head movements not only signals the need for recalibration of the VOR, but also specifies if an increase or decrease is needed in VOR gain. Therefore, the brain constantly monitors its performance, and in response to any kind of retinal slip adjusts accordingly[6;13;51;52]. This adaptation process is called motor learning. Both visual and vestibular inputs are necessary for motor learning. The VOR does not recalibrate during head turns in the dark or during retinal image motion with the head stationary[7]. When a visual-vestibular mismatch occurs during head movements, the VOR is under adaptive control to correct its performance. This mismatch could be internally generated, due to the

effects of age, disease, or trauma on the vestibular apparatus, circuitry, and/or eye muscles. Alternatively, the mismatch could be externally created by changing the relative movement of the visual scene in response to head movements, such as would occur when putting on prescription eyeglasses or image magnification. Regardless of how the mismatch occurs, the VOR is capable of making adaptive changes to its gain and phase to correct for differences and to re-stabilize the image. Retinal slip provides a neural signal that is used to modify the VOR output and recalibrates the VOR performance by parametrically adjusting VOR gain and/or phase. Once adaptation is complete, clear vision is restored, for either the short term or the long term[7;19;23;51;53-55].

The current belief is that adaptation can be non-conjugate (monocular) or conjugate. Conjugate adaptation of the human VOR has been investigated using different methods. It was demonstrated in humans by having them wear reversing prisms[56-58]. VOR gains were substantially reduced and the phase of the VOR reversed; head rotation caused eye rotations in the same direction, so the retinal images were once again stabilized. Gonshor and Jones[56] demonstrated that wearing reversing prism for many days could reduce VOR gain by 75%, while Jones et. al.[57] found that 6 hours of wearing reversing prisms decreased VOR gain by 66%.

One common clinical response of VOR to optically induced changes in vision is adaptation to habitual wearing of corrective spectacles. In addition to their linear magnification, spectacle lenses have a prismatic effect, which causes the VOR gain to vary systematically with each diopter of correction. With negative spectacles, perfect fixation requires a smaller eye rotation than head rotation. Positive spectacles have the opposite effect. Thus, in individuals who wear high positive lenses, eye rotations will need to be

larger to hold gaze steady during head rotation. The same applies to myopia except that eye rotations must be smaller than without glasses. Therefore, myopes who are corrected by spectacles tended to have lower gains and hyperopes have higher gains. Adaptive increases in gain were demonstrated in subjects wearing telescope lenses as well. Fifteen minutes of adaptation to telescopic spectacles, exhibited a 7-46% VOR gain increase, while wearing them for several days, showed a 70% increase in VOR gain[13;21;23;59;60].

It had been presumed that, because of the conjugate neural connection and linking between the two eyes, only conjugate adaptation was possible. It has been argued that asymmetrical vergence do not necessarily violate Hering's law[61]. If this law was interpreted as the two eyes' movements being equally large, then adaptive nonconjugacies would violate Hering's law of equal innervation. However, Hering's observation was that eye movements are so coordinated that the two eyes are always aimed at the same object. Thus, nonconjugate adaptation actually contributes to this coordination, instead of violating it[62-66].

Non-conjugate adaptive changes in the VOR occur in response to different visual stimuli between two eyes. It is expressed as differences in magnitude between the movements of the two eyes, which adequately match the differences in image-size. Retinal slip differences in the two eyes are the stimuli that drive monocular adaptation. Non-conjugate ocular motor adaptation is believed to be an adjustment of the relative innervation to the two eyes to ensure optimal binocular visual-ocular motor performance[24;64;67;68].

1.7.1 Neural Design of Adaptive Control of VOR

VOR gain is adapted until retinal stability is restored. In the light, retinal slip provides an error signal, which recalibrates the brain. Visually driven eye movement controls have

priority over vestibular commands, causing the eyes to fixate or follow a visual target accurately in the light[69;70]. If a visual–vestibular mismatch continues, then learning is influenced and the VOR gain changes[6;71]. To evaluate this new reflex gain, the VOR is tested in the dark.

It is still not clear which part of the brain is specifically responsible for VOR adaptation. In this regard, the focus of the research is on three possibilities, each of which has its advocates. Firstly, the cerebellar flocculus has been considered to play a crucial role in VOR adaptation[6;69;71-74]. Secondly, The brainstem is considered exclusively responsible[50;75]. Finally, the hypothesis which is presently most accepted, suggests roles for both the flocculus and brainstem[70;76-78].

1.7.2 Non-Conjugate Adaptation

Non-conjugate adaptive changes in the VOR occur in response to different visual stimuli between two eyes[24]. There are some conditions which require asymmetrical adaptation in order to maintain binocular fixation. Neuromuscular asymmetry, such as paresis of some of the muscles of one eye[63;79], unilateral peripheral ocular motor palsies, such as III, IV, VI nerve palsies[24;26;80;81], amblyopia[82;83], unilateral eye patching[84] are some examples of conditions in which non-conjugate adaptation has been investigated in humans and animals. Monocular adaptation of VOR was observed after surgically weakening one or two horizontal recti in one eye of a monkey. One day after surgery, during patching of the affected eye, VOR gain showed a decrease in the affected eye without loss of function in the normal eye[63;79]. In human subjects with unilateral peripheral sixth nerve palsy, VOR gain in the paretic eye showed a decrease during abduction and adduction[24]. In unilateral fourth

nerve palsy, VOR gains were reduced during incyclotorsion, depression and abduction of the paretic eye, as anticipated from paresis of the superior oblique muscle. VOR gains during excyclotorsion, elevation and adduction of the paretic eye were also reduced[26]. In third nerve palsy, VOR gains of the paretic eye decreased during abduction, adduction, elevation, depression, excyclotorsion and incyclotorsion[80]. In all these studies VOR gains were normal in the non-paretic eye. In another study[84], one week of patching of one eye in monkeys created a decrease in VOR gain in that eye, which returned to baseline within 24 hours of removing the patch. The gain remained unaffected in the other eye.

The effect of anisometropic spectacles on monocular VOR adaptation has been evaluated less. Because of the prismatic effect of the corrective lenses away from their optical centers, retinal disparity occurs for targets when the head moves[85]. Asymmetrical saccadic adaptation in response to long-term and short-term wearing of anisometropic corrective spectacles has been demonstrated[62;64;66;67]. As such, monocular adaptation of VOR should also be possible with spectacles. Collewijn et. al.[22] magnified one eye and minified the other eye for 24 hours, using convex and concave spectacle lenses (10 D anisometropia by spectacle). Their method created considerable blurring of the target, which may explain their finding that monocular VOR adaptation did not occur.

2 RATIONALE, PURPOSE AND HYPOTHESIS

It is known that VOR adapts conjugately[13;21;23;57-59]. It is also known that VOR adapts non-conjugately to unilateral peripheral ocular motor palsies, such as III, IV, VI nerve palsies[24;26;80;81], paresis of some of the muscles of one eye[63;79], discrepancies between visual and vestibular stimulation, such as investigated in amblyopia[82;83]. Moreover, it is known that saccades adapt non-conjugately to anisometropic spectacles[62;64].

Review of the VOR literature shows that adequate experiments have not been done on optically induced monocular adaptation of VOR in humans. If non-conjugate VOR adaptation is possible in response to other stimuli, it should also be possible with spectacles. One study[22] did not find monocular adaptation to anisometropic spectacles, but their method left the subjects without clear vision. The purpose of this study is to test whether horizontal angular VOR is capable of monocular adaptation in normal human adults as a result of induced anisometropia (without the confound of blur). We hypothesize that humans are capable of monocular adaptation of the VOR to induced anisometropia. The VOR gain, after monocular adaptation, is expected to show an increase in one eye and a decrease in the other eye.

2.1 Significance

Anisometropic spectacles may cause different prismatic effects, aniseikonia, suppression, diplopia or poor stereopsis due to the dioptric difference between the two eyes. Because of this, some wearers may experience some distortion and discomfort. With adaptation these symptoms are reduced[6]. The VOR is one system that needs to adapt. Generally, the compensatory changes in the VOR system to optical manipulations of the visual inputs are in the appropriate direction to enhance image stabilization.

This study will contribute to our understanding of VOR recalibration in response to visual-vestibular mismatches to anisometropic spectacles. It has the potential to influence clinical practice with regard to spectacle adaptation. Potentially, asymmetric VOR adaptation in response to anisometropic spectacles should be accounted for when interpreting the results of vestibular function tests.

3 METHODS

3.1 Participants

Nineteen participants between 19 and 45 years (11 female, 8 male) took part in this experiment. None had vestibular defects, neck motility problems, amblyopia, strabismus or any known binocular vision anomaly that could disrupt binocular viewing. All had best corrected vision of 6/6 (20/20) in both eyes and 40 sec of arc or better stereo acuity as tested by Randot Stereo Test (Table 3-1). For all the subjects except two of them, the right eye was the dominant eye as determined by self report based on their previous eye examination in the clinic, or by a push-up method done by the examiner.

Participants were recruited from the graduate student and summer research assistant population within the University of Waterloo. Each subject was required to attend one session, which took approximately 7 hours. Approval for the study was obtained from the Office of Research Ethics at the University of Waterloo. Informed consent was obtained from all the participants. An honorarium was paid to participants for their time.

3.2 Description of Contact Lenses and Spectacle Combination

During adaptation, the subjects were asked to wear a magnifier in one eye and a minifier in the other. This was achieved, without blurring of the image or substantially reducing the visual field, by using a combination of soft contact lenses and spectacles[64;86;87]. The desired magnification or minimization would be obtained with convex and concave spectacle lenses. To allow for a comparison between horizontal and vertical adaptations, spherical lenses were used to provide equal magnification and minimization factors in all meridians.

The defocus and blurring, created by the spectacle lenses, was neutralized with the contact lenses. I used one-day 13.8mm diameter contact lenses (Focus Dailies®, CIBA Vision) in my experiment. A contact lens does not cause any changes in the size of eye movements, because it moves with the eye. Under these circumstances, not only would the VOR of the two eyes be required to adapt differently, but they would be required to adapt in the opposite direction as well.

3.2.1 Power of the Contact Lenses and Spectacles

The power of the spectacles, which were used for all subjects, was +5.00 dioptres in front of the right eye and –5.00 dioptres for the left eye. The power of the contact lenses was equal to the subjects' habitual correction, summed with the power necessary to compensate for the spectacle lenses. Consideration was given to the fact that changing the position of a

correcting refractive lens changes its dioptric power. It is known that a lens of power P will require a modified power of

$$\frac{P}{1 - dP}$$

if it moves the distance d (meters) toward the cornea (i.e., spectacle lens vs. contact lens)[88;89]. For those subjects whose refractive errors were less than 5 dioptres, there was no significant difference in the effective power, in the contact lens and spectacle plane and therefore, no adjustment was made (Table 3-1).

Subject	Rx (OD)	Rx (OS)	LENS (OD)	LENS (OS)	SA
1	-1.50	-1.75	-6.5	+3.25	35 sec/arc
2	-1.75	-1.75	-6.24	+3.25	35 sec/arc
3	plano	plano	-5.00	+5.00	25 sec/arc
4	plano	plano	-5.00	+5.00	20 sec/arc
5	-2.50	-2.75-0.50x175	-6.88	+2.00	20 sec/arc
6	-1.50-0.50x175	-1.50-0.50x155	-6.24	+3.25	40 sec/arc
7	-3.75	-3.75	-8.12	+1.25	25 sec/arc
8	plano	plano	-5.00	+5.00	20 sec/arc
9	-3.75	-3.75	-8.12	+1.25	20 sec/arc
10	plano	plano	-5.00	+5.00	20 sec/arc
11	-6.00	-6.00	-9.71	-1.00	20 sec/arc
12	plano	plano	-5.00	+5.00	20 sec/arc
13	-2.00-0.50x75	-1.75-1.00x87	-6.88	+2.75	20 sec/arc
14	-5.50	-5.50	-9.32	-0.50	35 sec/arc
15	-2.50-0.50x5	-1.50-0.50x5	-6.88	+3.25	20 sec/arc
16	plano	plano	-5.00	+5.00	20 sec/arc
17	plano	plano	-5.00	+5.00	20 sec/arc
18	-2.75	-2.50	-6.88	+2.50	20 sec/arc
19	plano	plano	-5.00	+5.00	20 sec/arc

Table 3-1: Rx (OD) = Right eye prescription, Rx (OS) = Left eye prescription, Lens (OD) = Right eye lens power, Lens (OS) = left eye lens power, SA= Stereo Acuity, 20 sec/arc = limit of test.

3.2.2 Base Curve and Central Thickness of the Spectacle

The central thickness of the spectacle we used in my experiment was 4.8 mm for the right lens and 2.4 mm for the left lens. The right lens's base curve was +8.25D and the left lens's was +3.25D. The spectacle magnification was calculated by[88]:

$$M = \left(\frac{1}{1 - KV}\right)\left(\frac{1}{1 - \left(\frac{d}{n}\right) F_1}\right)$$

It shows that the magnification depends upon the power factor $(\frac{1}{1-KV})$ and the shape factor $(\frac{1}{1-(\frac{d}{n})F_1})$;

K= the vertex distance in meters; V= the back vertex power in dioptres; d= the centre thickness in meters; n= the index; F_1= the power of the front surface. Therefore, for the right lens the magnification was 1.09 and for left lens was 0.94. This means that the right lens magnified images by almost 9% and the left lens minified them by almost 6%.

3.2.3 Aniseikonia Created by the Contact lenses/spectacles Combination

Immediately upon wearing the contact lenses and spectacles combination, *The Aniseikonia Inspector 1.1 (Richmond Products p/n 4544)* software was used to measure the induced perceptual aniseikonia. Although chromatic stimuli are used which have chromatic aberration, this software has been shown to be a useful tool in measuring aniseikonia in patients[90]. The test is based on a direct comparison method[91]. The two eyes are offered a different image by means of color.

The subject sat in a dimly lit room, approximately 1 m away from the computer screen, looking through red/green glasses. Presented on the computer screen were red and green targets which the subject adjusted in size until he/she perceived the target sizes as equal.

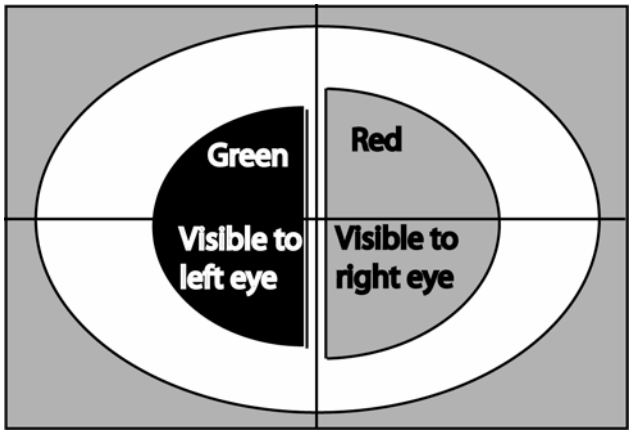

Figure 3-1: The direct comparison test of the Aniseikonia Inspector. Two size-adjustable half circles, red and green, color optimized by the software for viewing through red-green goggles.
Adapted from "The Aniseikonia Inspector 1.1 Manual"

3.3 ELMAR Eye Tracker and Head Tracker: Model 2020 - Binocular System

A combined head-eye-tracking device was used in my experiment for collecting eye and head movement data. The Elmar Eye Tracker, Model 2020 is a video based eye-tracking system. The optical components of the eye-tracking system are mounted on a lightweight headset and goggles (~200 g). Corneal reflections and center of the pupil are generated for each eye by illumination with four infrared light emitting diodes (LED). Two angled and transparent "hot-mirrors" are mounted on each side of the goggles frame, below the subject's line of sight (Figure 3-2). Reflections from these mirrors are captured by two cameras on the headset. Images from the cameras are processed in real time to obtain estimates of the corneal reflection and pupil centre locations. The information from the video generated from the cameras is digitized and converted to eye position (deg) as a function of time. The relative distance between the corneal reflections and the centre of the pupil is used to calculate eye position in degrees[92] (Figure 3-3). With translation of the

eyeball, both the corneal reflections and the pupil centre move by the same amount, thus the relative distance between them is independent of horizontal and vertical translation and lateral translation artifacts are eliminated[93;94].

The system records eye position in a linear range of approximately ±40 degrees horizontally and ±30 degrees vertically with a resolution of ±0.1 deg. The eye tracking system permits a field of view of 60° horizontally and vertically while the eyes are in primary position[95;96]. Images are sampled at 120 Hz, thus providing eye position signals every 8.33 msec. This instrument is non-invasive, and generally well tolerated by the majority of participants.

The eye tracking system is linked to a head tracker 'Flock of Birds®, Real Time Motion Tracking' (Ascension Technology Corporation) including a magnetic transmitter and receiver (Figure 3-1). The small and lightweight receiver is mounted to the eye-tracker headset, on top of the head, close to the centre of head rotation. A transmitting device radiates a magnetic field in which the head-mounted receiver is sensed and processed to provide position information about head movements. The transmitter is placed perpendicular to the display screen, above and behind the receiver, during the test. To minimize the noise during data collection, nearby metal objects and magnetic fields were removed, and the subjects were positioned such that their head was within 24cm of the transmitter[95].

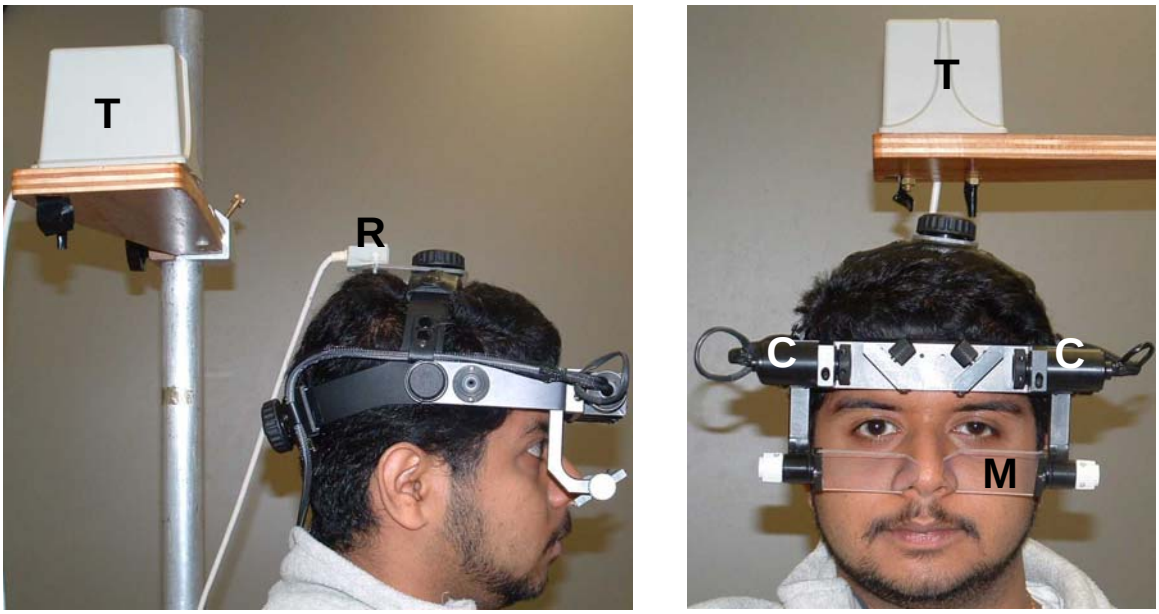

Figure 3-2: ELMAR eye tracker and Flock of Birds Head Tracker system; T: Transmitter, R: Receiver, C: Cameras, M; Hot-Mirror

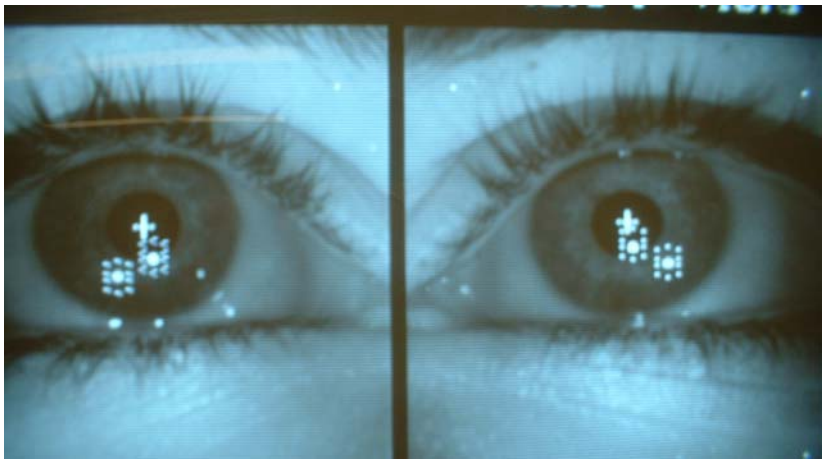

Figure 3-3: Pupillary marker (cross) and corneal reflections (square frame)

3.3.1 Evaluation of the Combined Head-Eye Tracking

There is a time delay between the signals received from eye and head trackers. Despite synchronization of eye and head trackers, there remains a fixed delay between the samples of data. For proper comparison of eye and head data, this delay should be known and compensated for[95].

The eye-head delay was measured during active head rotation in a lit room while fixating on a stationary target, and when VOR phase shift was close to zero. A delay estimate was made, at the highest power spectral elements of eye and head movements, in the frequency domain. A positive sign (+) indicates that the eye data was delayed compared with the head data and a negative sign (-) indicates that eye data led the head data. With our eye and head tracker, the eye led the head by -0.009 ± 0.004 s (mean ± 95% confidence interval) (Appendix 7-1). The average expected delay between the eye and head (physiological delay), with a stationary target is 0.0085s[46;48]. The expected delay was subtracted from the measured delay. The calculated delay, after this procedure, was -17.5 ± 4 ms, which means the head data was delayed by 1.5 to 2.5 samples relative to the eye data due to post processing of the head tracker data. This range of 1.5 to 2.5 samples is due to physiological variability and not a lack of instrumental synchronization.

Therefore, the expected head to eye delay for my equipment was calculated to be 2 samples, and incorporated into the instrument's set up prior to data collection. My calculated delay was similar to the delay found by DiScenna et. al. in their study[96].

3.3.2 Set-up and Calibration

The subject was seated in a chair facing the display screen, wearing the headset, with her/his head held still. The display screen (height: 111cm, width: 153cm) was aligned so that the subject's midline corresponded to the centre of screen and the eyes were aligned with the centre of the display. Prior to calibration, a set-up procedure was done to adjust the level of the infrared illumination for the corneal reflections and pupil centre[96].

Seven equally spaced calibration points were presented at known visual angles along the horizontal and vertical axes of the eye, between –10° and +10°. The corresponding changes in the distance between the pupillary marker and corneal reflections for every change in fixation were used to calibrate the instrument. The distance from the eye to the screen was carefully measured to ensure the targets would appear at the correct angle (distance: 200cm). During the calibration procedure, movements of the corneal and pupillary images, in pixels were transformed to eye positions in degrees. The calibration procedure minimized any horizontal-vertical crosstalk and undesired signals[96].

3.4 Experimental Set-up

The experiment was performed in a completely dark room, in order to isolate the vestibular system[5;6]. There was no fixation target. Subjects were instructed to fixate on an imagined, stationary visual target located straight ahead while making active horizontal head movements. To assist them with this, a small target was presented at a distance of 2m before each trial began. The target was a white square (1mm/1mm) on a black background.

3.4.1 Baseline Measurement

Following calibration, subjects were instructed to generate horizontal head rotations (approximately sinusoidal) for two one-minute trials, with a short rest between them. A metronome was used to guide subjects' head rotations at a specific frequency (0.833 Hz, 100 beeps per minute). At the beginning of each trial, the subject practiced keeping head movements at an amplitude of approximate 10°-20° for a few minutes (to keep the movements within the range of the recording system) and to become familiar with the task. Occasional reminders to keep fixation steady and to keep the eyes wide open were given to the subjects throughout the experiment.

3.4.2 Adaptation Period (Learning or acquisition phase)

After the baseline measurements were taken, the participants were asked to wear their combination of contact lenses and spectacles for a period of 4 hours. During this adaptation period the participants were asked to do whatever normal activities they felt comfortable doing.

3.4.3 Recovery (Memory retention phase)

Following the 4 hour adaptation period and immediately after removing the contact lens/spectacle combination, eye/head movements measurements were repeated, in exactly the same way as the baseline measurements. Subsequently, eye and head movements were recorded approximately every 30 minutes for 2 hours. This was done to investigate if the

VOR returned to baseline or not. For each trial the calibration was repeated, to allow subjects to move around freely between trials.

3.5 Data Analysis

Raw digital eye (p_e) and head (p_h) position data obtained from the trials, were exported as ASCII files for off-line analysis (Figure 3-4).

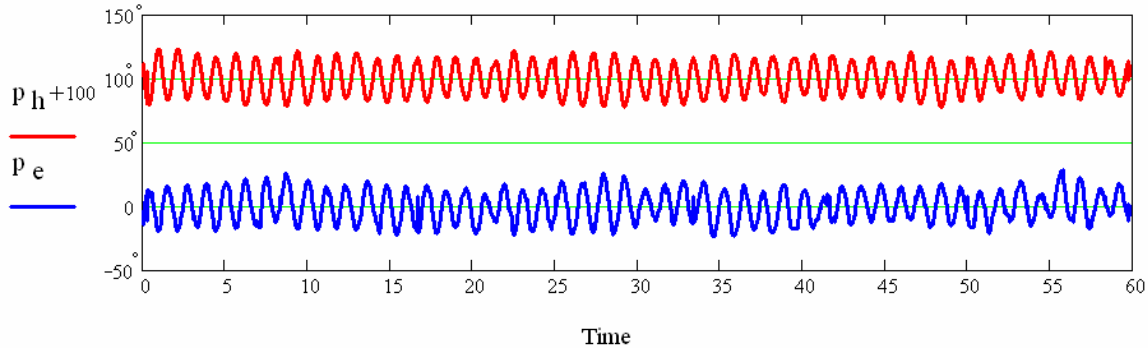

Figure 3-4: An example of eye position data (p_e) and head position data (p_h) of one of the subjects in 60 seconds. To show it better, the eye and head position graphs were purposely separated.

The data were analyzed with programs written in MATHCAD$_{TM}$ 11.1 software. In my experiment, the VOR gain was computed but not the VOR phase. Eye and head position data were transformed from the time domain to the frequency domain (P_e and P_h in frequency domain) by a Complex Fast Fourier Transform (CFFT). There is a dominant frequency for both eye and head signals in the range under 2 Hz. In all other frequencies the signals are only noise (Figure 3-5).

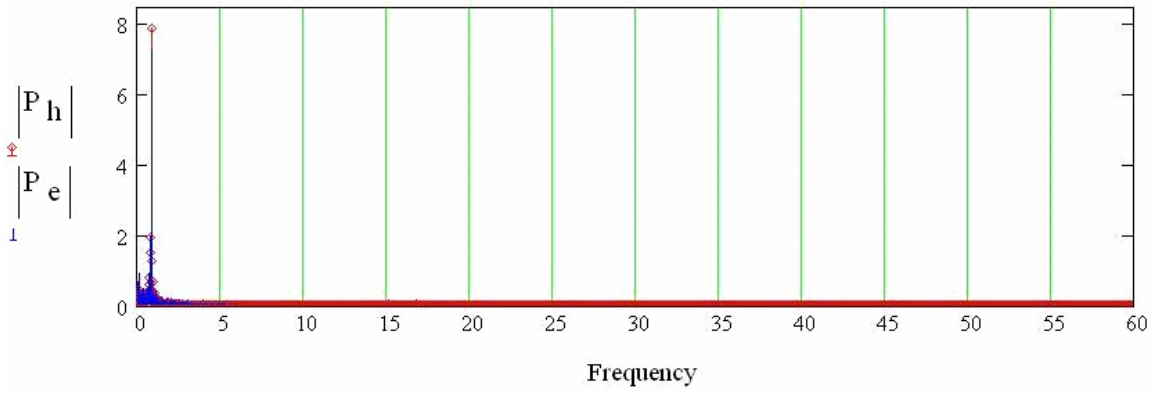

Figure 3-5: Eye (P_e) and head (P_h) position data are transformed from the time domain to the frequency data by a Complex Fast Fourier Transform (CFFT).

The dominant frequency (F_{max}) of eye and head movements was found where there were the largest absolute values of the amplitude of the CFFT of eye ($|P_{e_{max}}|$ and head position ($|P_{h_{max}}|$) data. The dominant frequency was the same for both eye and head signals and was close to the metronome frequency of 0.833 Hz (Figure3-6).

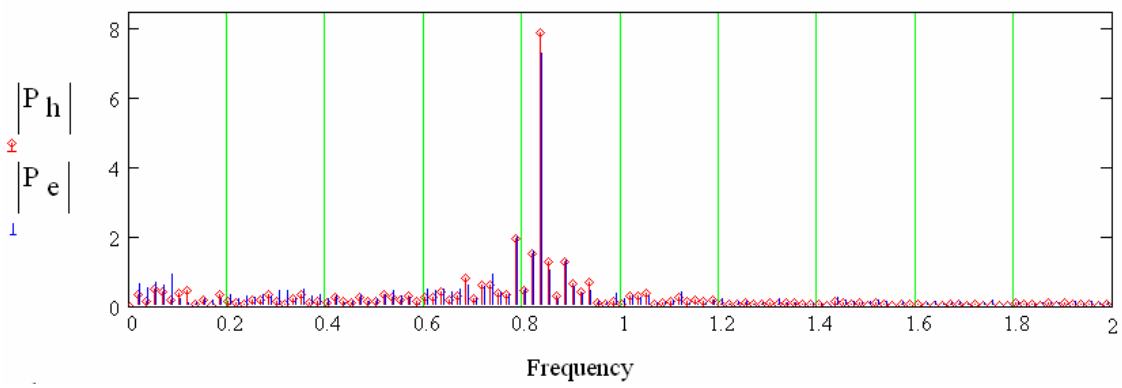

Figure 3-6: The largest absolute values of the amplitude of the CFFT of eye and head position data in dominant frequency.

VOR gain was calculated as the ratio of the absolute value of eye position amplitude to that for the head, in the dominant frequency.

$$Gain = \frac{\left| P_{e_{\max}} \right|}{\left| P_{h_{\max}} \right|}$$

We also divided the head movements into rightward and leftward direction. For each direction, eye and head position data were transformed from the time domain to the frequency domain by CFFT (the direction not being analyzed was set to zero). Gain, as we noted earlier, was calculated separately for each section of rightward and leftward head rotation in the dominant frequency (Figure 3-7, 3-8, 3-9, 3-10).

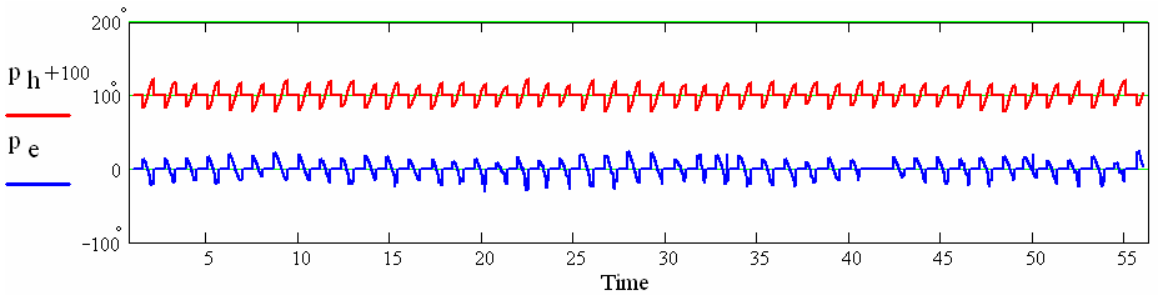

Figure 3-7: Rightward head rotation. Eye and head position data in time domain

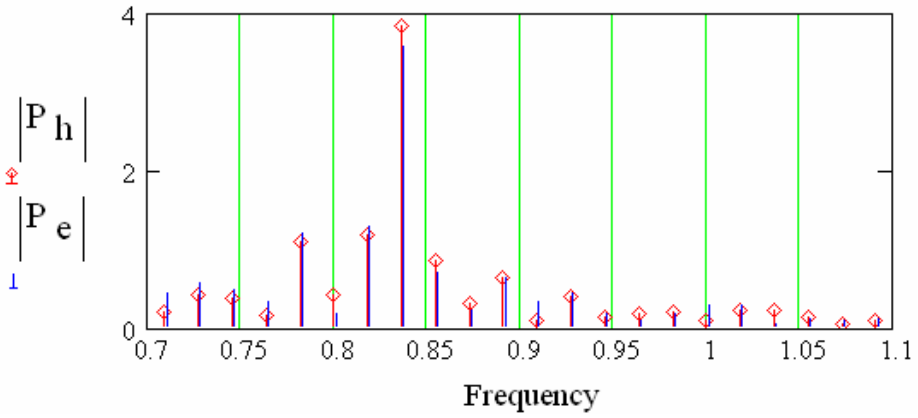

Figure 3-8: Rightward head rotation. Eye and head position data in frequency domain.

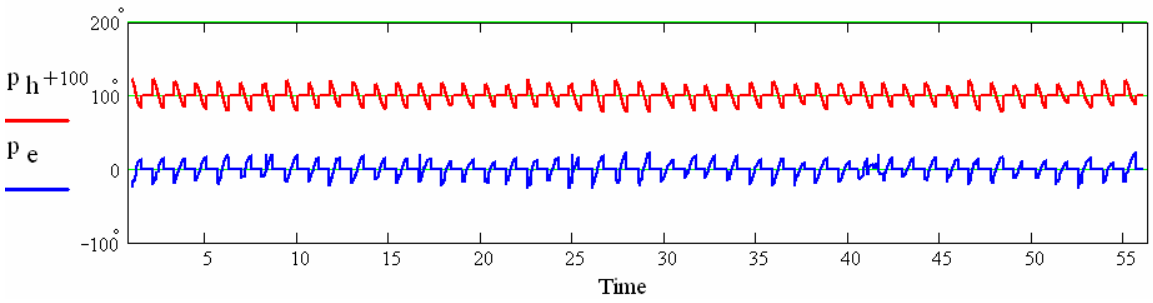

Figure 3-9: leftward head rotation. Eye and head position data in time domain

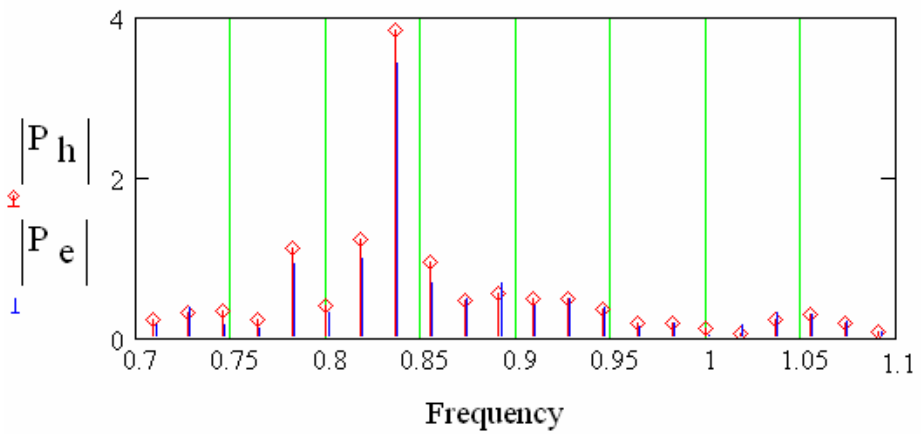

Figure 3-10: leftward head rotation. Eye and head position data in frequency domain.

4 RESULTS

4.1 Symptoms of Wearing the Contact lenses/spectacles Combination

In my study, the average measured aniseikonia with spectacles/contact lenses combination was approximately 15%, ranging from 7.5% to 20%. Almost all of the subjects reported spatial disturbance which they were unable to describe exactly. According to subjects' statements and observation of subjects by the examiner during the adaptation period, some of the subjects learned to turn their head rather than their eyes, so that they looked through the optical centers of the spectacle lenses. This helped them to reduce the spatial disturbance. Otherwise, during the first hour, some of the subjects behaved cautiously, and tended to decrease the frequency of their head movements, which reduced the amount stimuli for adaptation. This effect decreased after a while and behavior appeared more natural, according to the subjects' self report and the examiner's observation.

Twenty one percent of the subjects developed a headache during or after wearing the lens combination. Oscillopsia was not reported. One subject reported nausea, but did not vomit. Almost all of the subjects complained about diplopia at the beginning of wearing the contact lens/spectacle combination. For approximately 30% of the subjects, diplopia remained by the end of adaptation period and for the rest, it was not noticeable. For 70% of the subjects, 4 hours of wearing the combination was acceptable. The rest, who were the ones with persistent diplopia, found the adaptation period tough to tolerate but they completed the experiment.

4.2 Raw Data

A part of the raw data for one of the subjects obtained from EL-MAR eye tracker is shown in table 4-1. LXp represents for horizontal angular left eye position data, RXp represents horizontal angular right eye position data and HXv represents horizontal angular head position data. Eye position data were sampled every 8.33 msec, as the sampling frequency of the eye tracker was 120 Hz, while head position was sampled at 30 Hz. As noted earlier, positive and negative signs show the direction of eye and head movements. Positive was for rightward data and negative for the leftward direction. When the head was rotating toward right, the eyes were rotating in opposite direction, toward the left.

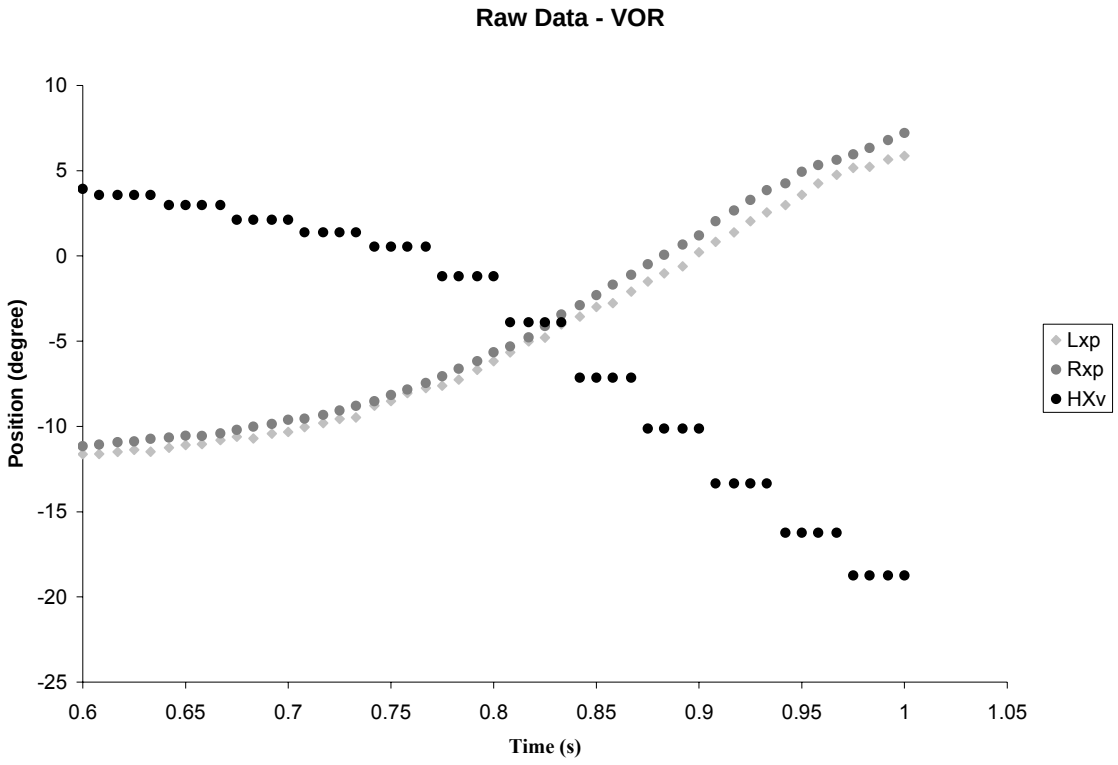

Figure 4-1: Raw data plot, for the right eye, left eye and head position data through the time.

Time	LXp	RXp	HXv
0.600	-11.632	-11.163	3.933
0.608	-11.616	-11.062	3.582
0.617	-11.491	-10.921	3.582
0.625	-11.374	-10.874	3.582
0.633	-11.476	-10.734	3.582
0.642	-11.249	-10.656	2.988
0.650	-11.085	-10.538	2.988
0.658	-11.031	-10.554	2.988
0.667	-10.804	-10.413	2.988
0.675	-10.609	-10.195	2.131
0.683	-10.702	-10.015	2.131
0.692	-10.421	-9.851	2.131
0.700	-10.320	-9.609	2.131
0.708	-10.038	-9.546	1.384
0.717	-9.804	-9.328	1.384
0.725	-9.562	-9.070	1.384
0.733	-9.476	-8.789	1.384
0.742	-8.781	-8.523	0.549
0.750	-8.515	-8.148	0.549
0.758	-8.039	-7.828	0.549
0.767	-7.742	-7.445	0.549
0.775	-7.617	-7.062	-1.187
0.783	-7.257	-6.609	-1.187
0.792	-6.679	-6.171	-1.187
0.800	-6.164	-5.648	-1.187
0.808	-5.648	-5.312	-3.889
0.817	-5.007	-4.773	-3.889
0.825	-4.789	-4.117	-3.889
0.833	-4.015	-3.429	-3.889
0.842	-3.562	-2.890	-7.141
0.850	-2.984	-2.297	-7.141
0.858	-2.765	-1.680	-7.141
0.867	-2.094	-1.109	-7.141
0.875	-1.500	-0.492	-10.129
0.883	-1.023	0.062	-10.129
0.892	-0.609	0.672	-10.129
0.900	0.219	1.203	-10.129
0.908	0.836	2.039	-13.337
0.917	1.383	2.672	-13.337
0.925	2.039	3.281	-13.337
0.933	2.555	3.859	-13.337
0.942	2.992	4.258	-16.238
0.950	3.586	4.929	-16.238
0.958	4.258	5.328	-16.238
0.967	4.758	5.640	-16.238
0.975	5.172	5.961	-18.743
0.983	5.234	6.336	-18.743
0.992	5.664	6.796	-18.743
1.000	5.867	7.218	-18.743

Table 4-1: One of the subject's raw data in the time between 0.6s till 1s.

4.3 Gain Results

4.3.1 Gain: Right Eye vs. Left Eye in Baseline Trial in 2 Directions of Head Rotation

All the results were calculated as the mean ± SD of the gain. Student's paired t-tests were used to examine the statistical significance of changes. The head movements were first divided into rightward and leftward direction. The gain was calculated in each direction for each subject. During the rightward head rotation, the average right eye VOR gain for all of the subjects in the baseline trial was 0.820 ± 0.128 and for the left eye VOR gain was 0.851 ± 0.108. There was no significant difference between the right eye VOR gain and left eye VOR gain for rightward head rotation ($p=0.075$) (Figure 4-2). For leftward head rotation, the average VOR gain for the right eye in the baseline trial was 0.839 ± 0.136 and for the left eye was 0.821 ± 0.144. No significant difference was observed between the right eye and left eye VOR gain for leftward head rotation ($p = 0.124$) (Figure 4-3). Therefore, rightward and leftward head rotation was collapsed for each eye.

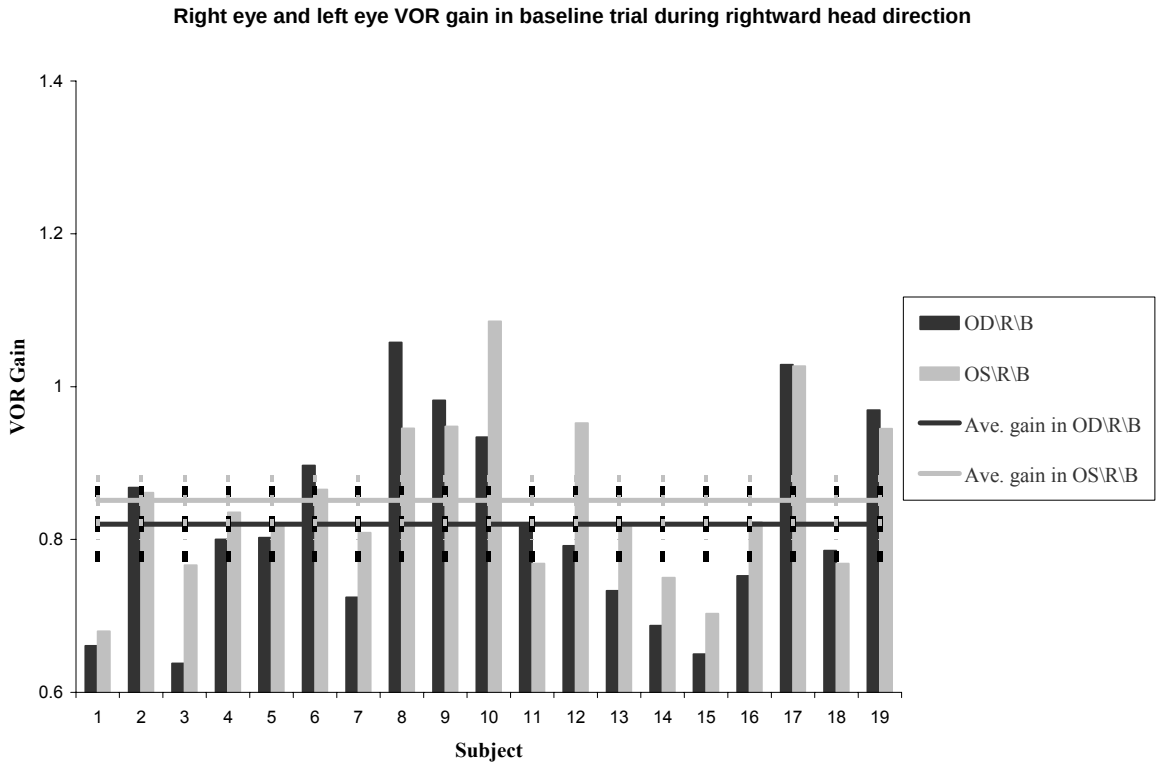

Figure 4-2: Right eye and left eye VOR gain during rightward head direction in baseline trial for each subject. The dashed lines represent 95% confidence intervals. OD\R\B: Right eye VOR gain during rightward head rotation in baseline trial. OS\R\B: Left eye VOR gain during rightward head rotation in baseline trial.

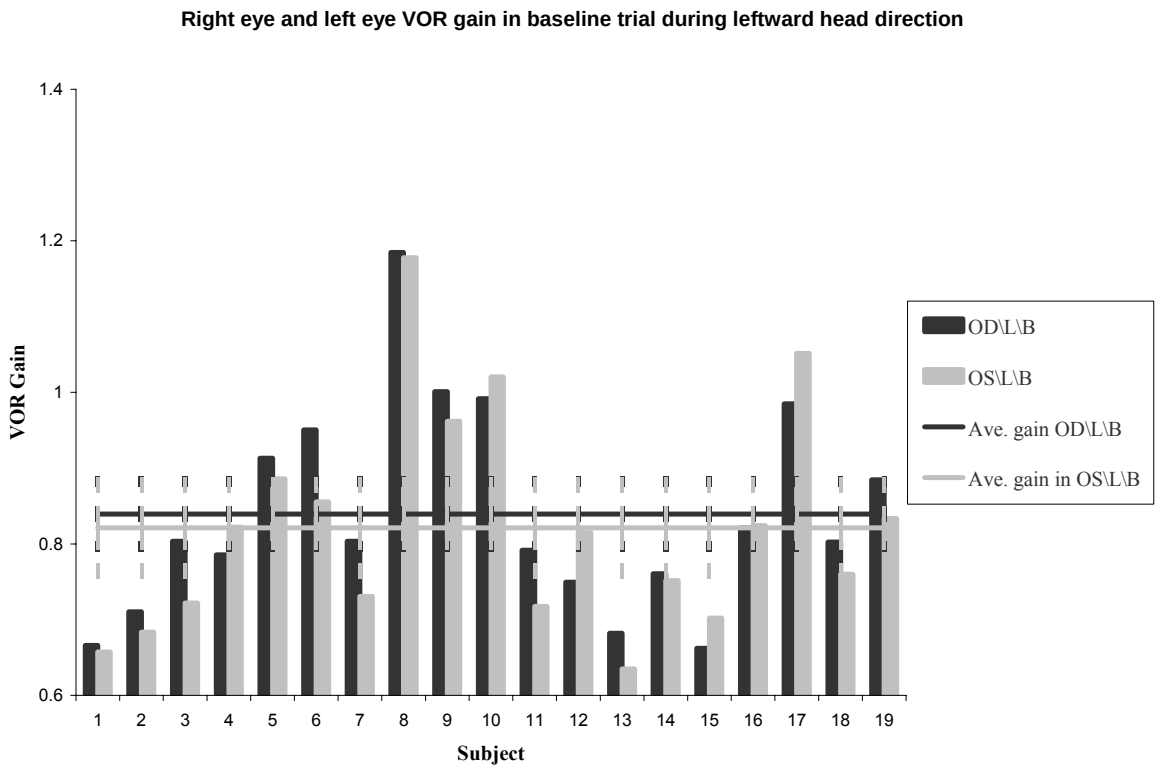

Figure 4-3: Right eye and left eye VOR gain during leftward head direction in baseline trial for each subject. The dashed lines represent 95% confidence intervals. OD\L\B: Right eye VOR gain during leftward head rotation in baseline trial. OS\L\B: Left eye VOR gain during leftward head rotation in baseline trial.

4.3.2 Gain: Right Eye vs. Left Eye in Baseline Trial

In the baseline trial, the average VOR gain in all of the subjects for the right eye and left eye was 0.831 ± 0.126 and 0.840 ± 0.117 respectively. There was no significant difference between the right eye VOR gain and left eye VOR gain (p= 0.38).

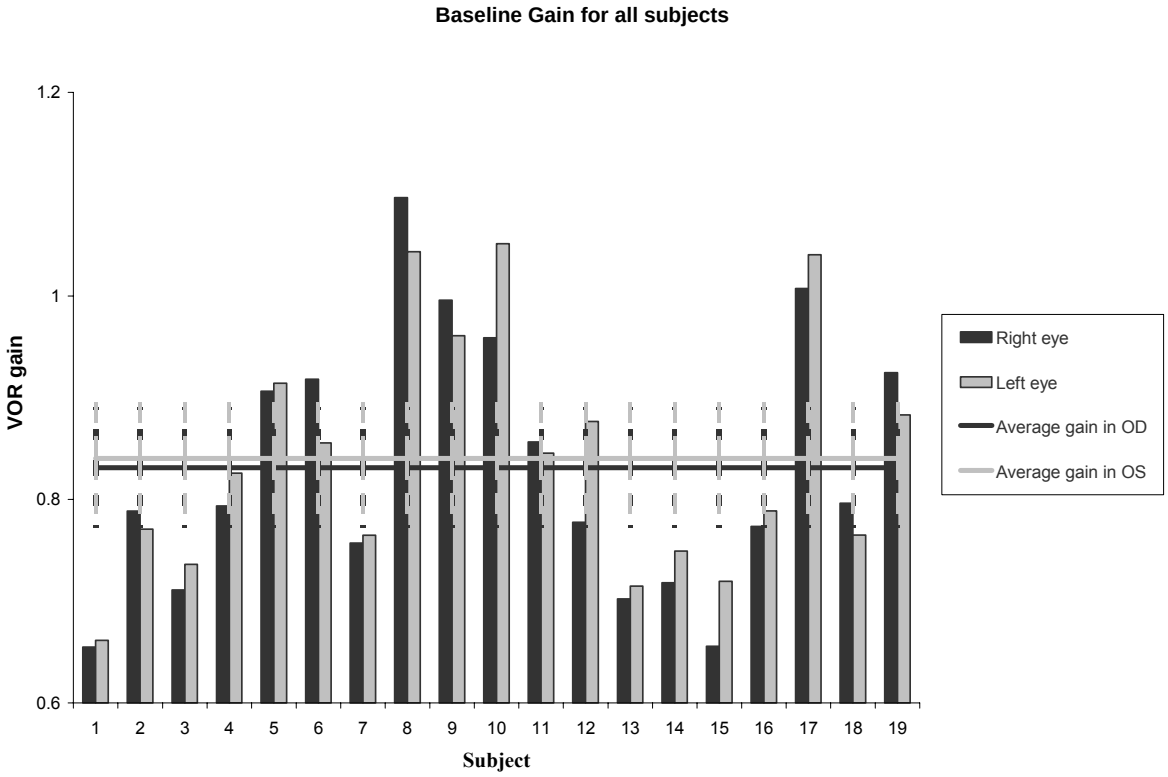

Figure 4-4: Right eye and left eye VOR gains in the baseline trial between the subjects. OD: Right eye, OS: Left eye. The dashed lines represent 95% confidence intervals.

4.3.2.1 Baseline Gain on Consecutive Days

Pre-adaptation (baseline) trials were performed on three consecutive days prior to my main experiment in 6 subjects, and the average VOR gain in the right and left eye was calculated on each day. There was no significant difference between VOR gain in right eye and left eye on different days (Figure 4-5). Using multiple t-tests, no significant difference was observed for the right and left eyes between the days ($p>0.05$).

Days	Right eye	Left eye
First day	0.901	0.893
Second day	0.857	0.842
Third day	0.896	0.921

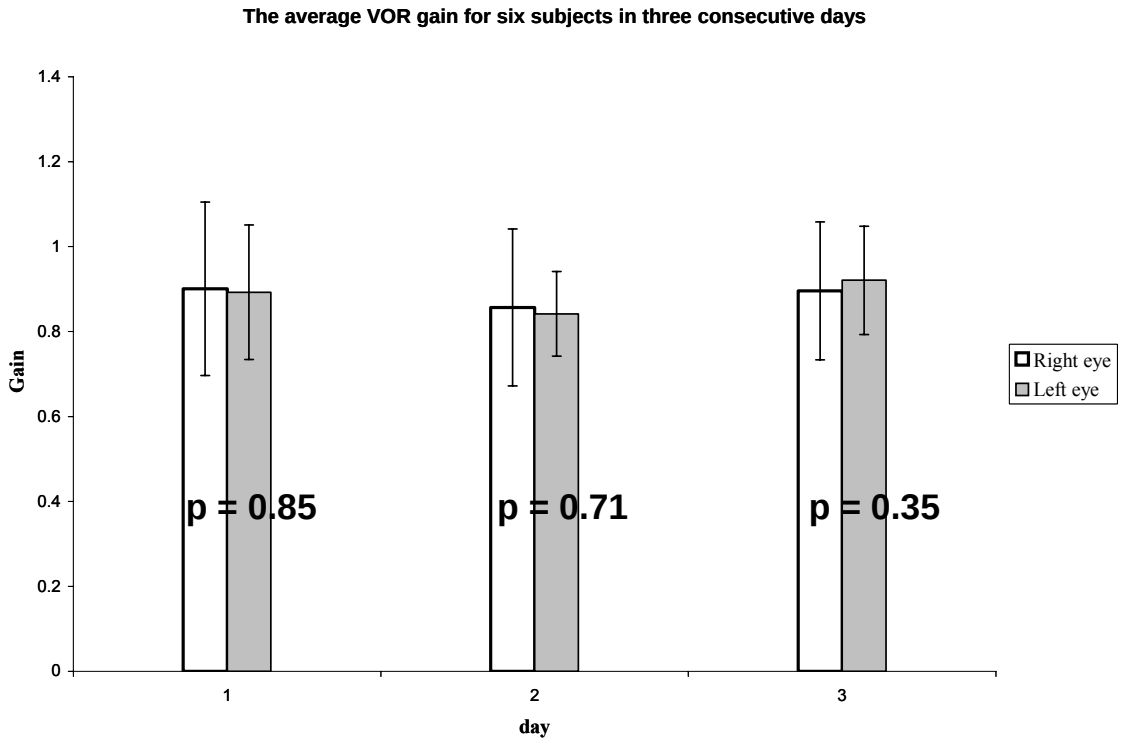

Figure 4-5: The average VOR gain for six subjects on three consecutive days ($p > 0.05$). The error bars represent standard deviation from the mean. P values show that there is not significant difference between right eye and left eye VOR gain on different days.

4.3.3 Gain: Baseline vs. First Post-Adaptation Trial in Right and Left Eye in 2 Directions of Head Rotation

The VOR gain difference between baseline and first post adaptation trial ($Gain_{baseline} - Gain_{post\text{-}adaptation}$) was calculated for each subject in the right and left eyes. During rightward head rotation, the average VOR gain difference between baseline and first post adaptation trial ($Gain_{baseline} - Gain_{post\text{-}adaptation}$) for the right eye was 0.049 ± 0.126 and for the left eye was 0.09 ± 0.147 (Figure 4-6). During leftward head rotation, the average VOR gain difference between baseline and post adaptation trial for the right eye was 0.03 ± 0.102 and for the left eye was 0.06 ± 0.127 (Figure 4-7). There were no significant differences between rightward and leftward head rotation for right eye ($p = 0.381$) and for the left eye ($p = 0.08$) VOR gain changes. Therefore, since there was no significant difference between rightward and leftward head rotation in both eyes, two directions of head rotation were collapsed for each eye.

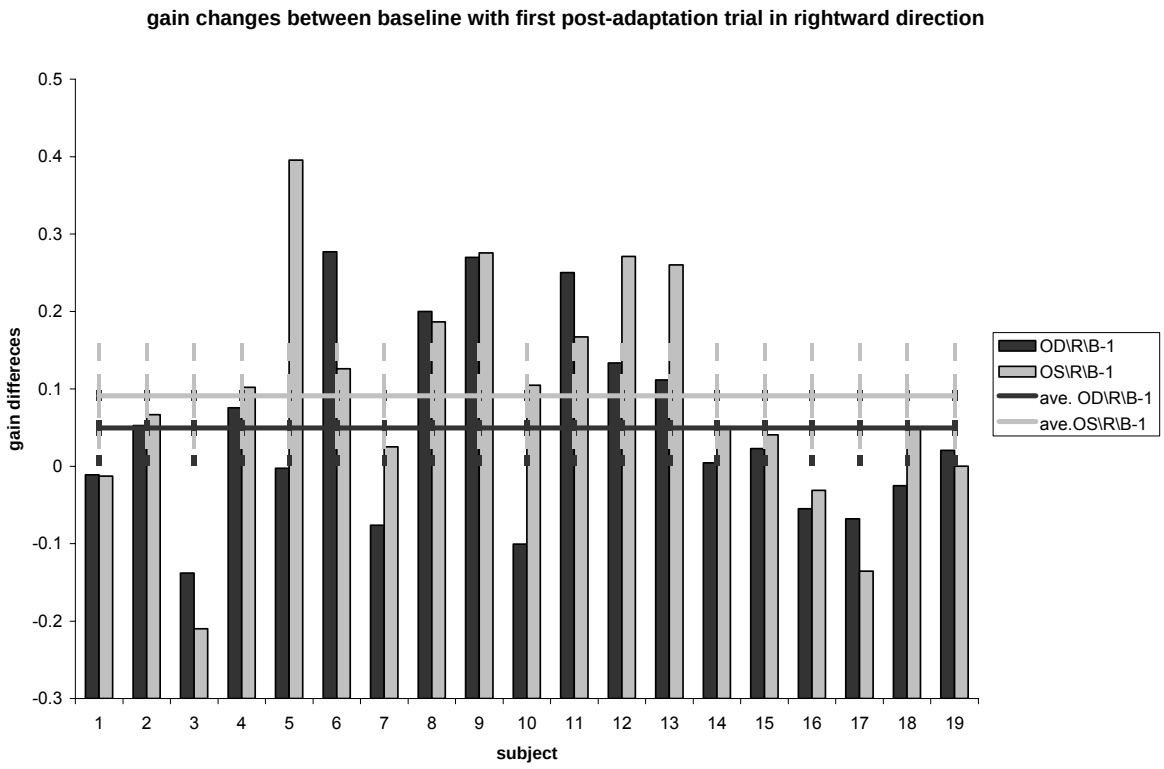

Figure 4-6: OD\R\B-1: Right eye VOR gain difference between baseline and first post adaptation trial during rightward head rotation, OS\R\B-1: Left eye VOR gain difference between baseline and first post adaptation trial during rightward head rotation. The dashed lines represent 95% confidence intervals.

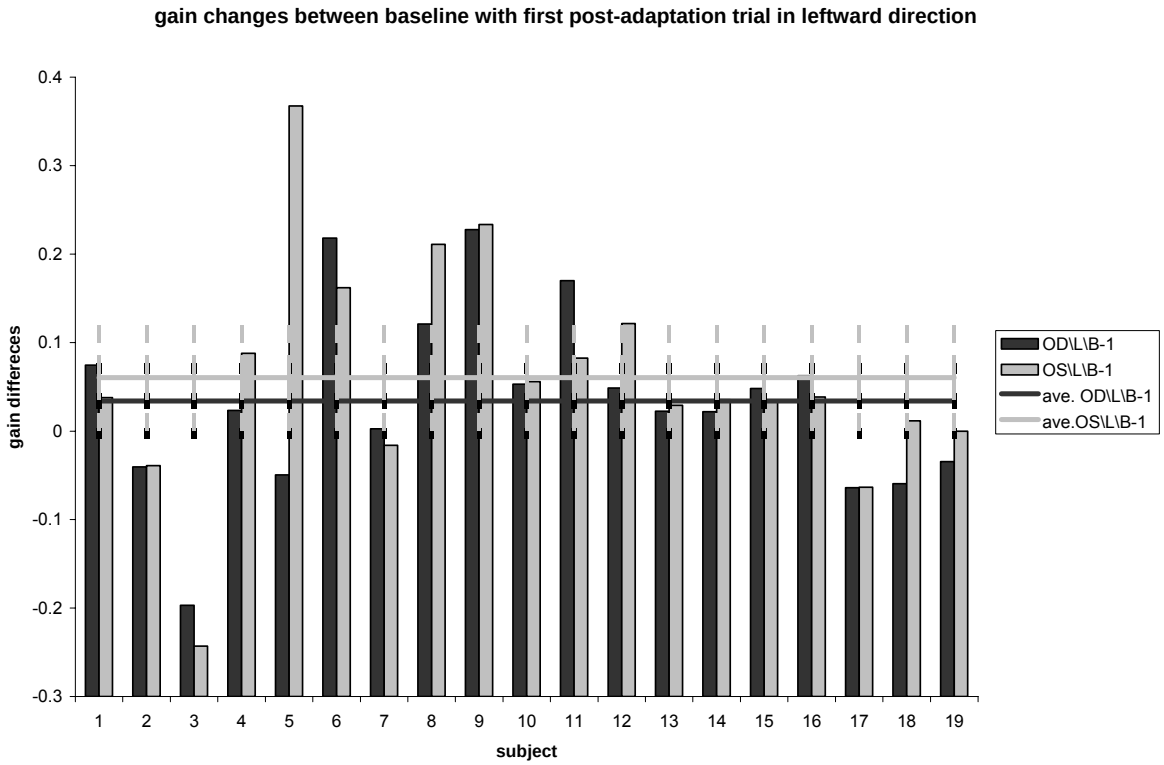

Figure 4-7: OD\L\B-1: Right eye VOR gain difference between baseline and first post adaptation trial during leftward head rotation, OS\L\B-1: Left eye VOR gain difference between baseline and first post adaptation trial during leftward head rotation. The dashed lines represent 95% confidence intervals.

4.3.4 Gain: Baseline vs. First Post-Adaptation Trial in Right and Left Eye

The average right eye VOR gain and left eye VOR gain was 0.789 ± 0.131 and 0.782 ± 0.140 respectively in the first post-adaptation trial (immediately after removing the contact lens/spectacle combination). There was a significant difference between the left eye VOR gain in baseline trial and the left eye VOR gain in the first post-adaptation trial ($p= 0.04$). For the right eye VOR gain, there was no significant difference between baseline trial and the first post-adaptation trial ($p= 0.124$) (Figure 4-8).

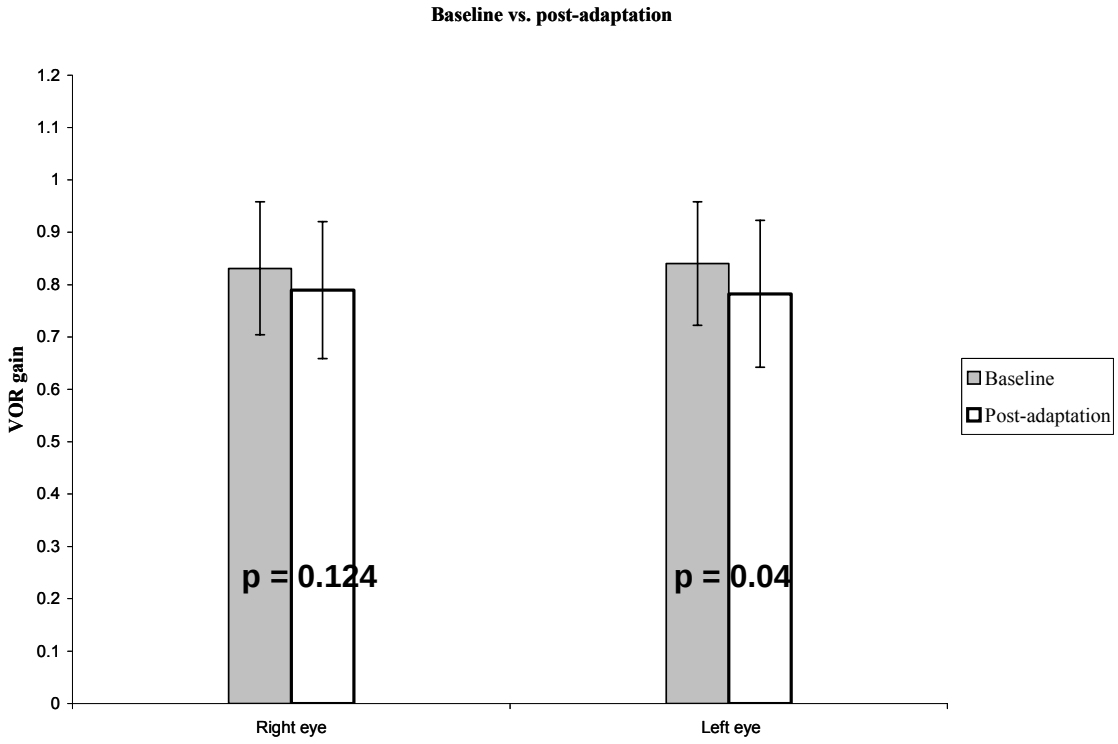

Figure 4-8: The average right eye and left eye VOR gain in baseline vs. first post-adaptation trial. p values show that left eye VOR gain significantly decreased after adaptation (p=0.04), while there was not a significant difference in right eye VOR gain between baseline and first post-adaptation trial (p=0.124). The error bars represent standard deviation from the mean.

The VOR gain changes between the baseline and first post-adaptation trials (Δ gain= Gain $_{\text{baseline}}$ - Gain $_{\text{post-adaptation}}$) were obtained for each subject's eye. The average right eye Δ gain for all subjects was 0.04 ± 0.112 and the average left eye Δ gain for all subjects was 0.05 ± 0.116 (Figure 4-9). However, there was no significant difference between the right eye Δ gain and the left eye Δ gain (p = 0.203).

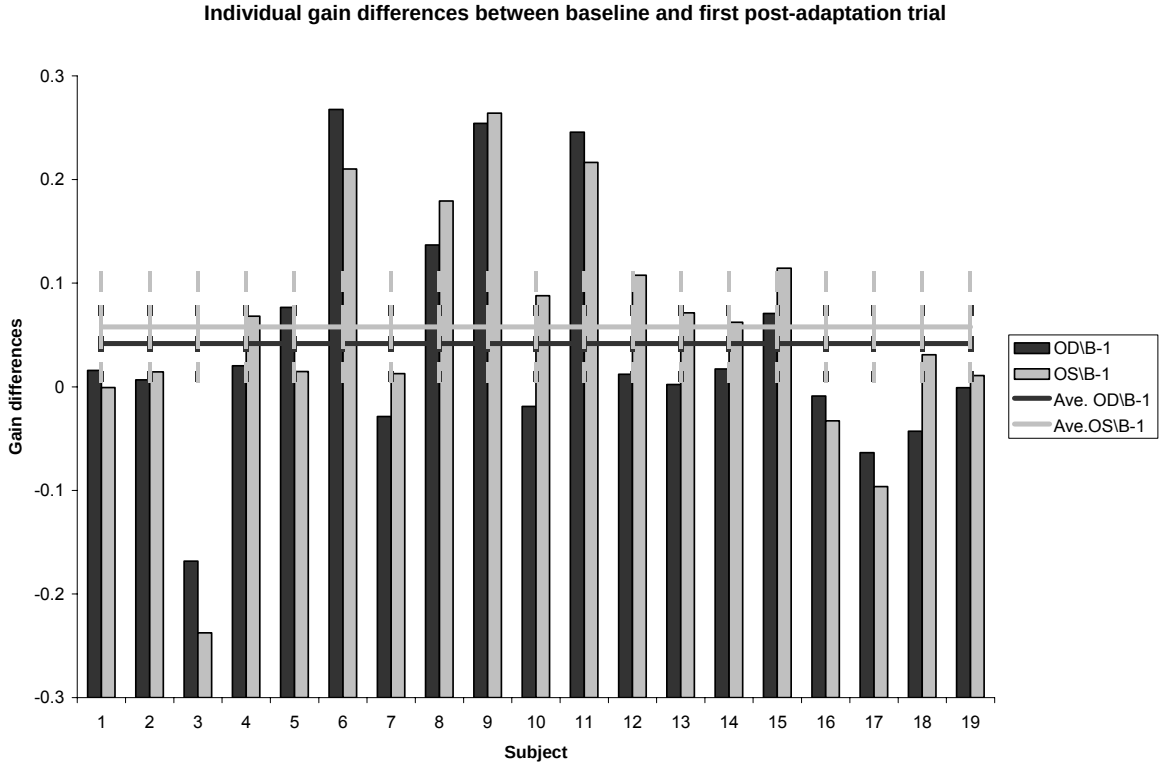

Figure 4-9: Δ gain between baseline and first post-adaptation trial in right eye and left eye. OD: Right eye VOR gain, OS: Left eye VOR gain, B: Baseline trial, 1: first post-adaptation trial. B-1: The difference between VOR gains in baseline with first post-adaptation trial. The dashed lines represent 95% confidence intervals.

The percent gain change (%ΔG) for each subject in right eye and left eye VOR gain induced by wearing the combination of contact lens/spectacle, was also calculated according to the relation:

$$\% \Delta G = 100(G'-G)$$

(G) was the subject's VOR gain in the baseline trial and (G') was the gain in the first post-adaptation trial. The average gain change in left eye was -5.77% ± 11.64 and in right eye

was -4.17% ± 11.29. It means that the left eye VOR gain after 4 hour lens adaptation was reduced 5.77% ± 11.64, while the right eye VOR gain showed 4.17% ± 11.29 reduction after adaptation (Figure 4-10). There was not a significant difference between right eye VOR gain changes and left eye VOR gain changes ($p = 0.133$).

Subject	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
% Δ gain in OD	-1.57	-0.66	16.84	-2.01	-7.65	-26.8	2.87	-13.7	-25.4	1.905	-24.6	-1.2	-0.21	-1.71	-7.06	0.9	6.355	4.285	0.095
% Δ gain in OS	0.065	-1.43	23.75	-6.81	-1.48	-21	-1.26	-17.9	-26.4	-8.8	-21.7	-10.8	-7.13	-6.21	-11.4	3.285	9.65	-3.1	-1.07

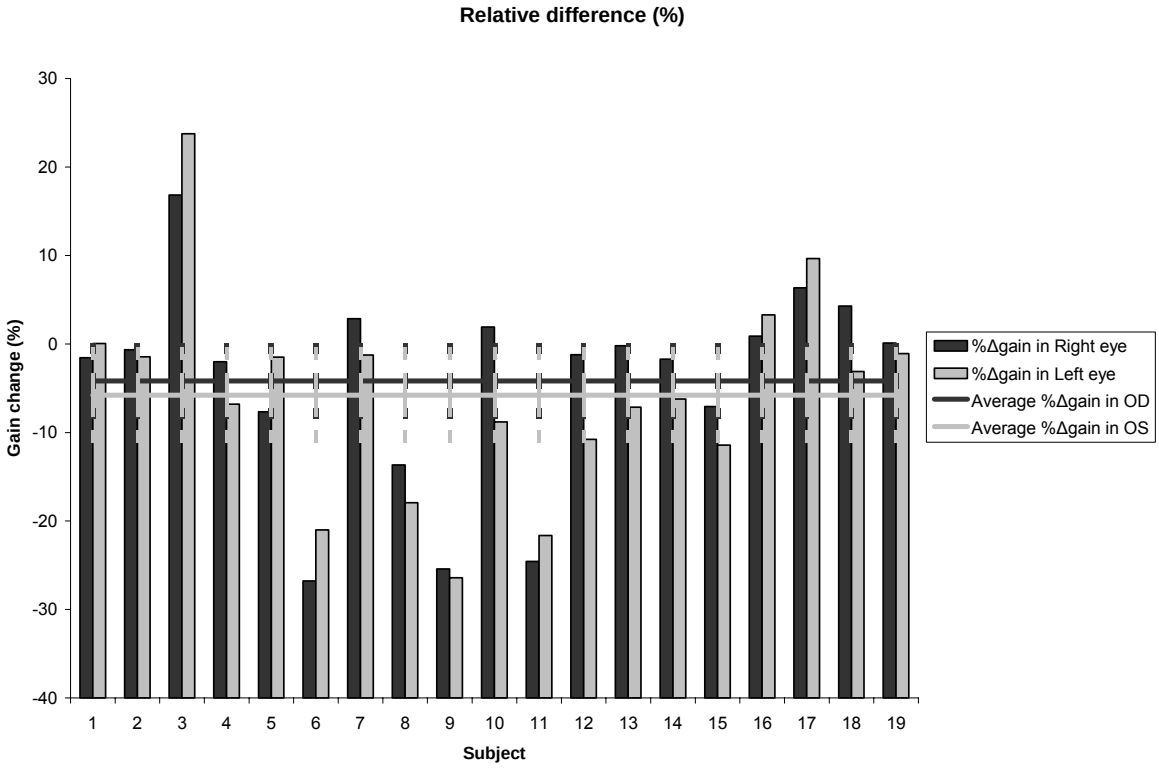

Figure 4-10: %Δ Gain between VOR gain at baseline and VOR gain at the first post-adaptation trial for each subject in right eye and left eye. The dashed lines represent 95% confidence intervals.

4.3.5 Gain: Baseline vs. 2 hours After Adaptation in Right and Left Eye

VOR gain was monitored every 30 minutes for 2 hours after removing the combination of contact lenses and spectacles. VOR gain in the right eye was reduced from 0.789 ± 0.131 (mean ± SD) in the first post-adaptation trial (zero minutes) to 0.718 ± 0.141 in the last trial (120 minutes) with the p = 0.06. In the left eye, VOR gain showed reduction from 0.782 ± 0.140 to 0.708 ± 0.141 during two hours after adaptation with p = 0.01 (Figure 4-11).

Eye	Baseline	0 minute	30 minutes	60 minutes	90 minutes	120 minutes
OD	0.831	0.789	0.752	0.713	0.761	0.718
OS	0.84	0.782	0.755	0.718	0.75	0.708

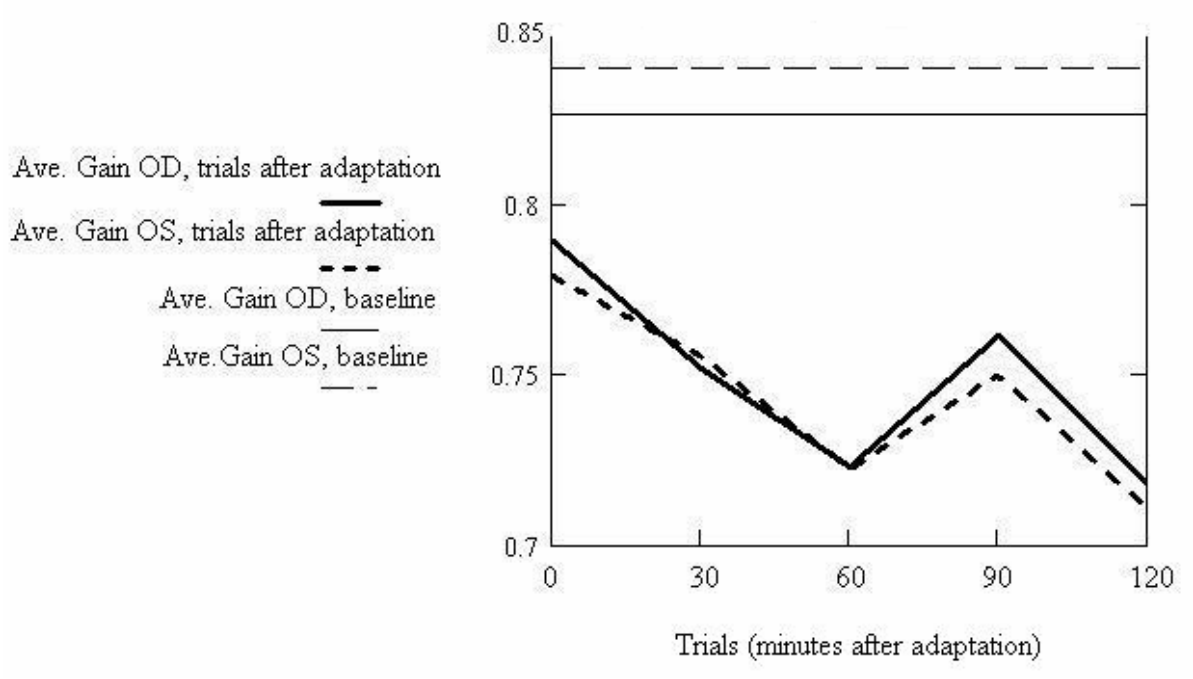

Figure 4-11: Changes in average right eye and left eye VOR gain; during the post adaptation trials (Minutes are after the removal of the contact lens/ spectacle combination).

According to Figure 4-9, which was confirmed by Figure 4-10, the results of four subjects (# 3, 6, 9, and 11) were greater than 2 SD from the mean. The same four subjects would also be considered outliers using 1.5 IQR (inter-quartile ranges). By excluding these subjects, a significant difference was obtained between right eye VOR gain changes (Δ gain= Gain $_{\text{baseline}}$ - Gain $_{\text{post-adaptation}}$) and left eye VOR gain changes ($p = 0.03$). The average VOR gain changes for the right eye was 0.01 ± 0.05 and for the left eye was 0.04 ± 0.06 (Figure 4-12).

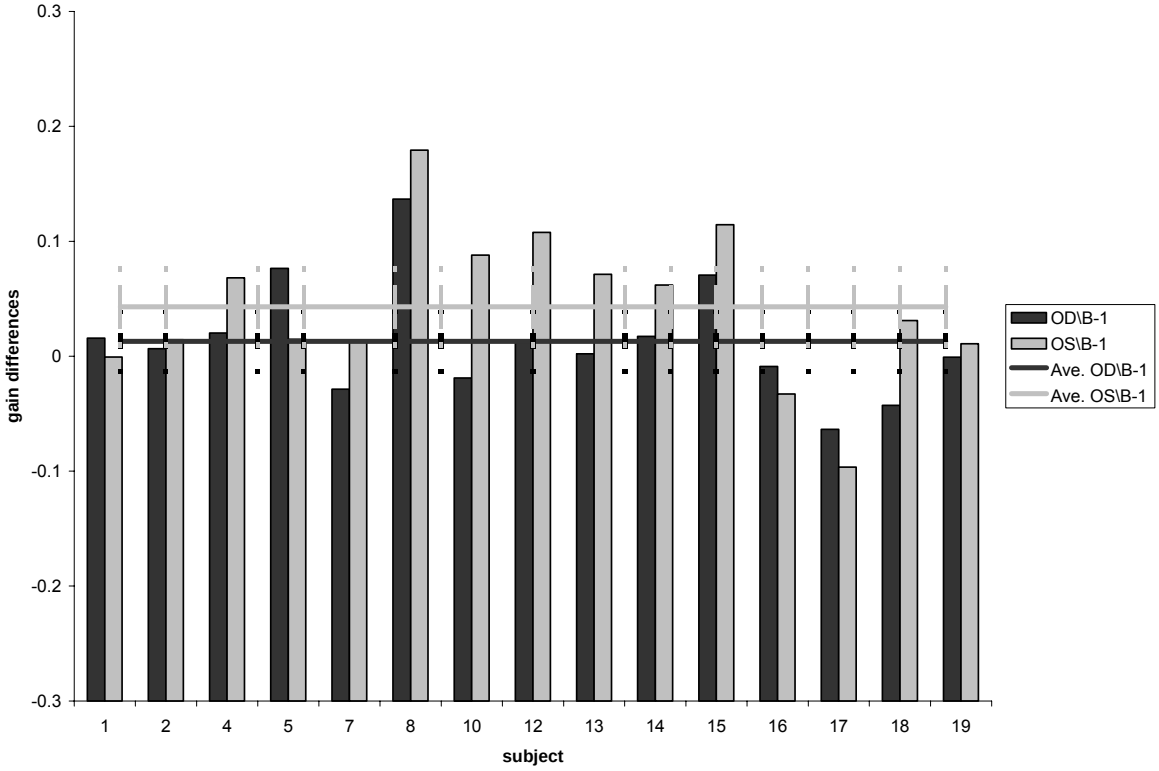

Figure 4-12: Results after excluding four subjects. OD\B-1: VOR gain differences between baseline and first post-adaptation trial for the right eye. OS\B-1: VOR gain differences between baseline and first post-adaptation trial for the left eye. The dashed lines represent 95% confidence intervals.

There was no significant difference between right eye VOR gain in the baseline trial and the first post-adaptation trial ($p = 0.33$), while there was a significant decrease in left eye VOR gain between the baseline trial and the first post-adaptation trial ($p = 0.02$) (Figure 4-13).

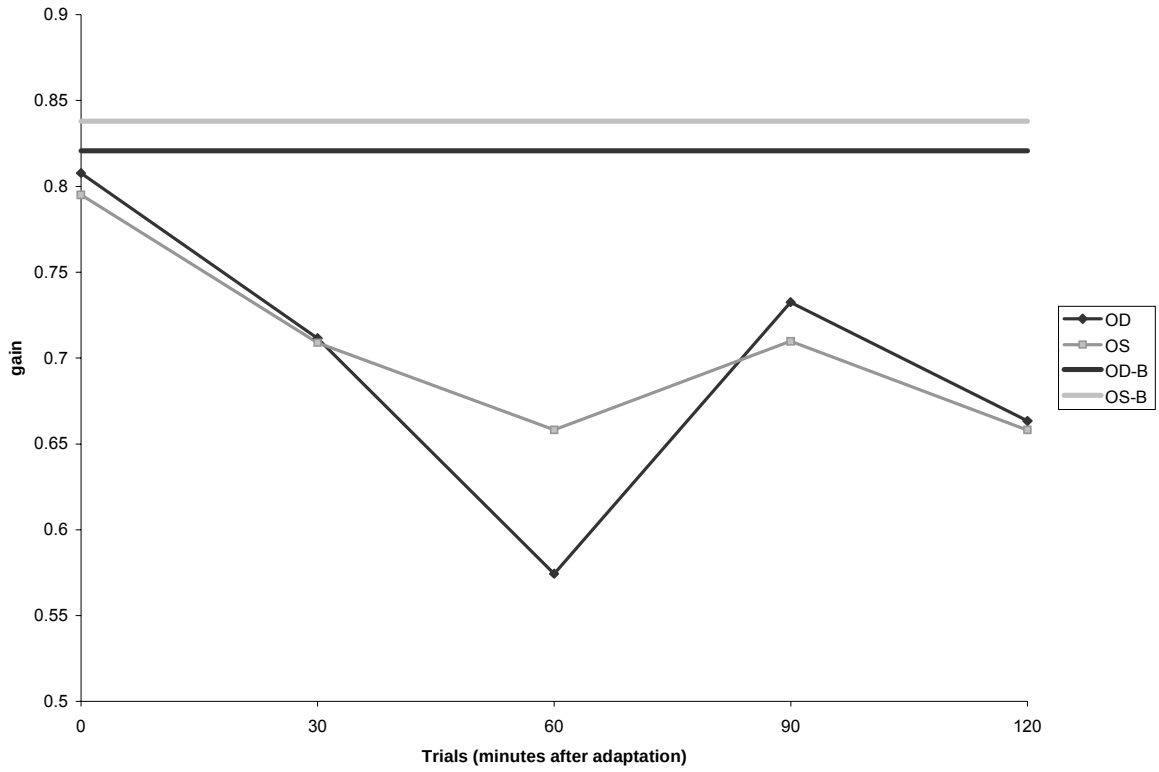

Figure 4-13: Average right eye and left eye VOR gain after excluding four subjects. OD: Right eye VOR gain, OS: Left eye VOR gain, B: Baseline trial.

The VOR gain for each trial and each subject is presented in table 4-2. For a few subjects, data from some of the trials were missing because of the problems in acquiring data, such as calibration and time overruns, and was noted as N/A in the table. These results were not included in the average values.

Subject	OD-B	OD-0	OD-30	OD-60	OD-90	OD-120	OS-B	OS-0	OS-30	OS-60	OS-90	OS-120
1	0.655	0.63935	0.622	0.65055	0.78895	0.7147	0.6615	0.66215	0.64705	0.6785	0.7693	0.70665
2	0.7886	0.78195	0.74225	0.8106	0.7469	0.8327	0.77065	0.75635	0.74225	0.7677	0.75655	0.78715
3	0.71115	0.87955	0.81765	0.8364	0.77095	0.9937	0.7363	0.97375	0.8561	0.88095	0.77835	0.96185
4	0.7937	0.7736	0.7375	0.753	0.72415	0.75805	0.8259	0.7578	0.6941	0.72335	0.73705	0.70405
5	0.9063	0.8298	0.8347	N/A	0.77195	0.72885	0.91415	0.8994	0.7426	0.75535	0.65535	0.74655
6	0.91825	0.6506	0.7854	0.8161	0.53355	0.72445	0.85565	0.64555	0.8198	0.9419	0.6253	0.7479
7	0.75715	0.78585	0.6876	0.3895	0.62625	0.4273	0.7648	0.7522	0.69955	0.4194	0.6127	0.41915
8	1.0965	0.9598	0.83195	0.88465	1.00905	0.73335	1.0435	0.86415	0.85245	0.7356	0.825	0.72795
9	0.9957	0.7415	0.6859	0.7304	0.65685	0.7254	0.96085	0.69675	0.69035	0.6761	0.7028	0.6231
10	0.95885	0.9779	N/A	0.7615	0.71595	0.80065	1.05125	0.9633	N/A	0.7672	0.75835	0.8074
11	0.8564	0.6108	0.57615	0.5661	N/A	0.5344	0.8454	0.62885	0.5995	0.55775	N/A	0.5511
12	0.77755	0.76555	0.739	0.70195	0.77025	0.48415	0.87665	0.769	0.7938	0.7535	0.7364	0.53085
13	0.70215	0.70005	0.7045	0.75375	0.7407	0.7933	0.7147	0.6434	0.6406	0.6783	0.68515	0.7168
14	0.71805	0.7009	0.71115	0.2313	N/A	0.6149	0.7492	0.68715	0.71175	0.6801	N/A	0.65435
15	0.6557	0.5851	0.6908	0.32595	0.7261	0.68355	0.7196	0.6052	0.6432	0.6137	0.7092	0.573
16	0.7734	0.7824	0.77575	0.6565	0.76215	0.72965	0.78865	0.8215	0.83865	0.69285	0.7926	0.7675
17	1.00745	1.071	0.90395	N/A	0.9131	0.94275	1.0405	1.137	0.93565	N/A	0.96215	1.0015
18	0.79635	0.8392	0.7643	0.7898	0.7756	0.7065	0.76495	0.73395	0.8272	0.71595	0.74595	0.72945
19	0.9245	0.92545	0.9269	0.90675	0.91785	N/A	0.88305	0.8723	0.865	0.89285	0.9012	N/A

Table 4-2: The VOR gain results. OD-B: Right eye VOR gain in baseline trial; OD-0: Right eye VOR gain in the first post-adaptation trial (immediately after the removal of the combination of contact lenses/spectacles); OD-30: Right eye VOR gain in the trial 30 minutes after adaptation; OD-60: Right eye VOR gain in the trial 60 minutes after adaptation; OD-90: Right eye VOR gain in the trial 90 minutes after adaptation; OD-120: Right eye VOR gain in the trial 120 minutes after adaptation; OS: Left eye VOR gain. N/A: Not applicable results.

To test the viability of the experimental procedure, I repeated my experiment on two subjects but tried to induce conjugate adaptation, as this is known to occur. I asked my subjects to wear +5D spectacles in each eye. The spectacle lenses magnified the images by 9%. Clear vision was obtained with compensating contact lenses. In the baseline trial, the average right eye VOR gain was 0.9855 ± 0.113 and left eye VOR gain 1.015 ± 0.05. The average VOR gain for the right eye in the first post-adaptation trial was 1.07 ± 0.121 and for the left eye 1.139 ± 0.05 (Figure 4-14). VOR gain significantly increased after adaptation in both eyes ($p<0.05$). Right eye VOR gain increased 8.57%, while left eye VOR gain increased 12.15%. The difference between the right and left eyes VOR gain changes were not significant ($p = 0.4$). However, only two subjects were tested.

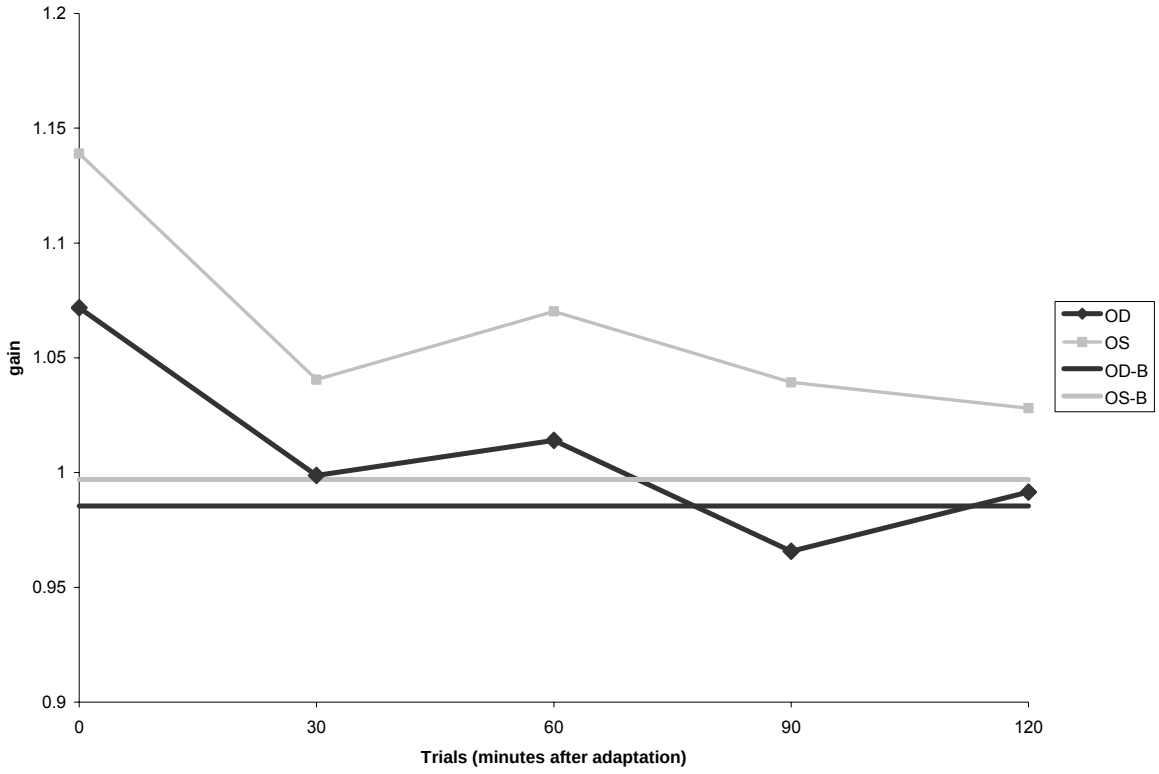

Figure 4-14: Average right eye and left eye VOR gain, in post adaptation trials compared with baseline trial, when subjects wore +5D spectacles in front of both eyes. OD: Right eye VOR gain, OS: Left eye VOR gain, B: Baseline trial.

5 Discussion

When we divided the head movement into rightward and leftward directions, no significant difference in VOR gain was found for either the right eye or the left eye. This is in agreement with the Collewijn and Smeets[46], and Viirre et. al.'s[35] studies. Therefore, data for leftward and rightward head rotation was collapsed for each eye. In the baseline trial, the difference in the VOR gain between the right eye and left eye was compared by a paired t-test, and failed to achieve statistical significance. Furthermore, as seen in figure 4-5, we confirmed that there was no significant difference between the right eye and left eye VOR gains on different days.

I analysed the position data instead of velocity data, because the velocity data was considerably noisier than the position data. The data collection was done at low frequency (0.833 Hz) and therefore, saccadic movements were minimal. As well, the gain was calculated from only the dominant frequency. Consequently gain calculated from position data would not be expected to differ significantly from that calculated from velocity data.

The average VOR gain for the right eye and the left eye was measured after 4 hours of wearing the contact lens/spectacle combination. The first post-adaptation trial was conducted immediately after the removal of the contact lens/spectacle combination (0 minutes) and then repeated every 30 minutes, for 2 hours after adaptation. In the first post-adaptation trial, the amount of gain change was expected to be the largest, and the adaptation the strongest. As noted earlier, the magnifying lens was placed in front of the right eye and the minifying lens, in front of left eye. In the first post-adaptation trial vs. baseline trial, left eye VOR gain significantly decreased, while right eye VOR gain did not show any

significant difference. In the rest of the post-adaptation trials, VOR gain for both the right eye and the left eye showed a significant decrease vs. VOR gain for the baseline trial.

In a study with goldfish[97] on the monocular adaptation of VOR, similar results were observed. In this study, one eye was stimulated to decrease the gain and the other eye was stimulated to increase the gain for 3 hours. During training, the goldfish was rotated at a specific frequency in the horizontal plane (vestibular stimulation), while a random pattern of dots of light (visual stimulation) was rotated 180° out of phase with the vestibular stimulation. This increased the VOR gain. To decrease the VOR gain, the visual and vestibular stimulations were rotated together. No significant change in gain (from 0.75 ± 0.05 to 0.61 ± 0.14) was observed on the eye (stimulated to increase the gain), whereas the other eye stimulated to decrease the gain, did produced a significant gain decrease over the adaptation period (0.57 ± 0.05 to 0.23 ± 0.03).

In another study[22], two human subjects wore a -5D spectacle lens in front of the right eye and a +5D spectacle lens in front of the left eye for 24 hours. The results show a decrease in VOR gain in the dark, by approximately the same amount for both eyes. Unfortunately, their method created considerable blurring for the subjects, except one of them who could restore sharp vision using accommodation in his right eye. Collewijn et. al.[22] suggest that the adaptive system has great difficulty adjusting the gain differently for the two eyes in darkness. They believe that if there is an advantage to using the signal from one eye only, which was the case with the subject who had sharp vision in only one eye, the gain of both eyes will adapt to that level.

Miles and Eighmy[52;98], in their experiments on monkeys, found that gain increases proceed more slowly than gain decreases. It has been suggested by McElligott and Wilsons[97]

that there are different mechanisms for gain increases and decreases. In their experiment with goldfish, it is shown that separate and conflicting visual stimuli presented to each eye produces only a gain decrease in the eye stimulated to decrease VOR gain. This provides further evidence that there are separate neuronal mechanisms for the 2 types of gain adaptations, which appear to be arranged in a ranked series. Also in the goldfish study, it was found that monocular adaptation of the VOR is possible for gain increasing but not for gain decreasing, when one eye was patched and the other eye was stimulated to increase or decrease the gain for 3 hours[97]. In the eye stimulated to increase the gain, VOR gain increased, whereas that of the occluded eye did not. In another set of experiments, the viewing eye was stimulated to decrease gain. In this case, both the viewing and the occluded eyes decreased VOR gain similarly. In Collewijn et. al.'s study[22], a human subject was fitted with a -5D lens for one eye, while the other eye was patched. A conjugate decrease in both eyes VOR gains was obtained after 24 hours.

In the current study, I found that in the first post-adaptation trial, the amount of VOR gain change in the left eye was equal to the predicted amount (≈ 6%) but for the right eye not only the amount of gain change was less (≈ 2-4% instead of the 9% that we expected), but the direction was also opposite (decreasing instead of increasing). As such, there was monocular adaptation, between 2% to 4% (depending on whether we excluded those four subjects whose results were greater than 2 SD from the mean) but it was not complete and it was not as expected. What are the possible explanations for these findings?

The first possibility is that a 9% gain increase is too much for the VOR system. However, in the conjugate adaptation control study using +5D spectacle lenses in front of both eyes, we confirmed that the VOR gain is able to increase by more than 9%. Second, the

average measured perceptual aniseikonia in this study was approximately 15%, which was equal to the total magnification difference with the spectacles. Therefore, the second possibility is that a 15% magnification difference between the two eyes might be too much for the VOR system. However, in a study on short-term nonconjugate adaptation of human saccades[64], it was noted that nonconjugate adaptation in one direction, while the size of the image was reduced by negative lenses, was possible within a 16% difference in the image size. A third possibility is that having the VOR system adapts in two different directions might be the problem. If the VOR gain in one eye needs to increase and in the other eye it needs to decrease after adaptation, this might be beyond the adaptive capabilities of the VOR system.

As mentioned in the Results section, the spectacle lenses might have had a subtle effect on the head movement characteristics during the adaptation period. Although we asked the subjects to behave as naturally as possible, head movement characteristic might not have been totally natural throughout the adaptation period. Also, all of the participants were graduate students and research assistants, whose "daily activities" are predominantly deskwork (i.e. passive actions). Since visual-vestibular stimulation drives VOR adaptation, it might be possible that the subjects were not exposed to enough stimuli to adapt. It might have been helpful if a chaperone had accompanied the subjects during the adaptation period—to encourage them to move around and to ensure uniformity of activity. On the other hand, it also might be possible that the adaptation period was not long enough, and the subjects need more than 4 hours to adapt to the spectacles.

In the current experiment, natural behavior was the adaptation stimulus. Most natural head movements occur at high frequencies (e.g. walking causes head movements between 1-

10 Hz)[6]. According to "channel" hypothesis[99], higher frequency channels are expected to receive more visual-vestibular interaction signals than lower frequency channels, and because of this they might be the stimulus for adaptive VOR gain change. However, the VOR gain in this study was measured at approximately 0.833 Hz as this frequency was the most comfortable frequency for the subjects to rotate their head. Therefore, the low frequency head movements at which the data were collected relative to the adaptation frequencies may be the reason for the small change in VOR gain after adaptation.

Two of the participants (#13, and #16) were left eye dominant. In all of the subjects, the vision of the two eyes was equal (less than one line difference). Although, we always put the magnifying lens in front of the right eye and minifying lens in front of the left eye, the VOR gain changes after adaptation in these two subjects were not different from subjects with dominant right eyes. Therefore, adaptation was not a function of eye dominancy.

Another interesting finding is that, 30 minutes after the removal of the contact lens/spectacle combination, and throughout the 2 hour follow up, VOR gain in both eyes did not return to the baseline trial level. Both eyes did show a significant decrease in VOR gain when compared to the baseline trial. The possible explanations for these findings are as follows: During the 2 hour follow up, for a few subjects, data from some of the trials were missing because of the problems in acquiring data, such as calibration and time overruns. Since data were collected data every 30 minutes, the subjects did not have enough time between the trials to move around and to recover. On the other hand, multiple measurements during the recovery time could have made the subjects tired and less motivated and this may have caused a decrease in the VOR gain. It is also known[6] that taking repeated VOR measurements, causes a decrease in VOR gain and maybe was a factor in this study.

However, Kuki et. al.'s study on monkeys[98] shows that there are different memory retention mechanisms for VOR gain increases and decreases. Learned decreased gain returns to the baseline slower than increased gain and therefore its time constant is longer. Therefore, a longer separation between trials and a longer follow-up time after adaptation, than those used in this experiment, would likely have resulted in a return to baseline.

6 Conclusions

The study showed that there was minimal monocular adaptation of VOR in response to the combined contact lenses/spectacles, but it was not complete and it was not as we expected. It was shown that the significant decrease in VOR gain was possible to minifying lens (≈6%), while the VOR gain increase in response to magnifying lenses did not happen (≈ 2% decrease instead of 9% increase that was expected). The study also showed that monocular adaptation of 4% did not return to the baseline trial throughout the two hours follow up.

Recommendation for future research include trying different amounts of anisometropia in one direction (e.g., using 15% magnifier or minifier spectacle lens in front of one eye and no spectacle lens in front of the other eye) or in two directions (using less than 10D anisometropic spectacles, e.g. +3D in front of one eye and -3D in front of the other eye), a longer adaptation period (more than 4 hours) might stimulate monocular VOR adaptation as was expected. Monitoring the gain for more than 2 hours after adaptation with a longer separation between trials also might show a return to the baseline after adaptation.

7 Appendix

7.1 Processing Delay Between Eye and Head Trackers in EL-MAR

Raw digital eye (p_e) and head (p_h) position data obtained from the trials, were exported as ASCII files for off-line analysis. The data were analyzed with programs written in MATHCAD$_{TM}$ 11.1 software (Figure 7-1).

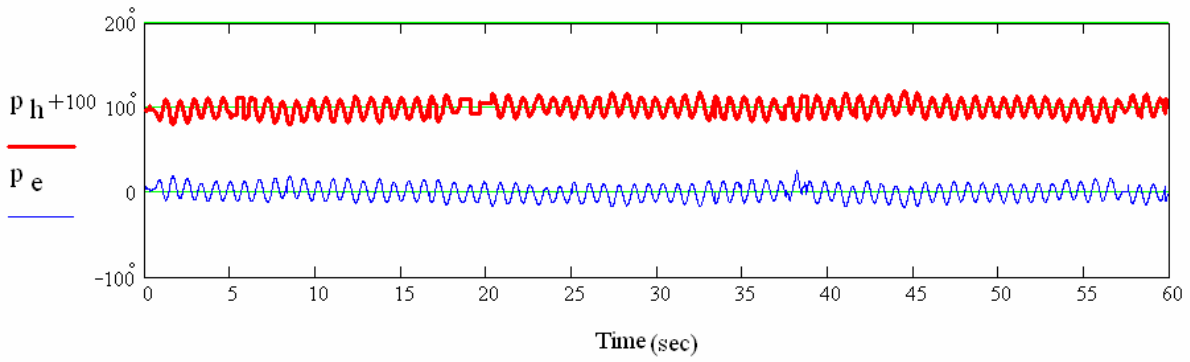

Figure 7-1: Eye position data (p_e) and head position data (p_h) of one of the subjects in 60 seconds. To show it better, the eye and head position graphs were purposely separated.

Eye and head position data were transformed from the time domain to the frequency domain (P_e and P_h in frequency domain) by a Complex Fast Fourier Transform (CFFT). The dominant frequency (F_{max}) of eye and head movements was found where there were the largest absolute values of the amplitude of the CFFT of eye ($|P_{e_{max}}|$ and head position ($|P_{h_{max}}|$) data. The dominant frequency was the same for both eye and head signals (Figure 7-2).

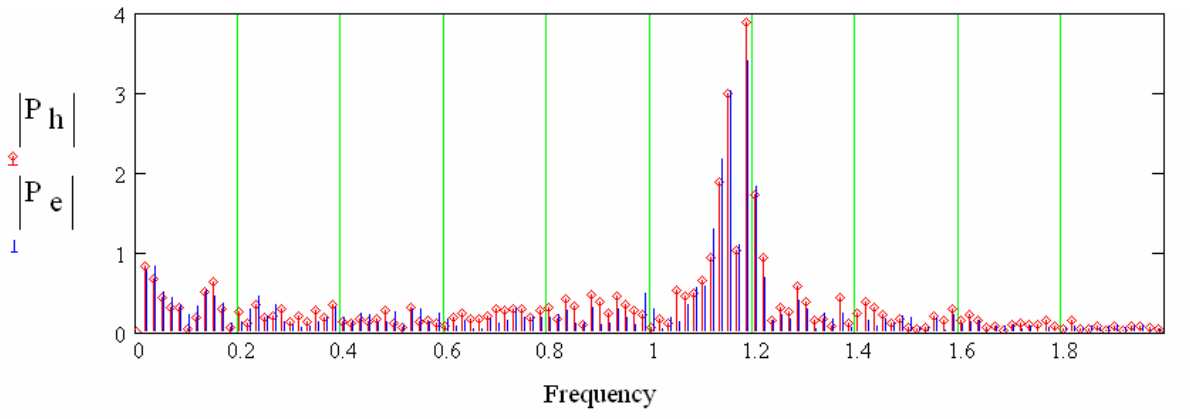

Figure 7-2: The largest absolute values of the amplitude of the CFFT of eye and head position data in dominant frequency.

A complex number of the form $z = |z|(\cos\theta + i\sin\theta) = |z|e^{i\theta}$ was used where i is the imaginary unit equal to $\sqrt{-1}$, $|z|$ is also a positive real number representing amplitude, and θ is a real number called the argument. The argument represents the phase. MATHCAD uses the "arg" function to calculate the phase shift between the eye and head signals as follows:

$$\text{Offset} := \arg\left[\left(-P_e\right)_{\max}\right] - \arg\left(P_{h\,\max}\right) \qquad \text{Offset} = 3.944\ \text{deg}$$

$$\text{Delay} := -\left(\frac{\text{Offset}}{2\cdot\pi}\right)\cdot\frac{1}{F_{\max}} \qquad \text{Delay} = -0.00924 \quad \text{[seconds]}$$

7.1.1 Analysis of Subdivisions of the Data

The analysis was repeated on subdivisions of the data to estimate DDelay for each subdivision. This was used to compute the confidence interval for Delay computed above. We divided the whole signals to 10 subdivisions (nsub=10).We chose this number of subdivisions as the dominant frequency (F_{max}) for all the data would be close to dominant frequency ($FF_{\max_s}$) in each subdivision (s). The number of data points in total was 7189, therefore, in each subdivision the number of point was ≈718. Eye and head position data for each subdivision were transformed from the time domain to the frequency domain (PP_{e_s} and PP_{h_s} in frequency domain) by a Complex Fast Fourier Transform (CFFT). The dominant frequency (FF_{max}) of eye and head movements for each subdivision was found where there were the largest absolute values of the amplitude of the CFFT of eye ($|PP_{e_{\max S}}|$ and head position ($|PP_{h_{\max S}}|$) data (Figure 7-3).

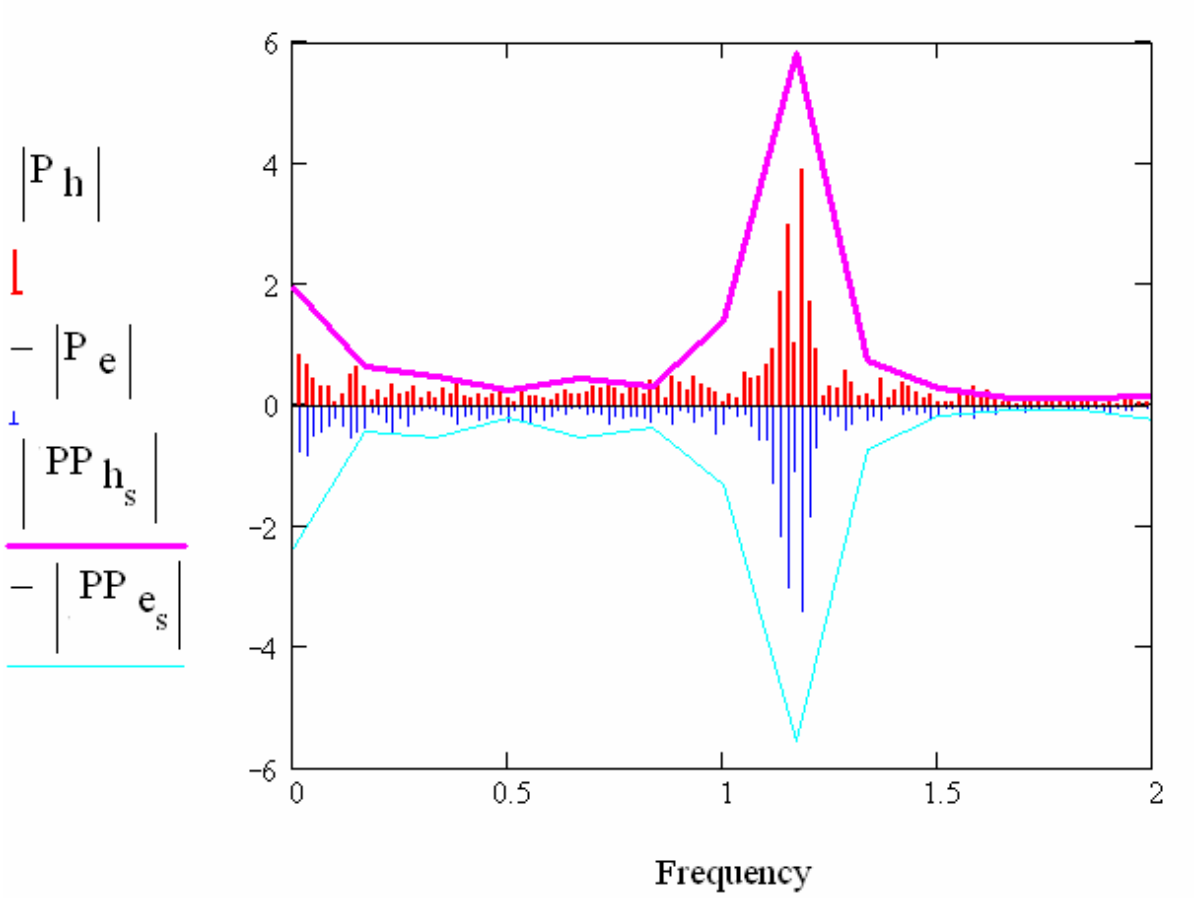

Figure 7-3: The largest absolute values of the amplitude of the CFFT of eye and head position data in dominant frequency in one subdivision (subdivision=5) compared with the whole signal.

The most common dominant frequency out of all subdivisions was found for eye and head signals (In my data, the dominant frequency was the same for both eye and head signals in all the subdivisions).

7.1.2 Compute $DDelay_s$ for Each Subdivision (s)

The phase shift and delay ($DDelay_s$), as noted earlier, was calculated separately for each subdivision. The results are as follows:

Subdivisions	1	2	3	4	5	6	7	8	9	10
DDelay	-0.032	-0.011	-0.011	-0.075	-0.0092	-0.0022	-0.02	-0.0052	-0.0051	-0.0071

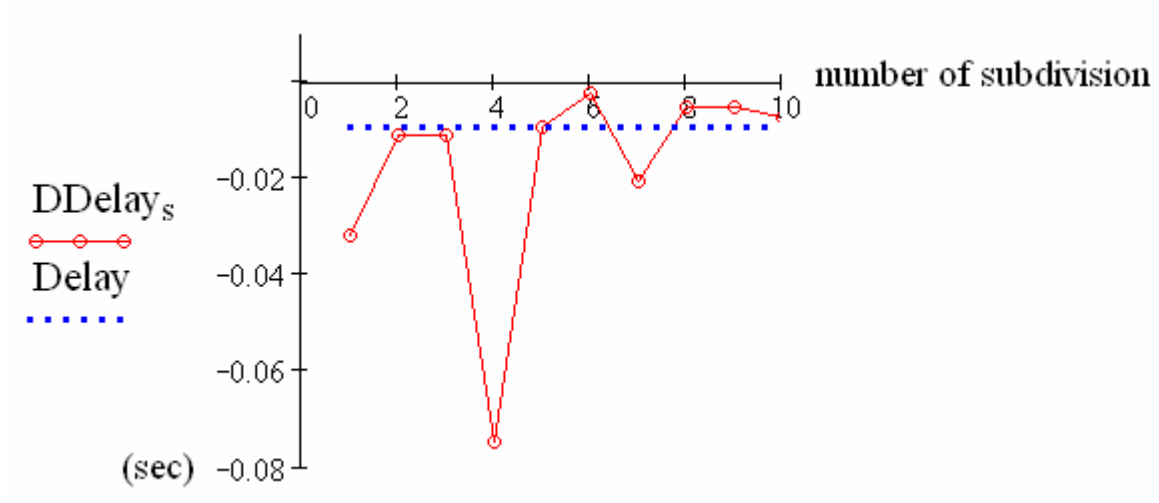

Figure 7-4: Calculated Delay (Delay) for the whole signal, compared with calculated delay for each subdivision ($DDelay_s$).

7.1.3 Compute Confidence Intervals for Delay

The Confidence Interval for delay was computed based on the Confidence Intervals for the mean of DDelay. Mean (DDelay) = -0.0179, while ΔDDelay was calculated as:

$$\Delta DDelay = x_{95} \times \frac{Stdev(DDelay)}{\sqrt{nsub}} = 0.0156 \ \text{(sec)}$$

Therefore, 95% confidence intervals were estimated to be:

mean (DDelay) = -0.0179

±

ΔDDelay=0.0156

Follow a student's t distribution, degrees of freedom, df was:

Df = nsub-1 = 9

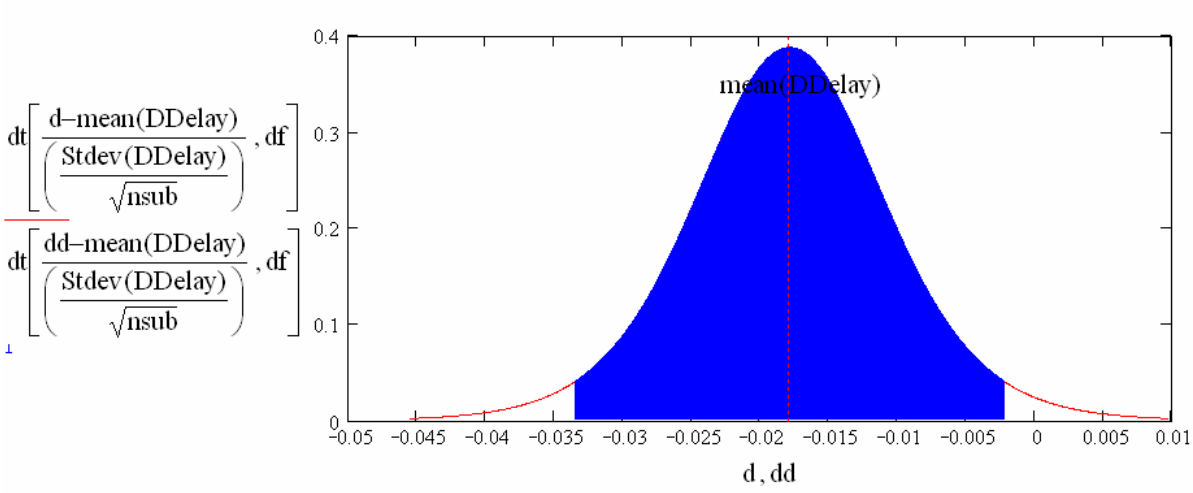

Figure 7-5: Plot of 95% Confidence Intervals for mean (DDelay) with unknown μDdelay (d).

As such, estimate Confidence Intervals for overall Delay was:

$$\Delta Delay = \frac{\Delta DDelay}{\sqrt{\text{nsub}}}$$

$$\text{Delay} = -0.0092$$

$$\pm$$

$$\Delta\text{Delay} = 0.0049$$

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