How Binocular Visual Performance Is Changed When One Eye Has Lower Vision:
Characterization Of Inhibitory Binocular Interactions

by

Kari Smith

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DEDICATION

I would like to dedicate this to the individuals in my life who have supported me through this journey. My family: Mom, Dad, Kim, Nana, and Papa for many years of encouragement, I am proud to finally have an answer to the never-ending question "when will you be finished school"? To Greg, thank you for being patient with me while spending hours in front of "your" computer and always keeping me positive. To my friends near and far, it is reassuring to know that I will always be able to count on you regardless of circumstances. Thank you Dr. Tremblay for your dedication, guidance, and knowledge on this project. I truly appreciate your compassion for my success in the midst of changing cities and starting a career. Also, to Joan Parkinson and all members of the IWK staff and classmates, I have made memories that will last forever with you all.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Purpose: To explore new methodologies to quantify binocular interactions and shed light on their possible neural generators.

Methods: Binocular inhibition (BI) was experimentally produced in 40 visually healthy subjects by inserting a series of neutral density (ND) filters in front of one eye. Visual evoked potentials were recorded with stimuli tuned for check size, location and contrast. The Pulfrich effect was investigated using computerized pendulums.

Results: Stimulus parameters required to generate maximal BI differ from those for maximal binocular summation (BS). The phase shift required to reverse the Pulfrich effect was proportional to the strength of the ND filter used, and the implicit time measured with VEPs and calculated with the PE correlate.

Conclusion: It appears separate neural generators are responsible for BI and BS.

LIST OF ABBREVIATIONS AND SYMBOLS USED

ANOVA	Analysis Of Variance
ARMD	Age Related Macular Degeneration
AUTC	Area Under The Curve
BI	Binocular Inhibition
BS	Binocular Summation
BSV	Binocular Single Vision
C	Contrast
CCW	Counter Clock Wise
cGMP	Cyclic Guanosine Monophosphate
cpd	Cycle Per Degree
CW	Clock Wise
DLS	Differential Light Sensitivity
DVD	Dissociated Vertical Deviation
ETDRS	Early Treatment Diabetic Retinopathy Study
IT	Implicit Time
L	Luminance
LE	Left Eye
LGN	Lateral Geniculate Nucleus
M	Magnocellular
mfVEP	Multifocal Visual Evoked Potential
MS	Multiple Sclerosis
ND	Neutral Density
ON	Optic Neuritis
P	Parvocellular
PE	Pulfrich Effect

PR-VEP	Pattern Reversal Visual Evoked Potential
RE	Right Eye
SR	Summation Ratio
VEP	Visual Evoked Potential
'	Minute Of Arc
"	Second Of Arc

CHAPTER 1: INTRODUCTION

1.1 Background

Binocular vision literally means vision with two eyes, and various types of binocular interactions can occur. In individuals with good vision in both eyes, numerous advantages exist and promote the use of the two eyes together. The presence of the second eye makes vision sharper, clearer, and more sensitive (Steinman, Steinman, & Garzia, 2000). This advantage is called binocular summation (BS), which is an increase in binocular visual performance when compared to monocular visual performance. Subjective reports of BS have been shown using Snellen visual acuity (Bdrdny, 2009), contrast sensitivity (Legge, 1984), absolute luminance thresholds (De Silva & Bartley, 1930), critical flicker frequency (Crozier & Wolf, 1941), and performance tasks (Jones & Lee, 1981). However, the use of the two eyes together does not always yield superior binocular performance (Donzis, Rappazzo, Burde, & Gordon, 1983). In certain eye conditions where vision is lower in one eye (i.e. optic neuropathy, maculopathy, amblyopia, cataracts), using both eyes together can be a disadvantage resulting in a decrease in binocular performance when compared to monocular visual performance in the better eye; this is called binocular inhibition (BI). Subjective reports of BI have shown improvement of visual performance when the eye with poorer vision is closed. Objective studies of BS and BI have compared the amplitude of the binocular and monocular visual evoked potentials (VEPs). In healthy eyes with equal visual stimulus presented to each eye, results consistently show the binocular VEP amplitude is larger than the monocular VEP amplitude. However, in healthy eyes with unequal visual stimulus presented to each eye, by means of a neutral density (ND) filter in front of one eye, the binocular VEP amplitude becomes equal to or smaller than the monocular VEP amplitude (Katsumi, Tanino, & Hirose, 1986a; Pardhan, Gilchrist, Douthwaite, & Yap, 1990).

BS may be explained purely on statistical grounds, given that the probability of two eyes detecting a target would be greater than the probability of one eye detecting it (Pirenne, 1943). However the performance of the two eyes together can exceed what is

predicted by probability summation, and is interpreted as evidence for some sort of genuine neural interaction (Blake & Fox, 1973).

The fact that the world does not appear half as bright when one eye is closed shows BS is more complex than just the linear sum of two inputs. Fechner's paradox refers to the observation that a bright stimulus viewed monocularly appears brighter than when it is viewed binocularly with a ND filter in front of one eye (Fechner, 1860). Although under binocular viewing conditions more total light is received, the stimulus appears dimmer compared to the unfiltered eye alone. It seems as though the perceived brightness is determined by some average of the two monocular inputs.

Using VEPs, Pardhan et al. (1990) reported under binocular conditions in the absence of a ND filter, maximum amount of BS of VEP amplitude was obtained. With increasing monocular retinal illumination differences induced by ND filters, the amount of BS decreased until BI was produced. A further difference in retinal illumination between the two eyes produced suppression of the filtered eye.

Another interesting phenomenon, called the Pulfrich effect (PE), can also occur under binocular conditions when visual input is decreased to one eye. The PE is defined as the binocular perception of a small target oscillating in the frontal plane as moving elliptically in depth (Pulfrich, 1922). This can be achieved experimentally by placing a ND filter in front of one eye (similar to Fechner's paradox) and it can also occur spontaneously with various eye conditions. The PE is most often measured qualitatively, however, a computer-based pendulum test has recently been used in attempts to quantify an induced PE (Stadelmann, Jiang, & Mojon, 2009). The effect was neutralized, and thus quantified, by changing the phase shift between the pendulums viewed with the right and left eye.

Both Fechner's paradox and the PE are visual phenomena experienced under binocular viewing conditions and can be experimentally induced with a ND filter over one eye, or can occur spontaneously in individuals with lower vision in one eye. Although the outcome measurements of these phenomena are different, it is of interest if the quantification of the PE will correlate with the objective measurements of the VEP.

1.2 Purpose Of The Study

The purpose of this study is to explore new methodologies to quantify BI using VEPs (to study Fechner's paradox) and computerized pendulum experiments (to study the PE). Furthermore, it is of interest to explore the possible neural generators of BS and BI.

1.3 Hypothesis And Research Questions

Little is known about BI and the visual conditions best susceptible to elicit the phenomenon. The hypothesis of this research is that unequal vision can induce binocular inhibition.

1) With the use of VEPs we want to determine: What are the VEP stimulus parameters that influence the strength of binocular inhibition in a paradigm using Fechner paradox? Of specific interest are the check size, location and contrast of the stimulus.

2) With the use of computerized pendulum experiments we want to determine: Can the Pulfrich effect be quantified reliably in relation to the interocular difference created by the interposition of neutral density filters?

3) Can the delay in VEP timing be correlated to the delay observed in the Pulfrich effect?

CHAPTER 2: LITERATURE REVIEW

2.1 The Visual Pathway

Light enters the visual system through the eye and strikes the retina located at the back of it. The retina is composed of specialized cells called photoreceptors (cones and rods), which convert light energy into neural activity. When light strikes the light-sensitive pigment in the rods or cones, it changes form, and thus activates a G protein called transducin. Transducin then activates another enzyme, phosphodiesterase, which reduces the conversion rate of cyclic guanosine monophosphate (cGMP); the reduction in available cGMP in turn reduces the number of open sodium channels in the membrane of the rod cells, thus hyperpolarizing the cell (Remington, 2012). As a result, fewer molecules are released into its synapse with the binocular cells. The receptive field of bipolar cells has two components: a central receptive field composed of the information that travels directly from the photoreceptors to the bipolar cell, and a peripheral receptive field composed of information that arrives via the horizontal cells. Membrane potentials are then synapsed onto retinal ganglion cells. Axons of the retina's ganglion cells collect in a bundle at the optic disc and emerge from the back of the eye to form the optic nerve, which is the pathway that carries the nerve impulses from each eye to the brain (Remington, 2012).

The optic nerves of the two eyes intersect at the optic chiasm, where axons from the nasal side of each retina crosses sides, so the left half of the visual field is perceived by the right cerebral hemisphere (and vise versa, Figure 1). Axons from the temporal side of each retina do not cross sides and proceed straight through the optic tract. From here, the vast majority of nerve fibers project to the lateral geniculate nucleus (LGN), which serves as the main relay in the pathway to the primary visual cortex. The projection from the LGN to the visual cortex is called the optic radiation. The primary visual cortex is where the brain begins to reorganize the image from the receptive field of the retina and is located in the most posterior portion of the brain's occipital lobe.
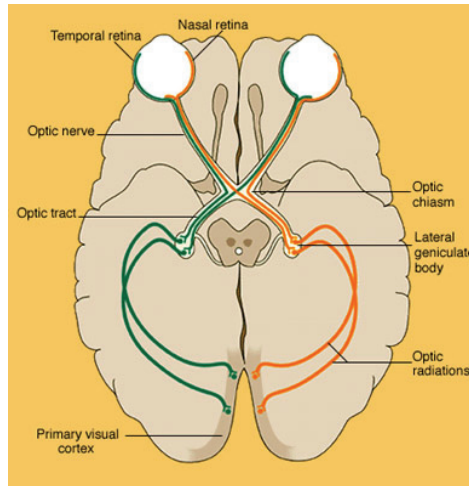
Figure 1. The visual pathway. Axons from the right half of each retina (left visual hemifield) project to the right visual cortex and those from the left half of each retina (right visual hemifield) project to the left visual cortex. (Adapted from Trobe, 2009).

2.2 Cellular Structure Of The LGN And Visual Cortex

Much research has been done on the cellular architecture of the LGN and the primary visual cortex. Anatomically, the LGN provides a good opportunity for information from the two eyes to come together at the level of the single cell, however this does not occur. The inputs from each eye are separated into layers in the LGN and geniculate cells are strictly monocular (Howard & Rogers, 1995). It is not until the signals reach the visual cortex that information from the right eye (RE) and left eye (LE) come together. Each geniculate axon ascends through the layers of the visual cortex terminating in layer 4C, and each group of cells in layer 4C receives inputs from only one eye. These inputs are then relayed to cells in other layers in the same vertical column of cortical tissue, and most of these cells also receive input from the other eye through cells in layer 4C in neighbouring columns (Howard & Rogers, 1995). Hubel and Wiesel (1962) first demonstrated the presence of cells in the primate visual cortex that responded preferentially to visual stimulation in both eyes as opposed to one eye alone, these are now known as binocular cells.

Columnar organization exists for visual modalities such as orientation and color. Cells sharing information from both eyes, responding to all orientations and colors form a hypercolumn. A hypercolumn is a generic structure seen in the cortex that is stretched

vertically through the layers of the cortex and is the base functional unit of the visual cortex. Each hypercolumn occupies about 1mm^2 of the cortical surface (Howard & Rogers, 1995).
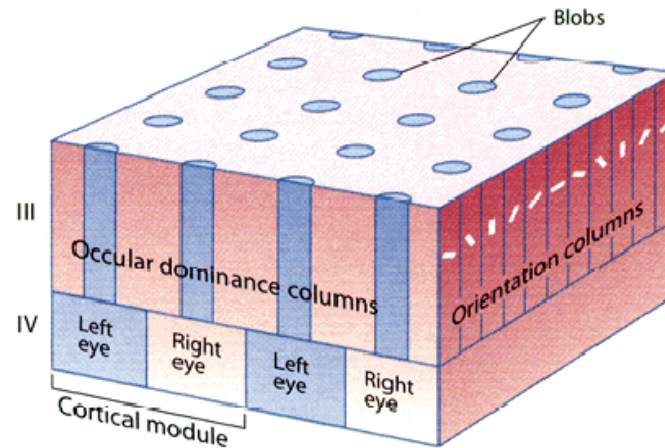
Figure 2. Schematic of a hypercolumn in the primary visual cortex. Alternating columns of neurons sensitive to input from the left and right eyes form ocular dominance columns. Neurons throughout orientation columns respond to stimuli oriented at the same angle, while color sensitive neurons form blob channels (Adapted from Gazzaniga, Ivry, and Mangun, 1998).

Other levels of cellular organization exist within the visual cortex. Horizontal stratification is based on various types of neurons that specialize in receiving or sending neural information, and is also divided radially into a multitude of columns in which all the neurons respond to the same characteristic of a given point in the visual field. The columns thus form functional units that run perpendicular to the surface of the cortex. Finally, monocular blob cells are arranged in lines and centered on an ocular dominance band in layer IV C and are sensitive to the wave length of light (color).

Each binocular cell in the visual cortex has two receptive fields, one from the RE and one from the LE. Each receptive field is similar with regards to its position on the retina, complexity, orientation, end stopping, and directional selectivity (Hubel & Wiesel, 1962). The similarities in receptive fields allow the visual system to match the images from the two eyes, which is a prerequisite for the creation of a unified binocular field. This means all visual stimuli located on the horopter (the locus of all object points that are imaged on corresponding retinal elements at a given distance) (Von Noorden, 1985)

are perceived optimally by binocular cells. However, visual stimuli located slightly in front of and behind the horopter plane are still perceived as single despite the fact they are not captured by retinal cells that are in identical positional correspondence. Cortical cells are good detectors of this disparity and this forms the basis of stereopsis (true depth perception within the so-called Panum's area (see next section). There are two plausible hypotheses for how cortical neurons encode binocular disparity. The traditional view is position encoding, in which the RE and LE receptive fields of a neuron have the same spatial profile but their positions are not necessarily at retinal correspondence (Nikara, Bishop, & Pettigrew, 1968). Alternatively, binocular disparity can be encoded through a difference in receptive field profile (phase) between the two eyes without receptive field position disparity (DeAngelis, Ohzawa, & Freeman, 1991).

2.3 Binocularity

The two eyes are positioned in different locations in the head separated by an interocular distance of approximately 50-75mm, providing two different vantage points for the object of regard (Dodgson, 2004). This parallax provided by the different position of the two eyes gives rise to depth perception. Binocular single vision (BSV) can be defined as the state of simultaneous vision that is achieved by the coordinated use of both eyes so that separate and slightly dissimilar images arising in each eye are appreciated as a single image by the process of fusion at the cortical level (Barlow, Blakemore, & Pettigrew, 1967). Fusion is the successful blending of the two similar images from each eye into one composite image, but fine binocular perception of depth is not necessarily perceived in conditions of fusion. Stereopsis is the highest binocular processing that arises from relatively small horizontal disparities and gives rise to the conscious experience of depth (Von Noorden & Campos, 2001). Stereopsis is the hallmark of binocular vision.

Normal BSV requires a clear visual axis, sensory fusion, and motor fusion (Bhola, 2006). A clear visual axis is necessary to produce a reasonably clear image in both eyes. Sensory fusion is the ability to appreciate two similar images, one with each eye, and interpret them as one blended image. For fine sensory fusion to occur, the images must be located on corresponding retinal areas and be similar in size, brightness and sharpness

(Von Noorden & Campos, 2001). Motor fusion is necessary to align the eyes in such a way that sensory fusion can be maintained. The stimulus for motor fusion eye movements is retinal disparity outside Panum's area. Panum's area is the region around the horopter in which single vision is present. To clarify: points lying on the horopter are seen as single but not in depth, points in Panums'a area are seen as single and in depth, and points lying outside Panum's area are seen as double (Pratt-Johnson & Tillson, 2001). Disparate retinal images can cause the eyes to move so that the images fall as near as possible onto corresponding retinal elements, these fusional movements eliminate disparity and the appearance of double images is prevented (Hershenson, 1999).

Normal binocular vision requires two normal monocular visual systems as well as normal interactions between these monocular systems (Huanh, Zhou, Lu, & Zhou, 2009). To develop and maintain binocular vision, certain anatomical and physiological factors must be present. Anatomically, the shape of the orbit, reciprocal innervation of the extra ocular muscles, and the presence of adjacent ligaments, muscles and connective tissues, results in the two eyes being situated in the orbit so that the visual axis is directed in the same direction. Physiologically, certain binocular reflexes are present which can be inborn or acquired as a result of appropriate stimulation. Binocular reflexes include a fixation reflex (orients the eyes onto a fixed target), refixation reflex (allows foveal refixation from target to target and maintenance of foveal fixation on a moving target), and the pupillary reflex (consensual constriction of the pupil in the response to light stimuli).

Other then the above-mentioned stereopsis, having two frontal eyes instead of one has further benefits. First, two eyes provide us with an extra eye that can be used as a spare if one is damaged or diseased. Second, the use of two eyes provides a larger field of view, allowing us to visualize more of the world around us. The human species has a maximum horizontal field of roughly 200° with two eyes, while a monocular field is limited to 160°. Since human eyes face forward, when the two eyes are used together the visual field overlaps by about 120°, this area is called the binocular visual field and is flanked on either side by monocular fields of roughly 40° each (Steinman et al., 2000). Third, having two frontal eyes gives rise to BS which in general means the performance of the two eyes working together is superior to that of either eye on its own.

The advantage of binocular vision comes at a cost, it requires the eyes to be aligned correctly, moving together, and be equally sensitive. Disrupted eye alignment (strabismus) can lead to diplopia (double vision) or suppression (ability to ignore the image from the deviated eye). Binocular diplopia is the perception of two images from one object (Evans & Doshi, 2001). This can be troublesome as individuals have difficulty judging which image is the true image. Closing one eye can alleviate binocular diplopia. The other compensatory mechanism to avoid binocular diplopia is suppression of the input from the deviated eye. Suppression occurs when the brain inhibits the cortical input from the deviated eye, so that when both eyes are open, the image from that eye is not perceived. If that eye is forced into use by covering the fixing eye, vision will appear normal. This type of suppression is a function of cortical plasticity that is present during the critical period of visual maturation (Von Noorden, 1985). If the suppression is longstanding and is not treated during the critical period it can lead to amblyopia, which is defined as a decrease of visual acuity in one eye caused by abnormal binocular interaction or occurring in one or both eyes as a result of pattern vision deprivation during visual immaturity, for which no cause can be detected during physical examination of the eye(s) and which in appropriate cases is reversible by therapeutic measures (Von Noorden, 1985).

Amblyopia occurs in approximately 2-2.5% of the general population and is the most common cause of decreased vision in childhood (Von Noorden, 1985). Classification of amblyopia includes strabismic amblyopia (caused by active inhibition of the deviating eye), anisometropic amblyopia (unequal refractive error), and visual deprivation amblyopia (under stimulation of the retina often due to opacities of the ocular media). Organic amblyopia is considered a different form of amblyopia that is caused by an irreversible defect in the afferent visual system that prevents the eyes from acquiring standard visual acuity (Von Noorden, 1985).

Disruption of the cortical binocular process can occur through other dysfunctions of the monocular input, such as unilateral or asymmetric optic neuropathy. More specifically, optic neuritis (ON) is an inflammatory condition of the optic nerve characterized by swelling and destruction of the protective myelin sheath that covers and insulates the optic nerve (Menon, Saxena, Misra, & Phuljhele, 2011) resulting in

temporary unilateral vision loss (Chan, 2007). ON commonly develops due to an autoimmune disorder that may be triggered by a viral infection, and can be an indication of multiple sclerosis (MS). Objective VEP tests are often useful in cases of ON, because compared to the unaffected eye, the VEP recording of the affected eye will have a longer implicit time (IT) and a lower amplitude (Atilla et al., 2006).

Age related macular degeneration (ARMD), optic atrophy, cataracts, and ischemic insult of the precortical pathways are other examples of visual disorders that may cause asymmetry.

2.4 Definitions Of Binocular Interactions

Several possibilities exist for the additive outcomes as a result of visual processing (Figure 3): 1) no summation refers to the case where the output of the common pool is equal to one afferent input, 2) complete/linear/additive summation refers to the case where the output of the common pool is the sum of the two afferent inputs (two eyes are twice as good as one), 3) facilitation refers to the case where the output of the common pool is greater than the sum of the two afferent inputs, 4) partial summation refers to the case where the output of the common pool is less than the sum of the afferent inputs yet greater than the response produced by a single input, 5) inhibition refers to the case where the output of the common pool is equal to or less than the response generated by a single input (the use of the second eye degrades the sensitivity of the fellow eye relative to its monocular sensitivity).

For this thesis, binocular summation (BS) is a collective term that can include the previously defined complete summation, facilitation or partial summation (2, 3,4). Binocular inhibition (BI) is represented by the previously mentioned definition of inhibition (5).

Ocular Input	Visual Cortex Output

+1.00 = No Summation(1)
+2.00 = Complete Summation(2)
+2.40 = Facilitation(3)
+1.80 = Partial Summation(4)
+0.40 = Inhibition(5)

Right Eye Input = +1.00
Left Eye Input = +1.00
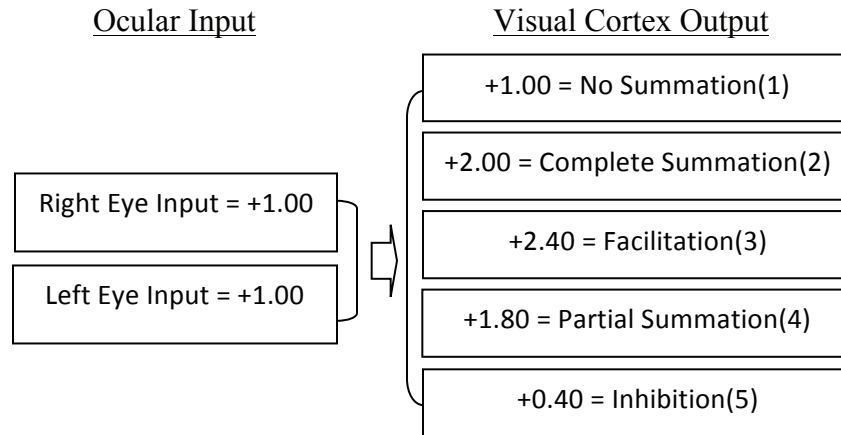
Figure 3. The addition of monocular inputs (left) can have various outputs from the visual cortex (right).

2.4.1 Probability Summation

As described above, the use of the two eyes together can be superior to that of either eye on its own, but what accounts for this? Various suggestions have been investigated as to whether superior binocular performance is simply a matter of statistics, or it is due to a physiological process that enhances the input from the two eyes. The probability theory suggests improvement of binocular vision occurs since two independent detectors (eyes) have a greater probability of detecting a stimulus compared to only one. For example, if each eye alone had a 0.6 probability of detecting a stimulus, the statistical probability of detecting the stimulus using two eyes would be:

$$P_b = P_r + P_l - (P_r \times P_l) = 0.6 + 0.6 - (0.6 \times 0.6) = 0.84$$

The improvement from one eye (0.6) to two eyes (0.84) represents a 1.4 fold increase. This was observed when Pirenne (1943) tested the monocular and binocular thresholds of detection of a dim light and found the binocular threshold was about 1.4 times lower than the monocular threshold.

2.4.2 Neural Summation

If the performance of the two eyes together exceeds that predicted by probability summation, the data is interpreted as evidence for some sort of neural summation to further enhance binocular vision (Blake & Fox, 1973). Neural summation occurs when

the two neural pathways stimulate a single cortical binocular neuron. By comparing the absolute light detection threshold in both binocular and monocular viewing conditions, Matin (1962) showed that optimal BS occurred when corresponding retinal points were stimulated with like targets, and when stimuli were presented to the two eyes simultaneously (within ~100msec). Martin concluded the two eyes were not independent detectors, and neural summation between the two eyes operated at some common sensory path in the visual system.

2.4.3 Signal To Noise Ratio

Another possible explanation of BS is the effect of background neural noise. Theoretically, neural noise (intrinsic electrical fluctuations assumed to be random and uncorrelated) from each eye would differ and partially cancel when combined, whereas visual signals from each eye would be similar and be added together. When the neural signal and noise are combined, an increase in signal-to-noise ratio is the result, which would improve the binocular threshold. Campbell and Green (1965) predicted this process alone would improve the binocular threshold by a factor of $\sqrt{2}$ (or 1.4) compared to the monocular threshold because sensitivity is proportional to the square root of the number of detectors. Although the assumptions underlying this model may not be entirely true (i.e. noise added together from the two eyes may not be uncorrelated), the model does predict threshold BS quite well.

2.5 Binocular Brightness Summation And Fechner's Paradox

Binocular combination of luminance has been studied for over 150 years, often by the means of psychophysical experiments. The sensitivity measure most widely used in BS research is the absolute threshold, where a small flash of light is presented to the fovea or periphery of one or both eyes and the minimum luminance and/or duration for the detection of the flash was determined (Blake & Fox, 1973). Although sensitive experiments are required to determine suprathreshold stimuli, a simple example of this can be done if one notes the brightness of an object using both eyes, and then observes if the brightness of the object appears reduced when one eye is closed. It is evident that there is no dramatic decrease in perceived brightness under monocular conditions, and

certainly no doubling of brightness under binocular conditions. The quadratic summation equation below predicts BS for luminance (B) and holds true when the RE and LE are equally stimulated (Blake & Fox, 1973):

$$R^2 + L^2 = B^2$$

However, this equation does not hold true if each eye is stimulated differently (ND filter placed before one eye), because Fechner's paradox demonstrates that binocular brightness is not greater than monocular brightness. If the binocular brightness is less than the monocular brightness, then some form of averaging process must have taken place. Fechner's paradox suggests the presence of an interocular inhibition mechanism and the quadratic summation model cannot account for this inhibitory phenomenon.

Fechner (1860) has done the majority of the early work on binocular brightness experiments and has been credited with what is now known as Fechner's paradox, as described above and depicted in Figure 4.
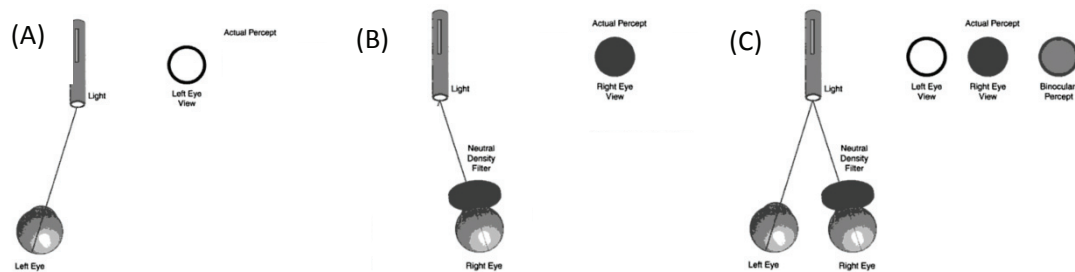
Figure 4. Fechner's paradox: A) a light is viewed under monocular conditions with the LE and the brightness perception is seen as bright, as indicated in the circle, B) a ND filter is placed in front of the RE under monocular conditions, the brightness perception is seen as dim (proportional to the ND filter strength), as indicated in the circle, C) the light is viewed with both eyes together, the light is seen as dimmer then when compared to the unfiltered eye alone (Adapted from Steinman et al., 2000).

Fechner's paradox for brightness is also evident in other areas of visual investigation. Using sensitivity to measure contrast, Gilchrist and McIver (1985) placed a ND filter in front of one eye and demonstrated that the binocular sensitivity is less than the sensitivity of the unfiltered eye. Similar results were obtained by Gottesman, Rubin, and Legge (1981) when they presented images with different suprathreshold contrasts to

the two eyes. Using VEPs to investigate visual performance when monocular sensitivities are unequal is a particular interest of this current study, and has been previously studied by Spafford and Cotnam (1989), and Heravain-Shandiz, Douthwaite, and Jenkins (1991).

2.6 Visual Evoked Potentials (VEPs)

Due to the high level of interconnectivity, cortical neurons tend to fire in synchrony, which generate fluctuating electrical fields that can be detected at the surface of the brain or on the scalp. Electrical fields generated by the visual cortex are known as VEPs. Pyramidal cells that run at right angles to the cortical surface form an electrical dipole when firing (pair of equal and opposite electric charges, the centers of which do not coincide) and are the most likely source of VEPs (Howard & Rogers, 1995). Since the visual cortex is activated primarily by the central visual field (magnification factor), the VEP depends on the functional integrity at all levels of the visual pathway (retina, optic nerve, optic radiations, and occipital cortex). Typically, the location, magnitude and form of the VEP response is related to the parameters of the visual stimulus.

The main parameters measured with VEPs are its amplitude and IT. Amplitude (μV) indicates "how much" information reaches the visual cortex, while IT (ms) indicates the time required for the electrical signal to peak. The general form of a VEP recording shows a prominent negative component (N1) at ~75 ms, a larger positive amplitude component (P1) at ~100 ms, and a more variable negative component (N2) at ~135 ms (Figure 5). Generators of early VEP components are attributed to the visual cortex, but the exact anatomical location of the generators is poorly understood. The source of the N1 component has been suggested to be the striate cortex, Brodmann's area 17 (Jefferys, 1977) or area 18 (Halliday & Michael, 1970), while the source of the P1component has been attributed to the extrastriate cortex areas 18 and 19 (Halliday & Michael, 1970), or to areas 17 and 18 (Maier, Dagnelie, Spekreijse, & van Dijk, 1987). The N2 component is generated from several areas including a deep source in the parietal lobe (Di Russo, Martínez, Sereno, Pitzalis, & Hillyard, 2002).
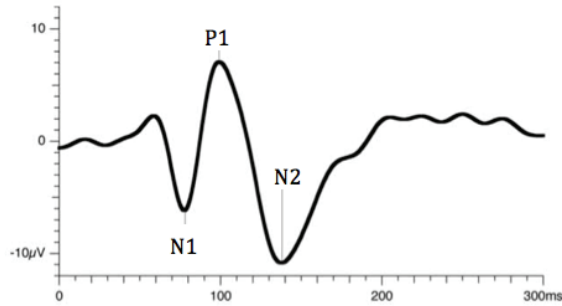
Figure 5. Components of a VEP waveform. (Adapted from Creel, 2011).

Checkerboard pattern reversal visual evoked potentials (PR-VEPs) are the preferred stimulus for clinical use, as they are less variable in waveform and timing. The International Society for Clinical Electrophysiology of Vision (Odom et al., 2010) recommends measuring the amplitude of the P1 from the preceding N1 trough to the P1 peak, since the P1 is usually a prominent peak that shows little variation between subjects, minimal within-subject interocular difference, and minimal variation with repeated measures over time.

Conventional VEPs have been recorded in clinic and laboratory settings for many years. The multifocal VEP (mfVEP) is a newer technique introduced by Baseler, Sutter, Klein and Carney (1994), which allow VEP responses to be recorded simultaneously from many regions of the visual field. mfVEPs use the same electrodes and amplifiers as conventional VEPs , however the display method of stimulation and the analysis of the raw recordings differ (Figure 6). The common stimulus for mfVEPs is a dartboard arrangement with each sector a contrasting reversing check pattern. The scaled circular checkerboard patterns are used to compensate for the magnification of the cortical representation of the central visual field. The mfVEP responses are recorded as a separate waveform for each testing region, and can be compared between eyes or to normative data. Each of the individual mfVEP responses in the array is derived from a correlation between the stimulation sequence of a particular sector and the overall, single, continuous VEP recording.

(A)   (B)
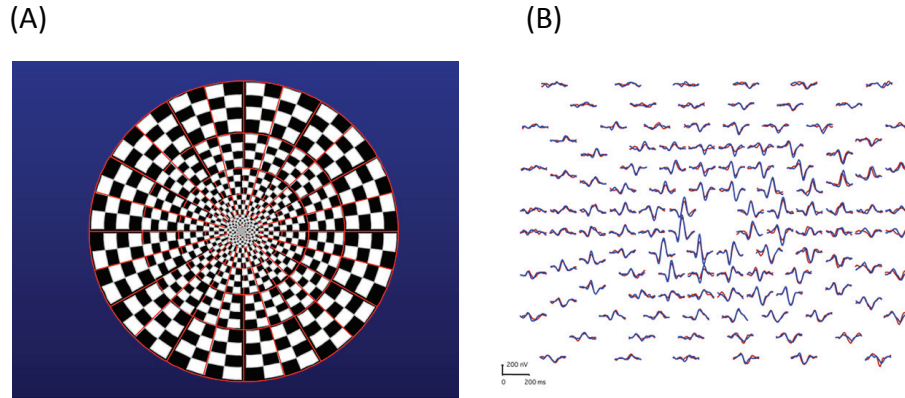
Figure 6. A) Schematic of dartboard stimulus used for mfVEPs. B) Schematic of recordings obtained from mfVEP stimulation (traces of the right eye in red, left eye in blue). (Adapted from Creel, 2011).

2.7 VEPs And Binocular Vision

Since binocular interactions occur for the first time at the level of the visual cortex, VEPs are an appropriate method to evaluate these interactions. In investigations of BS and BI using VEPs basic comparisons are made: the amplitude of the VEP response evoked by monocular stimulation of each eye is compared with the amplitude evoked by binocular stimulation (ratio=binocular/monocular), secondly, the response when the two eyes receive identical stimuli is compared to the response of when the stimuli are uncorrelated. The idea is that only similar stimuli summate their inputs, whereas dissimilar stimuli compete for access to binocular cells.

Trick, Dawson and Compton (1982) used VEPs to explore Fechner's paradox in subjects with normal binocularity using ND filters ranging from 0.3 to 2.0 log units to establish an interocular luminance difference. The stimulus used was a checkerboard pattern reversing at 3.75 Hz, contrast of 74%, and check size 14'. If the interocular luminance difference was less than 0.6 log units, the amplitude of the binocular response was greater than either corresponding monocular response, indicating BS, whereas if the interocular luminance difference was equal to or greater than 1.3 log units, the amplitude of the binocular response was below the level of either corresponding monocular responses, indicating BI.

Katsumi et al. (1986a) studied the effect of mean luminosity change on VEPs amplitude response using ND filters ranging from 0.2 to 3.0 log units. The checkerboard pattern reversed at 3Hz, the contrast level was 30%, check size 25', and mean screen

16

luminosity ~50cd/m^2. Results showed when the interocular luminosity difference was small (mild filter 0.3 log units), the binocular VEP amplitude was generally larger and peaked earlier than the monocular VEP (BS), and as the luminosity difference increased (stronger filter), the amplitude of the binocular VEP became equal to or smaller than that of the monocular VEP (BI). A further increase in luminosity difference caused the binocular VEP to return to monocular value. The authors suggested the binocular system might have a 3-phase response to differences in interocular luminosity. When the interocular luminosity difference is small, the binocular system will compensate for the difference (BS). When the interocular luminosity difference increases, the eyes interact and the binocular VEP amplitude becomes smaller than the monocular VEP amplitude (BI). When the interocular luminosity difference is too large there is no binocular interaction due to the large differences in visual input and suppression occurs as the monocular and binocular VEP become close to equal (total suppression).

Likewise, Pardhan et al. (1990) also investigated the electrophysiological binocular response to differences in monocular retinal illuminances using ND filters ranging from 0.3 to 3.0 log units. The checkerboard pattern reversed at 2Hz, contrast 96%, check size 41', and the mean screen luminosity was ~40cd/m^2. Results showed under binocular conditions in the absence of a ND filter, maximum BS was produced. Binocular sensitivity decreased to monocular level at ND filter strength 0.6 log units, and BI was maximal with a ND filter strength of 2.0 log units. Suppression of the filtered eye occurred when the ND filter exceeded 2.7 log units.

2.7.1 Size Of Pattern Elements

Dimensions of the individual checks are described by the visual angle subtended on the retina. Checks are traditionally expressed in minute of arc ('). The following equation can be used to calculate the visual angle of pattern elements:

$$a = \tan^{-1}(W/2D) * 120$$

where a is the visual angle in minute of arc, W is the width of the check in millimeters, D is the distance of the pattern from the corneal surface in millimeters, and $\tan^{-1}$ is arctangent expressed in degrees.

As a part of a series of experiments on the objective evaluation of binocular function with PR-VEPs, Katsumi, Hirose, and Tanino (1988) investigated the effect of various check sizes ranging from 7.5' to 100' under monocular and binocular viewing conditions of normal subjects. Results showed binocular VEP amplitudes were larger than the monocular VEP amplitudes at all spatial frequencies; the average VEP amplitudes were largest with 25' but not significantly different compared with the 12.5' and 50'. As check size increased or decreased from 25', the VEP amplitudes became smaller, resulting in an inverted U shape curve when VEP amplitude is plotted as a function of check size. However, when the binocular ratio was calculated (binocular/monocular amplitude), the smallest check size (7.5') showed the highest amount of BS and the largest check size (100') showed the lowest amount of BS (BS decreased as check size increased).

Adachi and Chiba (1979) also investigated the effect stimulus size (ranging from 4' to 111') on the monocular and binocular VEP amplitudes. Results showed the monocular and binocular VEP amplitudes were largest using 8', and binocular VEP amplitude showed a 20-30% increase compared to monocular (BS). Mitsuyu and Yanashima (1982) used check sizes ranging from 9.5' to 19' to examine monocular and binocular VEP amplitudes, and results showed BS was highest when the smallest check size of 9.5 was used. di Summa et al. (1997) studied the monocular and binocular amplitudes of PR-VEPs in response to different check sizes (15', 21', 38', and 85') in subjects with normal vision. It was found that binocular VEP amplitudes are higher than the monocular VEP amplitudes, and this effect was more pronounced using a small check size.

2.7.2 Contrast

Contrast is the degree to which light and dark areas of an image differ in brightness or in optical density. Contrast sensitivity is a measure of the ability to discern between luminance of different levels in a static image. For the purpose of this study, contrast is measured with a periodic non-sinusoidal luminance variation, where contrast is defined by the difference between the maximum and minimum luminance divided by

the sum of them. This type of contrast is referred to as Michelson Contrast (Barten, 1999).

Katsumi, Tanino, and Hirose (1985) used PR-VEPs to investigate the effect of stimulus contrast ranging from 20 to 95% under monocular and binocular viewing conditions. Results showed binocular VEP amplitudes were larger than monocular VEP amplitudes at all levels of contrast, the monocular VEP amplitude increased with increasing contrast (peaked at 50 to 80%), while the binocular VEP amplitude peaked at low contrast (20%) and decreased slightly with increasing contrast. BS was highest at 20 to 30% contrast and also decreased with increasing contrast. These results are similar to that of Mitsuyu and Yanashima (1982) who demonstrated higher levels of BS occurred with lower contrast levels (tested 11, 33, and 70%).

The magnocellular and parvocellular pathways (M and P pathways) are the major pathways of the visual system, accounting for most of the axons that leave the retina. The M and P pathways are anatomically and physiologically distinct: the M ganglion cells have a large cell body and project to layers 1 and 2 of the LGN, while the P ganglion cells have a smaller cell body and project to layers 3 to 6 of the LGN. Furthermore, the M pathway is tuned for low contrast, low spatial frequency, high temporal frequency information that is insensitive to color and has a transient response, while the P pathway is tuned for high contrast, high spatial frequency, low temporal frequency information that is color selective and has a sustained response (Liu et al., 2006).

2.7.3 Retinal Location Of Stimulus

Although there have been many studies investigating central BS (see Blake & Fox, 1973), less is known about BS in the periphery. Wood et al. (1992) used a contrast detection task to investigate BS for central and peripheral viewing as a function of eccentricity (7° to 75°) and target size (6.5', 26', and 103') along the horizontal and vertical meridians (normal subjects 19-30 years old). Results showed BS measured approximately the same (~1.4) for all target size in the fovea, but varied in the periphery with different target sizes. With the smallest target, BS decreased with eccentricity, with

the mid size target BS remained constant, and for the large target BS increased with eccentricity. Pardhan (1996) used a light detection task to compare BS at various eccentricities (0°-40°) of older (44-68 years old) and younger (18-26 years old) subjects with healthy eyes. Results showed a slight decrease of BS with increasing eccentricity for both age groups. BS was higher in the younger group compared to the older group at all eccentricities, and maximal BS of 1.9 was obtained at the fovea.

Katsumi, Tanino and Hirose (1986b) explored the effect of stimulus location using PR-VEPs of 30% contrast and check size of 25' by placing borders of increasing width on the stimulation display to study central filed stimulation, while the peripheral field was studied by blocking out areas of increasing size on the center of the stimulus display (central scotoma). Results showed when the center stimulus was less than 2.0x2.0° there was no significant difference between the monocular and binocular VEP amplitudes, but when the center stimulus was equal or greater than 2.4x2.4°, the binocular amplitude was significantly larger than the monocular. The highest amount of BS occurred when the center stimulus field size was 4.0x4.0°. The amount of BS decreased steadily with increasing size of the central scotoma and the peripheral stimulus field did not show any significant BS (Katsumi et al., 1986b).

Mitsuyu and Yanashima (1981) also used VEPs to investigate BS, and found the amount of BS was higher at 2° eccentricity with a 9.5' check size then at 4° with a 19' check size. Contrary to these results, Tsutsui and Fukai (1980) found BS was higher at the periphery then at the fovea.

Several other studies have reported the effect of peripheral stimulus field of the PR-VEP on the monocular VEP amplitude. Harter (1970) examined the VEP amplitude responses to checkerboard patterns and the effect of check size as a function of retinal eccentricity and found the check size that elicited the greatest amplitude depended on eccentricity of the retinal stimulation. Small checks (subtending 15-30') evoked the greatest amplitude response in the foveal area, and when progressively more peripheral areas of the retina were stimulated (up to 7.5° of eccentricity), progressively larger check-size (up to 60') evoked the greatest amplitude. More recently Katsumi et al. (1986b) found the monocular and binocular VEP amplitudes produced from the central 3.2° was larger than that produced from the peripheral stimulus field outside of 3.2°.

2.7.4 Non Structured Stimulus

Engel (1969), Fry and Bartley (1933), and Leibowitz and Walker (1956), claim contours and contrast in the visual stimuli presented to one eye will have a suppressing effect on the brightness seen by the other eye, so that the greater the amount of contour and contrast, the greater the suppression of the total binocular brightness. Bolanowski (1987) investigated contourless fields (Ganzfeld) with magnitude estimation techniques. Results showed brightness estimates given for a binocular Ganzfeld stimulus looked twice as bright as a monocular one, but when a 2° contoured stimulus target was introduced, the brightness was not perceived as being twice as bright. Given these results, the author suggests the presence of a single continuous contour leads to averaging of the monocular inputs, therefore under Ganzfeld stimulation where contour information is absent, binocular brightness is perceived as high.

Given that Ganzfeld stimulation can produce high BS of brightness, it became of interest as to whether Fechner's paradox is obtained with this stimulus. Bourassa and Rule (1994) reported no clear evidence of Fechner's paradox when binocular brightness summation was large. It was suggested that given nearly complete binocular brightness summation in the absence of contours, the visual system favors targets with low spatial frequency, and increasing contour (which introduces higher spatial frequency components) may act to reduce binocular brightness summation (Bourassa & Rule, 1994).

2.8 Clinical Considerations Of Fechner's Paradox

In a clinical setting, it is rare for a patient to complain of seeing better with one eye compared to two, suggesting some form of binocular visual adaptation may account for the lack of visual symptoms (MacMillan, Gray, & Heron, 2007). Although patients with an interocular brightness difference that is too large to be overcome by binocular adaptation may be symptomatic. Unequal pupil size, uncorrected anisometropia, unilateral or asymmetrical cataract, amblyopia and optic neuropathy are examples of deficient binocular vision where BI may occur in the absence of BS (Donzis et al., 1983).

Most research in amblyopia has focused on monocular defects of the amblyopic eye, but studies have also shown binocular vision is abnormal in amblyopia (Goodwin &

Romano, 1985; Holopigian, Blake, & Greenwald, 1988). Clinically, binocular assessment of visual acuity and other visual tasks appears to be the most appropriate measure of a person's vision, since a person functions with both eyes open on a day-to-day basis. It has been noted that in many clinical situations, the binocular measurement is often omitted when evaluating an amblyope, on the assumption that the amblyopic eye does not significantly contribute to binocular performance (Pardhan & Gilchrist, 1992). A study by Lanthony (1989) reported Fechner's paradox was abnormal in 78% of amblyopic subjects. Abnormal responses included monocular abolition (the paradox was not seen with a ND filter over one eye only- typically when filter was over the better seeing eye), binocular abolition (the paradox was not seen with a ND filter over either eye), and inversion of Fechner's paradox (binocular with ND filter appears brighter then the better monocular eye).

BS of visual acuity and low contrast stimulation is often reduced by ON and can lead to BI. BI is an important factor in the visual experience of a MS patient and may explain why some prefer to patch or close one eye in the absence of diplopia or strabismus, and it can also provide insight as to how visual function in a low contrast settings such as night time driving night be altered in patients with MS (Pineles et al., 2011). Furthermore, BI (longer peak time) of VEP latency is observed when there is a large difference in peak latency between the two eyes. For this reason, some ON patient may complain of objects appearing to move elliptically in depth, have difficulty judging distances or difficulty with sports.

2.9 The Pulfrich Effect

Another interesting phenomenon occurs when visual input is decreased to one eye. The PE is defined as the binocular perception of a small target oscillating in the frontal plane (a pendulum) as moving elliptically in depth (Figure 7). This was first described by physicist Carl Pulfrich in 1922, and occurs when visual input is decreased to one eye under binocular viewing conditions. The PE can be observed by individuals with normal vision when a filter is placed in front of one eye (similar experimental conditions as Fechner's paradox) and an object is moved in a frontal plane. A right filtered eye will

see counterclockwise (CCW) path and a left filtered eye will see a clockwise (CW) path, as viewed from above (Diaper, 1997).
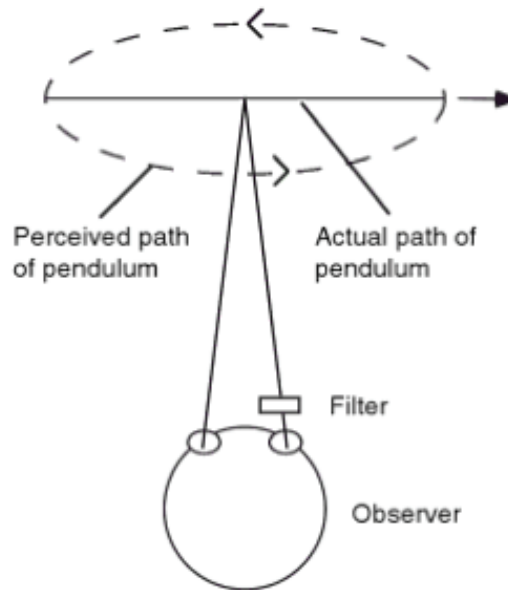
Figure 7. Schematic of the Pulfrich effect (top view). (Adapted by Harris and Jenkins, 2011).

The standard explanation is based on simple geometry. Due to the motion of the pendulum, the delay in the signal from the filtered eye reaching to visual cortex causes the position of the pendulum perceived by the filtered eye to lag behind that of the unfiltered eye in the trajectory of the pendulum at any given instant. This creates a simultaneous spatial disparity as the pendulum is seen at a different position by each eye simultaneously, this stimulates disparity tuned neurons to give rise to the perception of an object away from the plane of fixation (Pulfrich, 1922).

2.9.1 Literature Review

The size of the illusion experienced by the observer depends on a number of factors. Lit (1960) reported an increase in observation distance from the target resulted in a larger PE (larger ellipse perceived, increased depth). Later he reported that as the velocity of the target increased the size of the effect increased. Enright (1970) also reported both the apparent size and apparent velocity of the target increased as the

viewing distance increased. With regard to eye movements, some observers perceived an increase of the PE when the target was tracked, while other experience a more marked effect when the eyes were fixed on a central stationary target (Rogers, Steinbach, & Ono, 1974).

Retinal illumination is likely the most important factor influencing the size of the PE. A study by Vaphiades and Eggenberger (1997) reported only interocular luminance disparity needs to be present to induce the PE. This was accomplished by either reducing monocular illumination by placing a ND filter in front of one eye or constricting one pupil, or by increasing monocular illumination by dilating one pupil or directly illuminating one eye. With a 0.6 log unit ND filter in front of the LE, all subjects reported the pendulum moving in a CW direction, and with the filter in front of the RE subjects reported the pendulum moving CCW direction. Nine of ten subjects also reported the PE with monocular illumination (Welch Allen illuminator held 15 mm in front of the eye), however the effect was perceived as smaller and in the opposite direction as compared to the monocular placement of the ND filter (CW when the RE was illuminated and CCW when the LE was illuminated).

The PE was also observed after pharmacological anisocoria. With dilation of the left pupil with phenylephrine hydrochloride 2.5% and tropicamide 1% subjects reported the pendulum moving in a CCW direction (smaller than seen with just ND filter or monocular illumination), and when the intereye illuminance was enhanced by the addition of monocular illumination of the larger pupil, the PE appeared larger. With constriction of the left pupil with pilocarpine hydrochloride subjects reported the pendulum moving in a CW direction, and when the intereye illuminance was equalized by the addition of monocular illumination of the smaller pupil, no PE was perceived. The authors suggest that the PE relies on an interocular luminance disparity created by filtering or illuminating one eye and the physiologic mechanism probably lies in the latency difference of the two images perceived by the brain (Vaphiades & Eggenberger, 1997).

Many pendulum apparatus have been used to test the PE. If no pendulum apparatus is available, the swinging pen test can be done. For this test, the patient fixates on the examiner's thumb held close to the examiner's stomach, and a black pen is moved

from side to side in the frontal plane against the background of the examiner's white lab coat, the patient is asked to describe the oscillation of the pen and if an elliptical is perceived, and the thumb can be moved toward the patient to estimate the size of the illusion (Mojon, Rösler, & Oetliker, 1998).

A mechanical pendulum can be used for more precise quantification, examples include a steel bar with a letter attached to the bottom, a rod oscillating in the frontal plane in simple harmonic motion driven by a motor (Stadelmann et al., 2009), a string attached to the ceiling with a weight attached to the free end, or a simple pendulum which has the advantage of simple harmonic motion with gravity as a consistent driving force. With the mechanical pendulum, the patient is asked to indicate the apparent direction of the swinging pendulum (CW indicates a left sided defect, CCW indicates a right sided defect), and the magnitude of the PE can be estimated by positioning markers to indicate the apparent path of the ellipse (Thompson & Wood, 1993).

Computer based pendulums are also available and include a vertical bar moving back and forth sinusoidally along a horizontal path on a television monitor (Nakamizo, Nickalls, & Nawae, 2004), a dot of light produced by a sine wave of an oscilloscope (Tredici & Von Noorden, 1984), or simulation software to create swinging pendulums.

Stadelmann et al. (2009) compared a computer based pendulum test to a mechanical pendulum in order to determine if the computerized pendulum was an accurate method to measure the size of the PE. Their design of computerized pendulums was generated by 4 identical rectangles (12.5x1.5cm), within each rectangle, a black pendulum moved in simple harmonic motion with amplitude of 12cm and velocity of 0.226m/s at mid position. The movement in the top two rectangles had a phase shift of 90° compared to the bottom two rectangles. A base out prism was placed in front of each eye to fuse to the right and left half of the screen. When a ND filter (0 to 1.7 log unit) was placed in front of one eye to create the PE, the subject used arrows on a keyboard to neutralize the effect by adjusting the phase difference. The authors state three reasons as to why the exact quantification of the PE is important: 1) spontaneous elliptical movements of a small size were also found in normal subjects (Fleischhauer, Oetliker, Oetliker, & Mojon, 2002), 2) it will allow determination of the time course of a spontaneous PE, and 3) some patients require treatment with a ND filter in front of the

normal eye (Diaper, Dutton, & Heron, 1999). Stadelmann et al. (2009) were able to conclude a computerized pendulum allowing an interocular image phase shift can be used as an alternative to a mechanical pendulum for the quantification of the PE.

2.9.2 Clinical Considerations Of The Pulfrich Effect

Reports of a spontaneous PE have been documented with corneal opacities (Lanthony, 1984), traumatic anisocoria (Lanthony, 1984), unilateral cataract (Scotcher, Laidlaw, Canning, Weal, & Harrad, 1997), macular disease (Hofeldt, Leavitt, & Behrens, 1985), repaired retinal detachment (Lanthony, 1984), asymmetric pigmentary glaucoma (Tong, Borsting, & Ridder 3rd, 2001), optic neuritis (specifically when related to MS) (Rushton, 1975; Wist, Hennerici, & Dichgans, 1978), mid-facial injuries with unilateral traumatic optic neuropathy (Heron, McCulloch, & Dutton, 2002), pituitary tumors (Feinsod, Bentin, & Hoyt, 1979), and anisometropic amblyopia (Tredici & von Noorden, 1984).

Common symptoms experienced by patients with spontaneous PE include: oncoming traffic appear to swerve in towards the driver (Scotcher et al., 1997), difficulty parking (Diaper et al., 1999), fear of walking into people (Larkin, Dutton, & Heron, 1994), misjudgment when pouring liquids (Heron, Thompson, & Dutton, 2007), difficulty judging heights when placing objects on a flat surface (Diaper et al., 1999), and increased errors in recreational games such as tennis or golf (Heron et al., 2007; O'Doherty & Flitcroft, 2007). The majority of individuals who present with asymmetric visual input rarely complain of such symptoms, likely suggesting an adaptation mechanism. Symptoms of illusionary depth can usually be eliminated or much reduced by placing an appropriate ND filter in front of the eye with the shorter visual latency, so that its latency is increased to match that of the other eye (Plainis et al., 2012).

Diagnosis of the PE requires specific testing, as standard stereotests and typical VEPs will fail to detect this (Stadelmann et al., 2009). Tredici and Von Noorden (1984) found that gross stereopsis is required to appreciate the PE and a good correlation exists between the PE and random dot stereograms. However stereo blind subjects have been reported to see the PE despite their inability to see random dot stereograms (Thompson & Wood, 1993). To explain this disparity, the authors proposed the magno and parvo

cellular pathways (two depth mechanisms) are intact in normal subjects, whereas stereo blind subjects have lost their parvocellular pathway for central stereoscopic resolution but retain the low-resolution magnocellular pathway. Also, the lack of stereopsis does not exclude the possibility of binocular vision associated with some sensory and motor fusion (Thompson & Wood, 1993).

Predominately, assessment of the PE has been used to provide a sensitive means of detecting residual optic nerve defects (Feinsod et al., 1979). It has been found to be more sensitive than the relative afferent pupillary defect (Douthwaite & Morrison, 1975), however others have found that the relative afferent pupillary defect remains the most clinically sensitive test for optic neuropathy (Vaphiades & Eggenberger, 1997). The PE assessment (swinging pen technique) can be used as a quick and simple bedside test useful in confirming pathology in patients with subtle optic neuropathies, and especially in those with nonreactive pupils (Vaphiades & Eggenberger, 1997). Opinions of clinical application varies, some consider PE testing demanding (Remky, 1983), while others consider it is easy to administer and can be used in children as young as 3 1/2 years old (Tredici & von Noorden, 1984). Nevertheless, the computer based pendulum test to measure the PE has provided promising results as a method of quantifying the PE and it is less cumbersome and allows for easy variation of the stimulus parameters (Stadelmann et al., 2009).

CHAPTER 3: METHODS

3.1 Research Design

This study used a quasi-experimental design with independent measures. Five stimulus parameters were tested using electrophysiological VEPs: size of pattern elements (115', 29', 14', 6'), stimulus contrast (100%, 70%, 40%, 15%), stimulus location using VEPs (center and peripheral), stimulus location using mfVEPs (1.7°, 11.6°, 25°, 41° rings of eccentricity), and a Ganzfeld diffuse flash. These five stimulus parameters were tested under eight viewing conditions: monocular, binocular, and unequal binocular conditions induced by a ND filter (0.3, 0.6, 1.2, 1.8, 2.4, 3.0 log units) over the dominant eye. Additionally the psychophysical aspect of the PE was tested under five viewing conditions: binocular and unequal binocular conditions induced by a ND filter (0.3, 0.6, 1.2, 1.8 log units).

3.2 The Sample

3.2.1 Study Population

In total 44 participants who met the inclusion/exclusion criteria described in Table 1 took part in this study. Due to protocol refinements, we are reporting on 40 participants. Of these, some were tested on more than one stimulus parameter: one participant was tested with 3 stimulus parameters plus PE testing, 7 participants were tested with 2 stimulus parameters. The breakdown of number of participants per group is as follows and participants were assigned to stimulus parameters at random: check size (n=6), contrast (n=6), location using VEPs (n=11), location using mfVEPs (n=10), Ganzfeld (n=5), and PE (n=12).

3.2.2 Inclusion And Exclusion Criteria

The inclusion and exclusion criteria are summarized below in Table 1.

Table 1. Participant inclusion and exclusion criteria.

	Inclusion Criteria	Exclusion Criteria
General	• Between the ages 10 years to 65 years • Physically and cognitively capable of performing routine orthoptic testing and VEP testing • Ability to understand English • All in good health	• Presence of developmental delay or reduced co-operation • Extreme fatigue or inattentive behavior • Lack of consent
Eye Health	• Refraction within the past two years, wearing their most recently prescribed glasses for their refractive error • Free from organic ocular or neurological disease • Visual acuity better than or equal to 6/7.5 (20/25)	• History of ocular trauma • Manifest or latent nystagmus (shaky eyes) • Dissociated Vertical Deviation (DVD) • Optical media opacity (cataract)

To keep the population as homogenous as possible, the above inclusion and exclusion criterion were necessary. Individuals under 10 and over 65 were not eligible for this study because testing requires participant cooperation for an extended period of time. In an attempt to eliminate any confounding variables in the results, participants with organic amblyopia, nystagmus, cataracts, ocular trauma, DVD, or history of laser treatment to the eye were excluded. No participants were excluded on the basis of culture, religion, or sex.

3.2.3 Sample Size Determination

In a large normative sample taken from investigations carried on in the Visual Electrodiagnostic Laboratory at the IWK Health Centre, there is a normal interocular amplitude difference of $1.4 \pm 1.1 \mu V$. With an $\alpha = 0.05$ and statistical power of 0.80, a sample of 5 (per stimulus parameter) is required to test for an interocular difference of $2.5 \mu V$ (mean + 1 SD) or greater (~12%).

3.2.4 Recruitment Of Participants

      Participants were recruited by word of mouth between September 2010 and April 2011. Participants were informed of the study and contacted the principal investigator if they were interested in participating. In addition, a poster advertisement (Appendix B) was displayed in the Psychology department at Dalhousie University and posted online at www.psyc.me.ca, which advertises research ads for the Dalhousie Psychology Department. Interested participants were instructed to contact the principal investigator by phone or e-mail to obtain more information.

3.2.5 Risk And Benefit Analysis

      All tests performed were considered harmless based on the experience of the professional staff co-supervising this study. The participants may become tired from having to view visual stimuli for a long period of time, and a slight skin irritation may develop at sites where the electrodes were placed, but this is extremely rare and has not been a source of complaints at the IWK Electrodiagnostic Lab. In very rare cases, skin irritation may occur from the patch used during monocular testing. The testing was considered non-invasive, we did not touch the eye and no eye drops were used. Although we strive to protect confidentiality, a breach of confidentiality is always considered a potential harm. If previously unidentified abnormal results were found during testing suggesting pathology may exist, the participant was referred to the ophthalmology fellow in charge at the IWK Eye Care Clinic. The ophthalmology fellow would review the testing results and decide how to proceed with patient care.

      There were no anticipated benefits to the participant of this study. The knowledge gathered from the study may improve our ability to understand binocular interactions in clinical conditions affecting the use of the two eyes together. Our results may influence the way clinicians assess these conditions; the possibility of obtaining an earlier diagnosis based on BI may potentially lead to better visual outcomes.

3.2.6 Ethical Considerations

Ethical approval for the study was obtained by the IWK Health Centre Research Ethics Board. Consistent with this approval, all participants provided free and informed consent. The information and consent form used can be found in Appendix A.

3.3 Experimental Procedures

3.3.1 General Protocol

Participants willing to participate in the study signed the information and consent document before testing took place. A general orthoptic assessment was performed to ensure they were eligible to participate in further testing. Due to decreased attention and decreased quality of recording with prolonged testing, each participant was tested using only one stimulus parameter (willing participants underwent more testing or returned for more testing).

3.3.2 Orthoptic Assessment

Participants underwent the following orthoptic assessment to ensure inclusion and exclusion criteria were met. The participant's age, date of birth and sex were recorded. All testing was done with the participant wearing their most recent prescription for their refractive error. The prescription of the glasses was determined by lensometry. Near visual acuity of right eye and left eye was assessed using a Sloan card at 40cm, and distance visual acuity was assessed with an Early Treatment Diabetic Retinopathy Study (ETDRS) chart calibrated for 2.43m (8 feet). Eye alignment was assessed with alternate prism cover test at near (1/3m) and distance (6m), binocularity was assessed using the Titmus test, Bagolini lenses at near (1/3m) and distance (6m), and worth 4 dot flashlight at near (1/3m) and distance (6m). Pupils were assessed for relative afferent papillary defect using the swinging flashlight test, fixation was assessed using an ophthalmoscope, and the dominant eye was determined using a framing technique.

3.3.3 Electrode Placement

VEPs were recorded from a 10mm diameter gold disc FH-ESGH electrode (Grass-Telefactor Division Astro-Med Inc, West Warwick, USA) attached to the scalp

along the midline 2 cm superior to the inion (active electrode). A similar electrode, which served as a reference was placed on the scalp 4cm superior to the nasion on the midline, and an ear clip electrode that served as the ground was placed on one earlobe. All areas of electrode contact were cleaned with an alcohol swab then lightly abraded with a Q-tip and NU Prep ECC &EEG Abrasive Prepping Gel (D.O. Weaver & Co, Arora, USA). The electrode cup was filled with EC2 Electrode Cream (Grass Products Group, Astro-Med Inc, West Warwick, RI, USA) prior to placement on the skin and were secured to the forehead and inion with transpore tape (3M Compant, St. Paul MN). Electrode impedance was checked before each session using an EZM Electrode Impedance Meter (Grass Medical Instruments, Quincy MA.,USA) and kept below 5 kilo-ohms for the duration of the experiment.

3.3.4 Stimulus Presentation

The stimulus used varied depending on the specific stimulus parameter being tested.

3.3.4.1 Check Size

A 27cm high x 36cm wide cathode ray tube computer monitor (View Sonic, Graphics Series G90f) was used for the presentation of a pattern reversal checkerboard transient stimuli reversing at 1.2Hz. The main screen luminance was 77.5cd/m^2 (white: 152 cd/m^2, black: 3 cd/m^2). The visual angle subtended by the display was 23.8x31.7° at 65cm, contrast was 100% for all check sizes, and 4 dimensions of check sizes were tested and are presented in Table 2. The m-sequence was 6.

Table 2. Stimulus parameters for check size: contrast, size of patter element, and visual angle subtended by each check at a testing distance of 65cm.

Contrast (%)	Size of check (mm^2)	Number of pixels	Visual angle (degree (°))	Visual angle (min of arc ('))
100	21.7	64	1.9	115
100	5.5	16	0.48	29
100	2.7	8	0.24	14
100	1.2	4	0.11	6

3.3.4.2 Contrast

Contrast (C) is the luminance difference of adjacent dark and bright bands given a constant level of luminance (luminance), the Michelson Contrast Formula states $C = (L_{max}-L_{min})/(L_{max}+L_{min})$. Presentation of contrast stimuli was in the same manner as described above with check size. Check size was 29' for all contrast levels at a testing distance of 65cm. Four contrast levels were tested and are presented in Table 3. Luminance was measured with a luminance meter (Minolta LS-100, Minolta Camera Co., LTD., Japan).

Table 3. Stimulus parameters for contrast: contrast, white and black luminance and RGB coordinates.

Contrast in %	White luminance measure in cd/m^2	Black luminance measure in cd/m^2	White RGB coordinates	Black RGB coordinates
~100	152	3	255	0
~70	68	15	175	80
~40	51	21	151	99
~15	43	31	137	118

3.3.4.3 Location

Two methods were used to test stimulus location: VEPs using a central and peripheral stimulation, and more refined mfVEP. Central and peripheral stimulation VEP testing used the same presentation as described above with 29'check size and 100% contrast at a testing distance of 65cm. To determine the role of the central visual field in binocular interactions, a black border was created so that only the central 10° of visual field (stimulus diameter 11.5cm) remained. Alternatively, to determine the role the peripheral visual field in binocular interactions, an artificial scotoma was created so that the central 10° of visual field was blacked out, leaving the peripheral field stimulated.

Slightly different testing equipment was used to record the mfVEPs. A 31cm high x 41cm wide cathode ray tube computer monitor (View Sonic, Professional Series P815) was used for the presentation of the dartboard stimuli reversing at 35.7Hz. The main screen luminance was 86cd/m^2 (white: 172 cd/m^2, black: 2-3 cd/m^2). The visual

angle subtended by the display was 44x59° at 40cm, contrast was 100%, and the m-sequence was 13.

The stimulus was a dartboard arrangement consisting of 36 checkerboard polygons arranged in 4 concentric rings. Stimulus diameter was 29cm stimulating 41° of central visual field, and the eccentricity of the four rings were 0-1.7° (Ring 1), 1.8-11.6° (Ring 2), 11.7-25° (Ring 3), and 25.1-41° (Ring 4). The check sizes within the polygons were scaled based on cortical magnification.

3.3.4.4 Ganzfeld

A Ganzfeld bowl (VERIS^{TM} 2000 Ganzfeld Stimulator, Electro-Diagnostic Imaging Inc., Redwood City, CA) was used to provide a stimulus that consisted of homogeneous luminance. The flash duration was 1ms at 1s intervals presented 40 to 80 times. The overall flash luminance intensity was 3.34 cd*s/m^2.

3.4 Data Collection

3.4.1 Recordings

The active electrode gathered VEP recordings as the participant viewed the stimulus. Natural pupils were used and participants wore their appropriate distance optical correction. Lighting conditions were kept constant throughout each session and between experiments by turning off the ceiling lights, closing off the room curtain, and having a spot light directed to the corner of the room. Participants sat in a height-adjustable chair centered at eye level at a viewing distance that was determined based on the stimulus parameter being used. A chin rest was used to ensure a constant distance was maintained throughout recordings. A breadboard (Thorlabs, Newton, NJ, USA) with adjustable posts to hold ND filters was attached to the chin rest so that ND filters could be accurately positioned in front of one eye and easily changed.

Participants were instructed to focus on a red fixation cross (diameter 3°, fixation pen size 6%) on the center of the screen while concentrating on maintaining the checkerboard image clear and to relax (avoid squinting eyes, clenching teeth, scrunching forehead). Eight viewing conditions were recorded: binocular, monocular (MYI Occlusion Eye Patches, USA), and binocular with a ND filter with optical densities of

0.3, 0.6, 1.2, 1.8, 2.4, and 3.0 log units (Thorlabs Absorptive and Reflective Neutral Density Filter Kits, Newton NJ) over the dominant eye.

For check size and contrast recordings, the total recording time was 53.33 seconds (4 segments of 13.33 seconds), for VEP location stimulus total recording time was 1 minute 31 seconds (4 segments of 22.86 seconds), for Ganzfeld recordings the flash duration was 1ms and 40 to 80 flashes were presented, and because of the complexity of the stimulus used for the mfVEP, a total recording time was 3 minutes 38 seconds (4 segments of 54.14 seconds) was used.

The signal was amplified by a P511 AC Amplifier (Grass Instrument Division, Astro-Med Inc, West Warwick, RI, USA) bandwidth filters were set between 3-300Hz with an amplification of 100 000x. Visual Evoked Response Imaging System (VERIS) 6.0.10 software (Electro-Diagnostic Imaging Inc., Redwood City CA) was used to record and analyze the recordings. The mfVEP recordings used a slightly different amplifier (Grass Telefactor, model 15LT), with bandwidth filters set between 3-300 Hz and an amplification of 100,000x.

Three components of the VEP waveform were analyzed. The N1 amplitude was measure from peak ~50ms to trough ~75ms, the P1 amplitude was measured from trough~75ms to peak~100ms, and the N2 amplitude was measure from peak~100ms to trough~135ms (Figure 5).

3.4.2 Theoretical Graph Of Summation Ratio As A Function Of ND Filters

Figure 8 depicts a theoretical graph of the summation ratio (SR) as a function of ND filter strength. In this study, the SR is normalized to the monocular value and is defined as the ratio between the amplitude of the binocular VEP response (either binocular or binocular with a ND filter in front of one eye) to the monocular response of the non-dominant eye (SR=binocular/monocular). A SR of 1 indicates the amplitude of the binocular response is similar to the monocular response. A SR greater than 1 indicates the amplitude of the binocular response is larger than the monocular response (suggesting BS), while a SR less than 1 indicates the amplitude of the binocular response is smaller than the monocular response (suggesting BI). The y-axis indicates the SR, and the x-axis indicates the strength of the ND filter (log unit). The horizontal line at 1

indicates the monocular value to which the binocular values were normalized. Values above this line (area under the curve, AUTC), shown in blue indicate BS, while values below this line, shown in red indicate BI. Under binocular conditions BS is observed, with increasing ND filter strength the SR decreases until it reaches a level below the monocular value so that BI is observed. With a further increase in ND filter strength, the SR returns to the monocular value of 1.
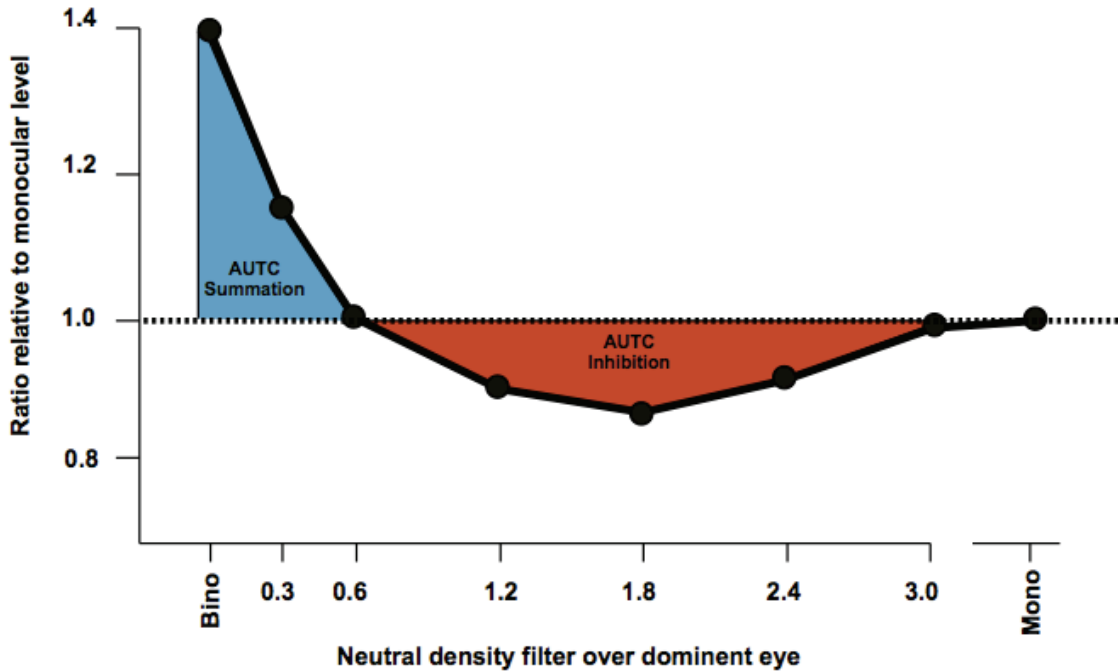
Figure 8. Theoretical representation of summation ratio as a function of ND filter strength.

For each VEP component, the AUTC was calculated from the average of individual normalized data the sum of all points less than 1 was divided by the sum of all points on the curve, multiplied by 100 to give the percentage of AUTC.

3.4.3 Statistical Treatment

The following statistical measures were calculated for each stimulus parameter:

1) An ANOVA ($p = 0.05$) to analyze the effect of ND filters on the SR.

2) A one-sample t-test to analyze the SR for each ND filter relative to the monocular value of 1.

3) An ANOVA (p = 0.05) to analyze the effect of the stimulus parameter on maximal binocular interactions (BS and BI).

4) An ANOVA (p = 0.05) to analyze the effect of the stimulus parameter on the area under the curve for BI.

3.5 Computerized Pulfrich Stimulus

3.5.1 Principles

The participant sat in a height-adjustable chair with their chin on a chinrest. A thin piece of wood (94x47x0.3cm) was painted black and spanned from the chin rest to the computer screen. It was centered on the computer screen so that with the RE saw the right half of the screen and the LE saw the left half of the screen. Fusion of the right and left half of the screen was achieved by placing a Risley rotary prism (Good-Lite Company, Elgin, IL, USA) in front of each eye mounted on the bread board, and the participant adjusted each prism to a base out orientation so that the pendulums on the right and left side of the screen were fused (sees 2 pendulums). To ensure fusion was maintained throughout testing, a horizontal bar at the bottom of the screen seen with the right eye intersected a vertical bar at the bottom of the screen seen with the left eye to form a cross.
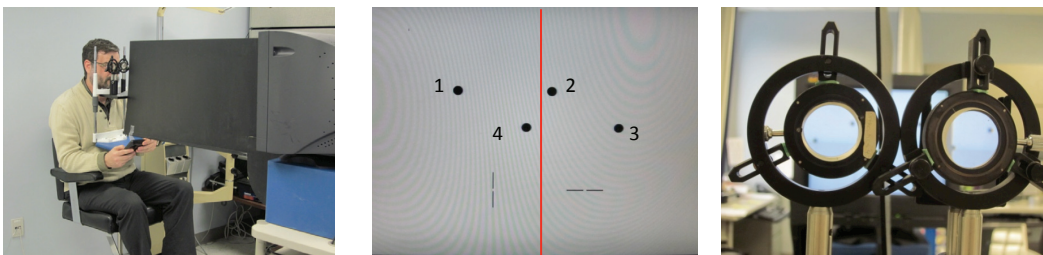
Figure 9. The PE stimulus set up showing the location and number designated to each pendulum.

When fusion is achieved, the pendulums should be viewed as rotating in a counterclockwise motion due to a -11.4° phase lag adjustment of the start values of the

pendulums on the right (2 and 3). The participant was given a cordless keyboard and was instructed to press and hold the indicated key (#3) until they noticed the pendulums rotating in the opposite direction (CW). The participant went through ~10 test trials to be certain they understood the concept and were able to recognize the direction change and release the key as soon as it was noticed it. Five viewing conditions were tested in random order: binocular and unequal binocular with ND filter of 0.3, 0.6, 1.2, 1.8 log units over the right eye. Each of the 5 viewing conditions was replicated 10 times.

3.5.2 Computerized Parameters

To quantify the PE, a computer-based test was developed using VPixx version 2.30 (VPixx Technologies Inc.). Four identical black pendulums arranged in a 2x2 design were created on a white background, each having a size of 1x1° (0.99484x0.99484cm). Table 4 and Figure 9 indicate the assigned number and start position for each pendulum. Each pendulum moved in simple sinusoidal motion with the bottom two pendulums (3 and 4) off set by a phase shift of 90° compared to the top two pendulums (pendulums did not cross midline).

The trigonometric sine function $f(x)=a*\sin(b*t+c+var1)$, d was used to develop movement of the stimulus where a is amplitude of motion (distance from the center of motion to either extreme), b is the frequency of motion (cycle per degree, Hz), c is the phase shift (the amount of horizontal displacement of the function from its original position), d is a vertical shift, and variable 1 is the phase shift controlled by the participants.
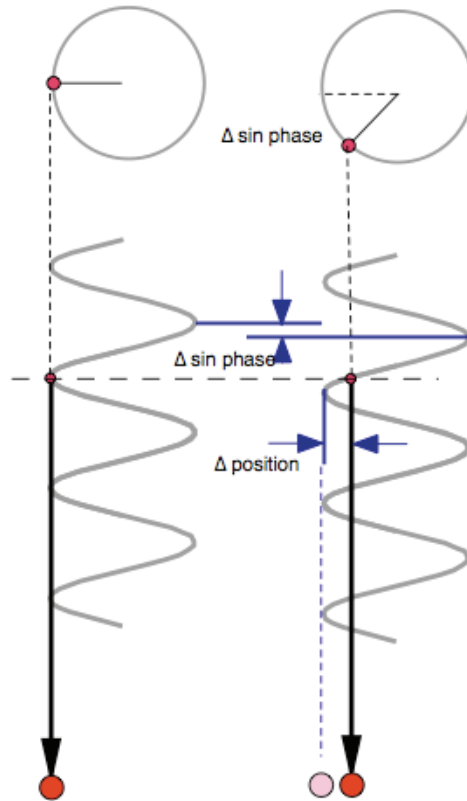
Figure 10. As the pendulum rotates around the wheel, the angle of rotation is plotted against time, resulting in a sine wave. The red pendulum indicates the position of the pendulum on the wave at a given time. When a phase change is introduced to the sine wave, the position of the pendulum is displaced, indicated in pink.

Table 4. Initial position of each pendulum and the sinusoidal function associated with the pendulum's movement.

Pendulum	X axis (degrees/cm from centre)	Y axis (degrees/cm from centre)	Formula
1	-5/ -4.97419	4/3.97935	(4*sin(4*t))-5
2	5/4.97419	4/3.97935	(4*sin(4*t+var1/100))+5
3	5.56448/5.53575	0/0	(4*sin(4*t+3.14+var1/100))+5
4	-4.43552/-4.41262	0/0	(4*sin(4*t+3.14))-5

3.5.3 Threshold Determination

        In all cases the pendulum was initially seen swinging in a CCW direction due to a -11.4° phase lag programmed into the pendulums on the right which induce a large PE due to retinal disparity. The participant was instructed to hold down the #3 key release the key as soon as they observed the pendulum swinging in the other direction (CW). The input from the participant continuously decreased the phase lag between the pendulums until they were neutralized to swing in 2D in the frontal plane, and a further decrease in phase lag changed the swinging of the pendulums to CW.

        Under binocular conditions, only the phase lag programmed into the computer was present (-11.4°) so the effect would appear in a CCW direction. The output value given from the software indicates the change in phase. The point of neutralization would be when the pendulum appeared to move without depth in the frontal plane, but because the "size" of the plateau during which the pendulums do not appear to have depth is quite large, we found this yielded large variability in the result, and for that reason, the paradigm was changed so that the end point was when the pendulums appear to swing in a CW direction, which we believe provided a more reliable threshold. Hence, with no ND filter in place, the output generated should be close to the theoretical neutral value of 11.4°, and likely larger to view CW.

3.5.4 Statistical Treatment

        The computer software measured the change of phase required for the participant to see the change in direction of the pendulums. In theory, when a filter was placed in front of the right eye, the effect should be larger, and thus require more of a phase change. The computer output calculates the average phase shift required (radians, which is converted to degree) per filter. A linear regression analysis was used to determine the relationship between the ND filter strength and the phase shift.

CHAPTER 4: RESULTS

4.1 Effect Of Check Size On Binocular Interactions

In the first series of experiments, the effect of check size on the SR was explored.

4.1.1 Between Filter Analysis

Data obtained from 6 individuals (age 19-37 years) for all 4 check sizes is summarized in Table 5 and Figure 11. Column A in Figure 11 depicts a sample set of raw VEP recordings obtained from one individual, with the N1, P1, and N2 components labeled for the monocular condition. Column B, C and D show the value of the SR for each VEP component, N1, P1, and N2 respectively, as a function of ND filter strength, and the standard error is present for each value. An asterisk paired with a SR value indicates at that given filter level, the SR is significantly larger (BS) then the corresponding monocular value of 1 (* signifies $p \leq 0.05$, ** signifies $p \leq 0.01$), while a dot next to a SR value indicates at that given filter level, the SR is significantly smaller (BI) then the corresponding monocular value of 1 (• signifies $p \leq 0.05$, •• signifies $p \leq 0.01$). ANOVA significance is denoted by * for $p \leq 0.05$, and ** for $p \leq 0.01$.

General trends of the VEP SR in response to ND filters are that the binocular and 0.3 log unit ND filter response show the highest levels of BS, and the SR is often slightly higher at 0.3 log unit. The response with a 1.2 and 1.8 log unit ND filter show prominent BI, and in most conditions, it takes 3.0 log unit nullify any interocular effect (SR~1).

By means of an ANOVA, the P1 component shows a significant difference between filters and their SR at all check sizes. The N1 component shows a significant difference between filters and their SR at only the two smallest check sizes, while the N2 component shows significance for all check sizes except 14' (Table 5)**.**

41

Table 5. Effect of check size and NDF strength on SR of N1, P1, and N2.

NDF	N	N1		P1		N2	
		Ave	SD	Ave	SD	Ave	SD
115'							
BINO	6	1.013	0.467	1.184	0.177	1.177**	0.093
0.3	6	1.331	0.553	1.163	0.201	1.142	0.220
0.6	6	1.099	0.565	0.958	0.172	0.936	0.162
1.2	6	0.832	0.560	0.790*	0.152	0.882	0.113
1.8	6	1.059	0.347	0.741**	0.153	0.751*	0.187
2.4	6	1.529	0.887	0.834*	0.119	0.857*	0.256
3.0	6	1.493	0.496	1.077	0.106	1.068	0.205
MONO	6	1.00	0.000	1.00	0.000	1.00	0
ANOVA		$F_{(7,40)}=1.319$ p=0.267		$F_{(7,40)}=7.893$ p=0.000**		$F_{(7,40)}=4.382$ p=0.001**	
29'							
BINO	6	1.159	0.256	1.253*	0.217	1.079	0.114
0.3	6	1.340*	0.294	1.315	0.336	1.068	0.146
0.6	6	0.934	0.453	0.927	0.320	0.963	0.188
1.2	6	0.953	0.181	0.805	0.213	0.747*	0.091
1.8	6	0.917	0.384	0.774*	0.144	0.780	0.227
2.4	6	0.927	0.386	0.953	0.156	0.968	0.218
3.0	6	1.003	0.174	1.021	0.162	1.004	0.113
MONO	6	1.000	0.000	1.000	0.000	1.000	0
ANOVA		$F_{(7,40)=}1.458$ p=0.210		$F_{(7,40)=}4.698$ p=0.001**		$F_{(7,40)=}3.847$ p=0.003**	
14'							
BINO	6	1.520*	0.382	1.472**	0.233	1.132	0.234
0.3	6	1.705	0.821	1.315	0.348	0.979	0.217
0.6	6	1.414	0.542	1.198	0.240	1.034	0.182
1.2	6	1.019	0.323	0.883	0.153	0.805**	0.115
1.8	6	0.976	0.382	0.910	0.290	0.931	0.388
2.4	6	0.915	0.249	0.996	0.142	1.058	0.116
3.0	6	0.985	0.388	1.020	0.099	1.008	0.0614
MONO	6	1.000	0.000	1.000	0.000	1.000	0
ANOVA		$F_{(7,40)}=2.842$ p=0.017*		$F_{(7,40)}=5.628$ p=0.000**		$F_{(7,40)}=1.414$ p=0.227	
6'							
BINO	6	2.020*	0.675	1.724*	0.365	1.349	0.413
0.3	6	2.308*	0.844	1.889*	0.374	1.346	0.404
0.6	6	1.881*	0.770	1.528*	0.468	1.181	0.280
1.2	6	1.395	0.565	1.078	0.144	0.930	0.135
1.8	6	0.820	0.234	0.772*	0.204	0.804*	0.083
2.4	6	1.068	0.379	1.119	0.242	1.188	0.219
3.0	6	1.370**	0.178	1.226	0.273	1.031	0.203
MONO	6	1.000	0.000	1.000	0.000	1.000	0
ANOVA		$F_{(7,40)}=5.981$ p=0.001**		$F_{(7,40)}=9.973$ p=0.000**		$F_{(7,40)}=3.488$ p=0.005**	
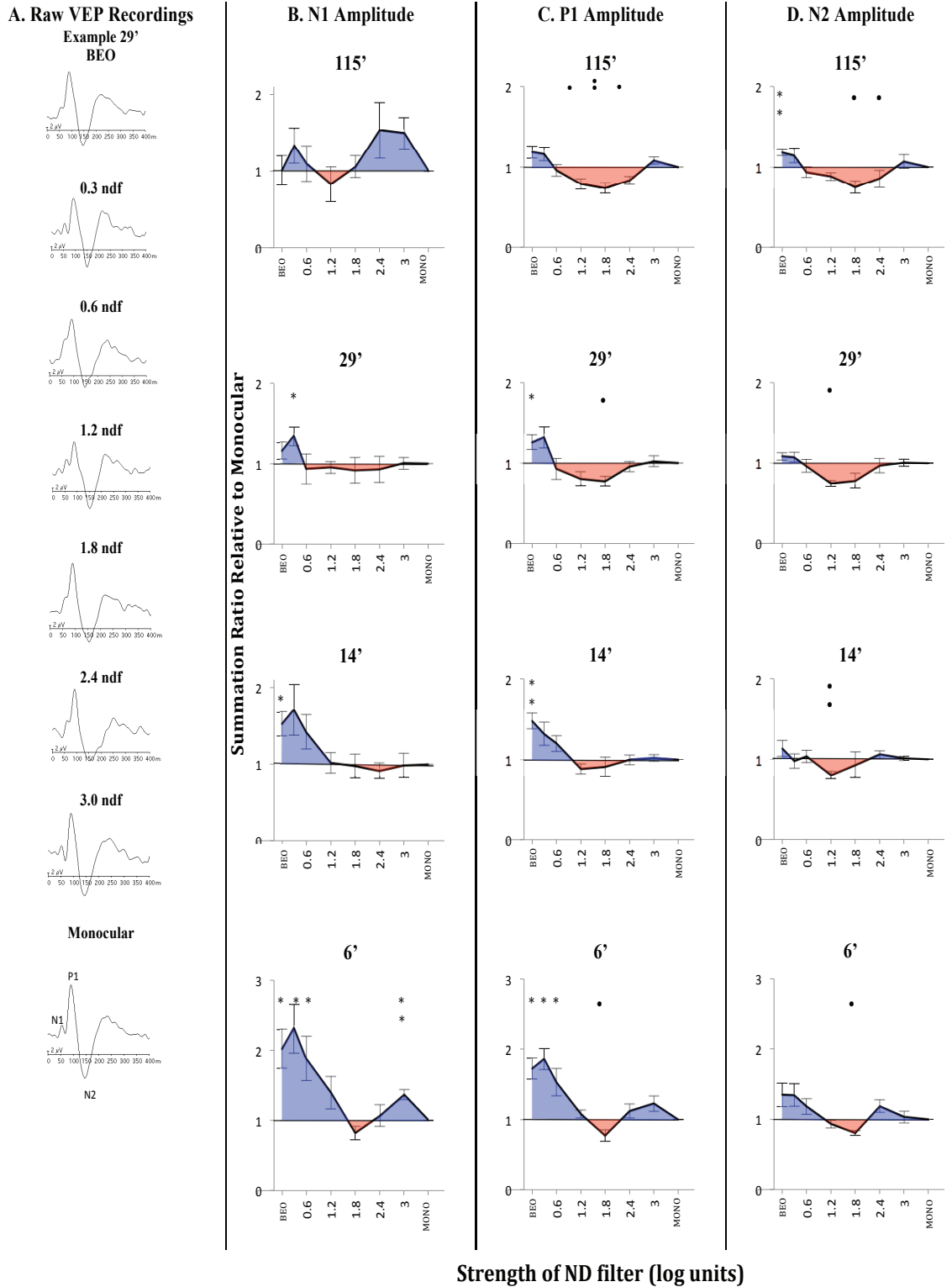
Figure 11. Effect of check size and NDF strength on SR of N1, P1, and N2. Column A depicts raw VEP recordings. Under the monocular condition the N1, P1, and N2 components are identified. Column B, C, and D represent the average SR for N1, P1, and N2 respectively for check size 115', 29', 14' and 6'.

4.1.2 Maximal Binocular Interactions

Results of an ANOVA to analyze the effect of check size on maximal binocular interactions reveal for the P1 component, check size influences BS: maximal BS occurs with smaller check sizes (Figure 12). Additionally, with each check size, maximal BS occurs under binocular conditions or when a mild ND filter is used. The highest amount of BS obtained was 1.8 with 6' check size and a 0.3 log unit ND filter (reduces luminance by 50%). Conversely, the effect of check size does not significantly influence maximal BI. With each check size, maximal BI occurred with a 1.2 or 1.8 log unit ND filter, and the highest amount of BI was 0.741 with 115' check size and 1.8 log unit ND filter (Figure 12).

ANOVA results for N1 and N2 components are not significant; check size does not influence maximal BS and BI. The highest amount of BS for N1 was 2.308 with 6' check size and a 0.3 log unit ND filter, and highest amount of BI was 0.820 with a 6' check size and a 1.2 log unit ND filter. The highest amount of BS for N2 was 1.349 under binocular condition, and highest BI was 0.747 with a 115' check size and 1.2 ND filter.

Table 6. Effect of check size on maximal binocular interactions.

Check Size	N	N1		P1		N2	
		Max(filter)	SD	Max(filter)	SD	Max(filter)	SD
BS							
115'	6	1.529(2.4)	0.887	1.184(B)	0.177	1.177**(B)	0.093
29'	6	1.340*(0.3)	0.256	1.315(0.3)	0.336	1.079(B)	0.114
14'	6	1.705(0.3)	0.821	1.472**(B)	0.233	1.132(B)	0.234
6'	6	2.308*(0.3)	0.844	1.889*(0.3)	0.374	1.349(B)	0.413
ANOVA		$F_{(3,20)}$=2.143, p=0.127		$F_{(3,20)}$=6.038, p=0.004**		$F_{(3,20)}$=1.421, p=0.266	
BI							
115'	6	0.832(1.2)	0.560	0.741**(1.8)	0.153	0.751*(1.8)	0.187
29'	6	0.917(1.8)	0.384	0.774*(1.8)	0.144	0.747*(1.2)	0.091
14'	6	0.915(2.4)	0.249	0.883(1.2)	0.153	0.805**(1.2)	0.115
6'	6	0.820*(1.2)	0.234	0.772*(1.8)	0.204	0.804(1.8)	0.083
ANOVA		$F_{(3,20)}$=0.210, p=0.882		$F_{(3,20)}$=0.861, p=0.477		$F_{(3,20)}$=1.415, p=0.268	
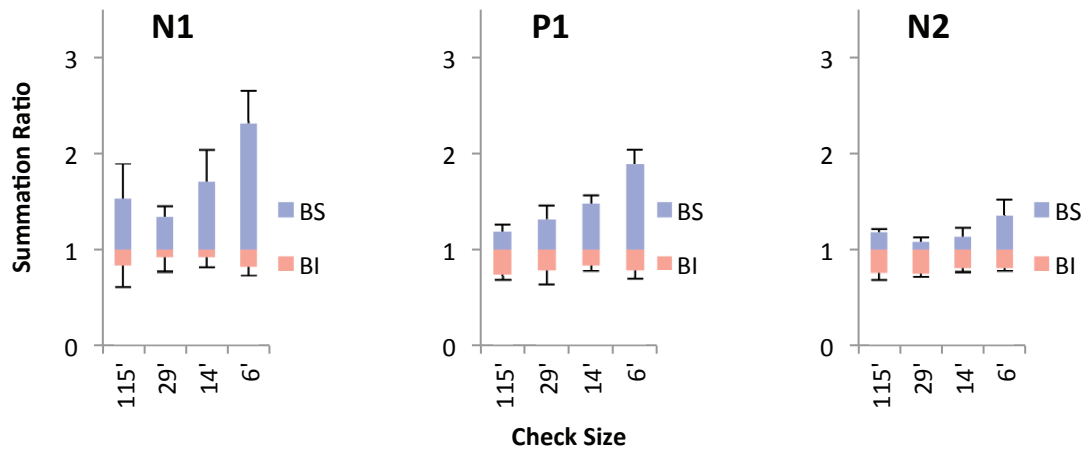
Figure 12. Effect of check size on maximal binocular interactions with standard error.

4.1.3 Area Under The Curve

To better represent the inhibitory process, the area under the curve (AUTC) was calculated (Table 7).

ANOVA results show the average AUTC is not significant between check size for the N1, P1, and N2 VEP components: check size does not influence average AUTC (BI). However the P1 component is very close to significance (p=0.056). For all three VEP components, there is a general trend that larger check size has the most average area under the curve, which decreases with smaller check size, and all show the smallest check size has the least AUTC (Figure 13).

Table 7. Effect of check size on AUTC.

Check Size	N	N1		P1		N2	
		AUTC	SD	AUTC	SD	AUTC	SD
115'	6	9.961	32.850	49.251	21.734	50.283	37.372
29'	6	51.580	24.752	49.089	14.287	52.324	15.939
14'	6	33.695	20.815	35.791	23.738	39.076	36.289
6'	6	7.551	11.843	8.296	22.697	22.154	19.059
ANOVA		$F_{(3,20)}=1.134$ p=0.359		$F_{(3,20)}=2.977$ p=0.056		$F_{(3,20)}=0.227$ p=0.877	
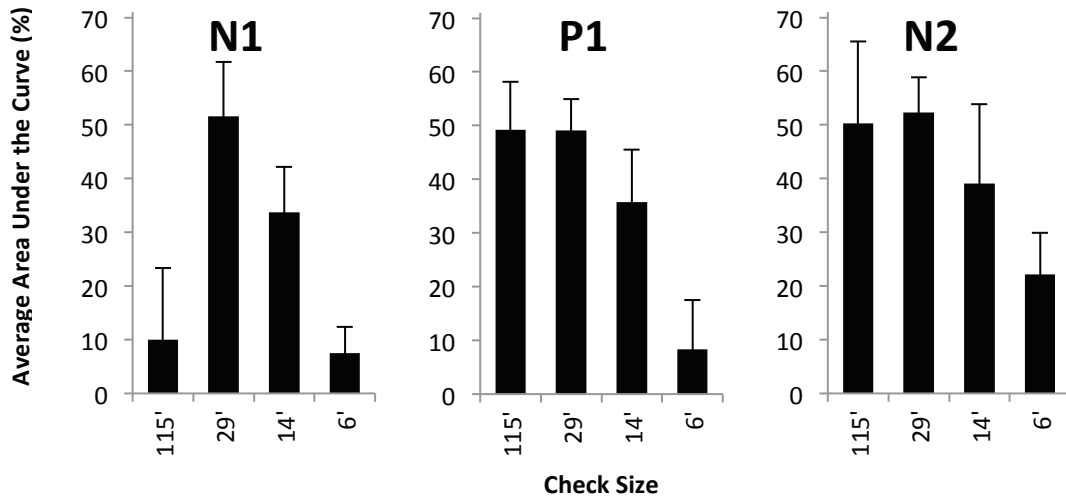
Figure 13. Effect of check size on AUTC with standard error.

4.2. Effect Of VEP Stimulus Location On Binocular Interactions

4.2.1 Between Filter Analysis

Data obtained on a group of 11 individuals (age 18-31 years) for central and peripheral VEP stimulation is summarized in Table 8 and Figure 14.

Results from an ANOVA of the P1 component shows ND filters have a significant effect on the SR for both center and peripheral stimulation. The N1 component shows a significant difference between filters and their SR with center stimulation only, while the N2 component shows significance with peripheral stimulation only.

Table 8. Effect of VEP stimulus location and NDF strength on SR of N1, P1, and N2.

NDF	N	N1		P1		N2	
		Ave	SD	Ave	SD	Ave	SD
Center Stimulation							
BINO	11	1.890*	0.952	1.340**	0.339	1.064	0.309
0.3	11	1.590*	0.723	1.182	0.365	1.012	0.332
0.6	11	1.316**	0.325	1.170*	0.222	1.107	0.366
1.2	11	1.396	0.699	0.903	0.275	0.924	0.330
1.8	11	1.287	0.713	0.803*	0.272	0.766**	0.243
2.4	11	1.040	0.3833	0.921	0.203	0.915	0.271
3.0	11	1.264	0.602	1.0168	0.236	1.092	0.337
MONO	11	1.000	0.000	1.000	0.000	1	0.000
ANOVA		$F_{(7,80)}=2.410$ p=0.027 *		$F_{(7,80)}=5.046$ p=0.000 **		$F_{(7,80)}=1.635$ p=0.138	
Peripheral Stimulation							
BINO	11	1.755	1.594	1.415*	0.477	1.287**	0.300
0.3	11	1.638	1.337	1.234	0.452	1.238*	0.341
0.6	11	1.808	1.325	1.163	0.345	1.155	0.332
1.2	11	1.462	1.0117	0.997	0.273	1.058	0.287
1.8	11	1.148	0.621	0.941	0.284	0.952	0.250
2.4	11	1.494	0.975	0.881	0.230	0.894	0.228
3.0	11	1.724	1.177	1.014	0.236	1.041	0.320
MONO	11	1.000	0.000	1.000	0.000	1	0.000
ANOVA		$F_{(7,80)}=0.772$ p=0.612		$F_{(7,80)}=3.382$ p=0.003 **		$F_{(7,80)}=2.701$ p=0.015*	
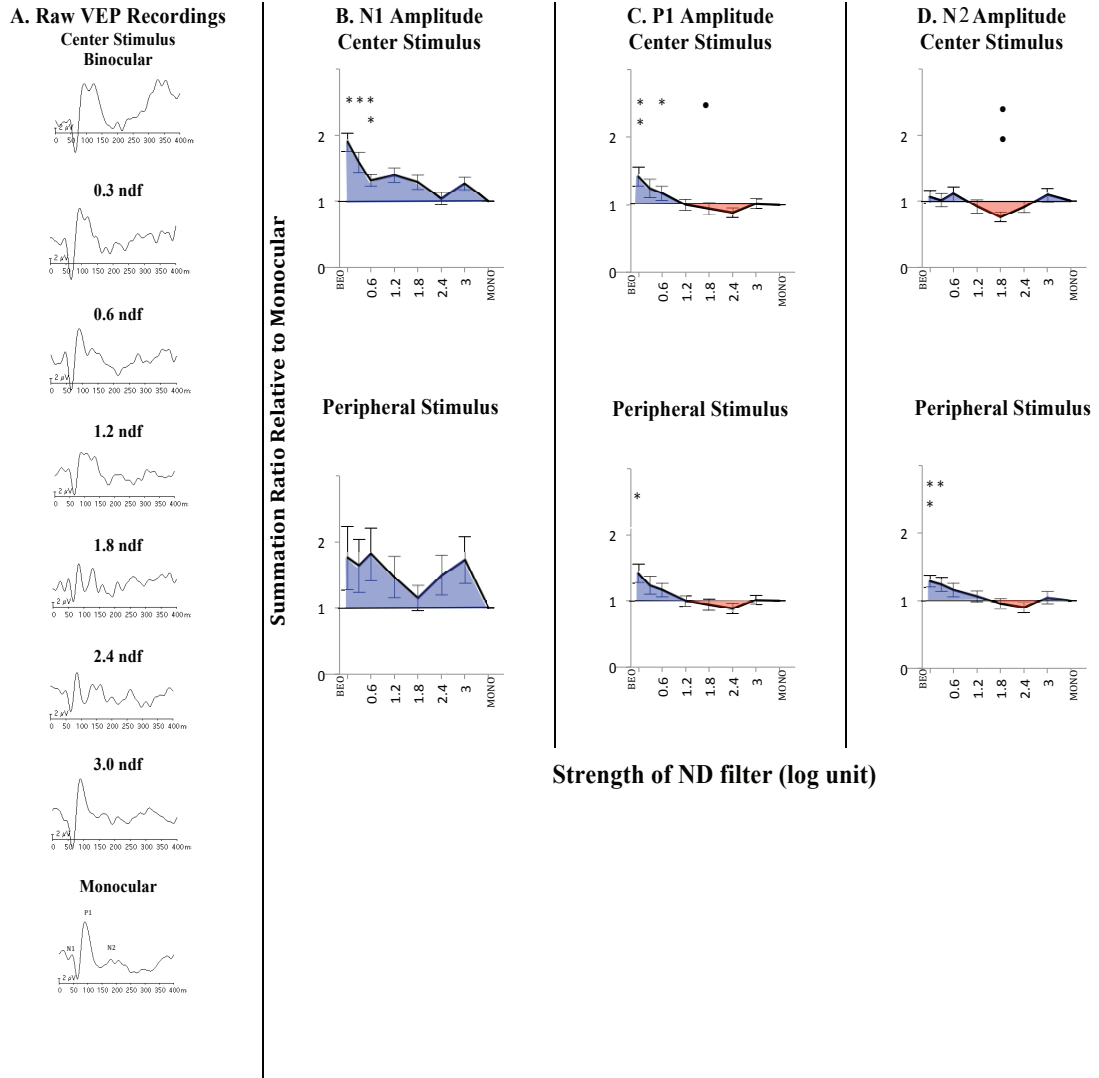
Figure 14. Effect of VEP stimulus location and NDF strength on SR of N1, P1, and N2. Column A depicts raw VEP recordings. Under the monocular condition the N1, P1, and N2 component are identified. Column B, C, and D represent the average SR for N1, P1, and N2 respectively for center and peripheral stimulus.

4.2.2 Maximal Binocular Interactions

ANOVA results to analyze the effect of VEP location on maximal binocular interactions are not significant for all three VEP components: VEP location does not influence maximal BS nor BI (Figure 15). The highest amount of BS for N1 was 1.890 with central stimulation under binocular conditions, and no BI occurred. The highest amount of BS for P1 was 1.415 with peripheral stimulation under binocular condition, and highest BI was 0.803 with central stimulation and 1.8 ND filter. The highest amount of BS for N2 was 1.287 with peripheral stimulation under binocular condition, and highest BI was 0.776 with central stimulation and 1.8 ND filter.

Table 9. Effect of VEP stimulus location on maximum binocular interactions.

Location	N	N1		P1		N2	
		Max	SD	Max	SD	Max	SD
BS							
Center	11	1.890*(B)	0.952	1.340**(B)	0.339	1.1079(0.6)	0.366
Periphery	11	1.808(0.6)	1.325	1.415*(B)	0.477	1.287**(B)	0.300
ANOVA		$F_{(1,20)}=0.087$, p=0.771		$F_{(1,20)}=0.181$, p=0.675		$F_{(1,20)}=1.067$, p=0.314	
BI							
Center	11	1	0	0.803*(1.8)	0.272	0.766**(1.8)	0.243
Periphery	11	1	0	0.881(2.4)	0.230	0.894(2.4)	0.228
ANOVA		$F_{(1,20)}=0.139$, p=0.713		$F_{(1,20)}=0.528$, p=0.476		$F_{(1,20)}=0.752$, p=0.397	
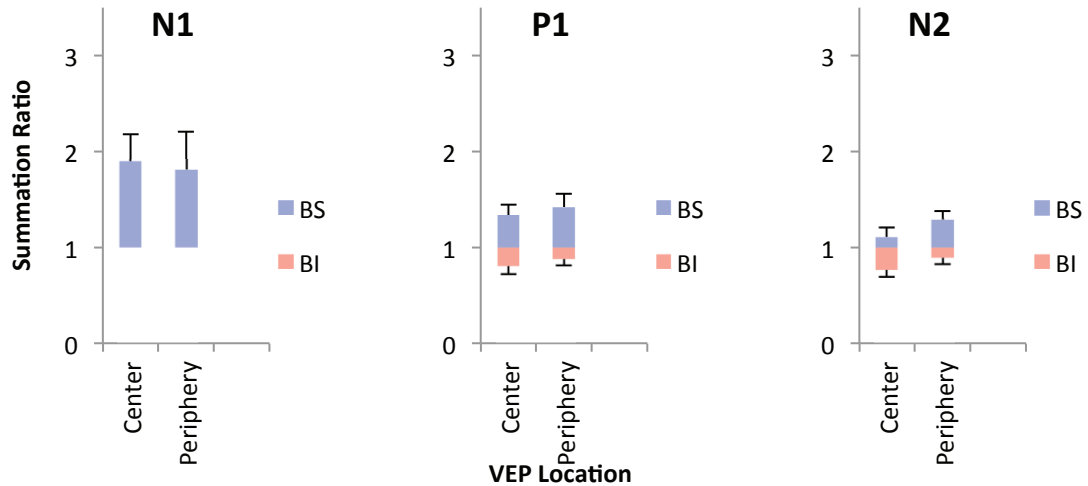
Figure 15. Effects of VEP stimulus location on maximum binocular interactions.

4.2.3 Area Under The curve

ANOVA results show the average AUTC is not significant between VEP location for the all three VEP components: VEP location does not influence average AUTC (BI). The N1 component shows no average AUTC, while the P1 and N2 component shows both center and periphery stimulus had similar amounts AUTC (Figure 16). As previously mentioned, the AUTC is calculated from the average of individual normalized data, resulting in zero AUTC for both center and peripheral stimulus of the N1 component. This zero value implies on average the there is no AUTC, but individually some subjects showed mild AUTC, thus allowing for some variability and the calculated SD.

Table 10. Effect of VEP stimulus location on AUTC.

Location	N	N1		P1		N2	
		AUTC	SD	AUTC	SD	AUTC	SD
Center	11	0	37.821	36.975	35.275	37.853	23.783
Periphery	11	0	28.510	35.052	34.493	24.218	31.526
ANOVA		$F_{(1,20)}=0.127$ $p=0.725$		$F_{(1,20)}=0.031$ $p=0.861$		$F_{(1,20)}=0.261$ $p=0.615$	
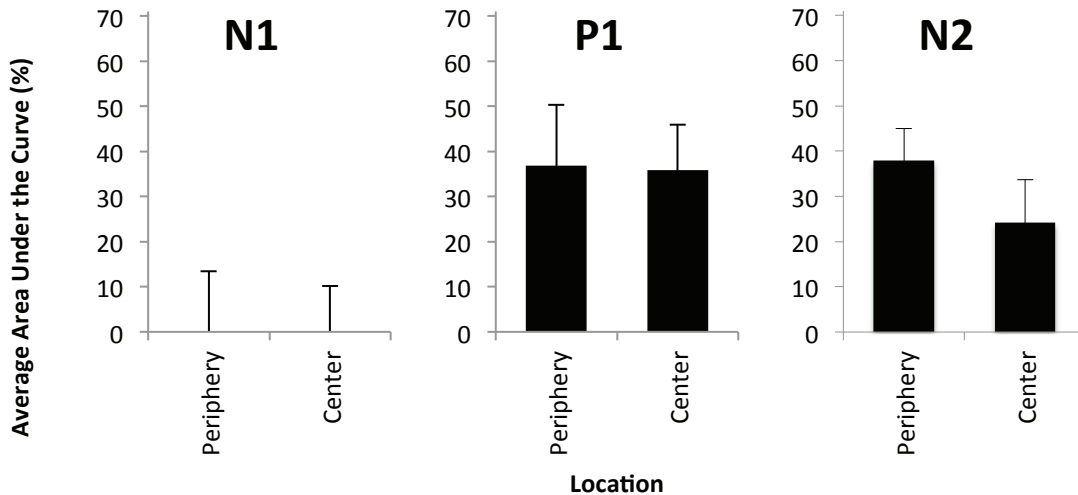
Figure 16. Effect of VEP stimulus location on AUTC.

4.3 Effect Of Multi Focal VEP Stimulus Location On Binocular Interactions

4.3.1 Between Filter Analysis

   Data obtained on a group of 10 individuals (age 18-31 years) for mfVEP ring locations is summarized in Table 11 and in Figure 17. Results from an ANOVA to analyze the effect of ND filters on the SR shows a significant difference for only the R2 location of the P1 component. As with previous results, highest amounts of BS are typically obtained under binocular conditions or with a mild ND filter. Overall very little amounts of BI was produced with all ring locations.

Table 11. Effect of mfVEP stimulus location and NDF strength on SR of N1, P1, and N2.

NDF	N	N1		P1		N2	
		Ave	SD	Ave	SD	Ave	SD
Ring 1							
BINO	10	1.348	.934	1.336**	0.269	1.605*	0.810
0.3	10	1.566	.786	1.230*	0.241	1.552	0.901
0.6	10	1.012	.447	1.056	0.500	1.455	0.814
1.2	10	1.102	.479	1.194	0.712	1.330	1.057
1.8	10	1.347	.884	0.981	0.328	1.155	0.620
2.4	10	1.283	1.083	0.930	0.254	1.010	0.422
3.0	10	1.596	1.278	0.989	0.219	1.313*	0.377
MONO	10	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,72)}=0.759$ p=0.623		$F_{(7,72)}=1.528$ p=0.172		$F_{(7,72)}=1.091$ p=0.378	
Ring 2							
BINO	10	1.752*	0.763	1.516*	0.585	1.668	1.224
0.3	10	1.693	1.441	1.317*	0.318	1.535	1.522
0.6	10	0.897	0.524	1.107	0.309	1.300	0.992
1.2	10	1.137	0.845	0.896	0.362	1.118	0.481
1.8	10	1.399	0.752	0.873	0.280	1.100	0.720
2.4	10	1.013	0.416	0.978	0.364	1.460	1.525
3.0	10	1.676	1.436	1.097	0.509	1.302	1.237
MONO	10	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,72)}=1.539$ p=0.168		$F_{(7,72)}=3.492$ p=0.003**		$F_{(7,72)}=0.463$ p=0.858	
Ring 3							
BINO	10	1.490	1.544	1.681	1.316	1.879	1.498
0.3	10	1.153	0.693	1.665	1.007	1.659	0.690
0.6	10	1.139	0.657	1.186	0.613	1.518	0.606
1.2	10	1.127	0.885	1.241	0.704	1.775	1.291
1.8	10	1.126	0.685	1.144	0.431	1.088	0.427
2.4	10	0.818	0.529	1.313	0.743	1.342	0.615
3.0	10	0.717	0.440	1.208	1.005	1.436	0.793
MONO	10	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,72)}=0.881$ p=0.526		$F_{(7,72)}=0.889$ p=0.520		$F_{(7,72)}=1.312$ p=0.257	
Ring 4							
BINO	10	1.305	0.686	1.881**	0.569	1.760*	1.020
0.3	10	1.864	1.411	2.311*	1.301	1.441*	0.684
0.6	10	1.317	0.769	1.948*	1.002	1.598	1.233
1.2	10	1.462	0.918	2.120*	1.493	1.743	1.469
1.8	10	1.487	1.626	1.475	0.838	1.536	1.180
2.4	10	1.516	0.825	1.879	1.318	1.128	0.719
3.0	10	1.401	1.361	2.071**	0.917	1.368	1.372
MONO	10	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,40)}=0.520$ p=0.817		$F_{(7,72)}=1.617$ p=0.144		$F_{(7,72)}=0.667$ p=0.699	
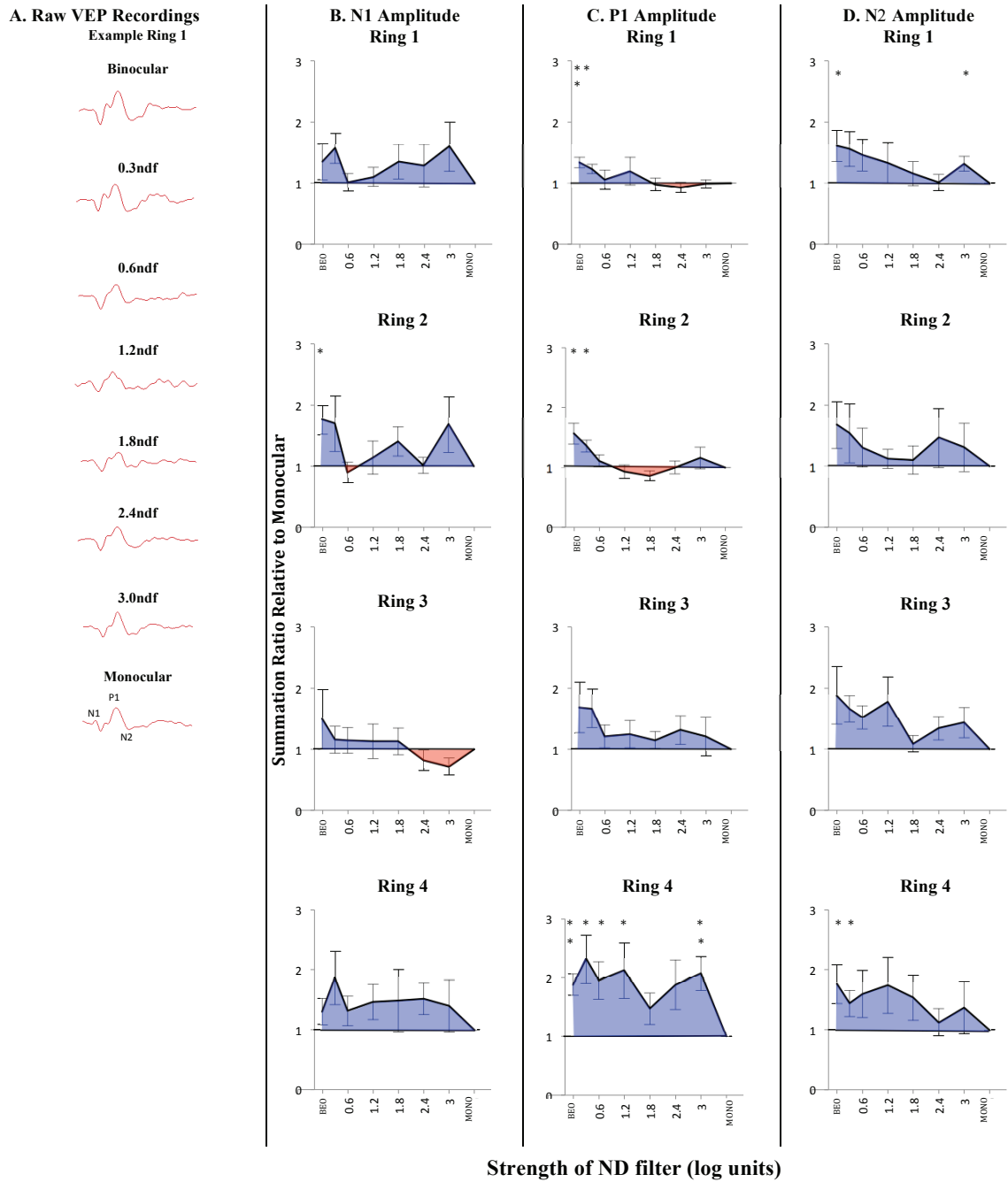
Figure 17. Effect of mfVEP stimulus location and NDF strength on SR of N1, P1, and N2. Column A depicts raw VEP recordings. Under the monocular condition the N1, P1, and N2 components are identified. Column B, C, and D represent the average SR for N1, P1, and N2 respectively for mfVEP stimulus location ring 1 to ring 4.

4.3.2 Maximal Binocular Interactions

Results of an ANOVA to analyze the effect of mfVEP ring location on maximal binocular interactions are not significant for all three VEP components: mfVEP ring location does not influence maximal BS and BI (Figure 18). Overall very little amounts of BI were produced. The highest amount of BS for N1 was 1.846 with ring 4 stimulation and 0.3 log unit ND filter, and highest BI was 0.717 with ring 3 stimulation and 3.0 log unit. The highest amount of BS for P1 was 2.311 with ring 4 stimulation and 0.3 log unit, and highest BI was 0.873 with ring 2 stimulation and 1.8 log unit ND filter. The highest amount of BS for N2 was 1.879 ring 3 stimulation under binocular condition, and no BI occurred.

Table 12. Effect of mfVEP stimulus location on maximal binocular interactions.

Ring	N	N1		P1		N2	
		Max(NDF)	SD	Max(NDF)	SD	Max(NDF)	SD
BS							
Ring 1	10	1.596(0.3)	1.278	1.336**(B)	0.269	1.605*(B)	0.810
Ring 2	10	1.752*(B)	0.763	1.516*(B)	0.585	1.668(B)	1.224
Ring 3	10	1.490((B)	1.544	1.681(B)	1.316	1.879(B)	1.498
Ring 4	10	1.864(0.3)	1.411	2.311*(0.3)	1.301	1.760*(B)	1.020
ANOVA		$F_{(3,36)}$=1.44, P=0.246		$F_{(3,36)}$=1.874, P=0.151		$F_{(3,36)}$=,1.809 P=0.163	
BI							
Ring 1	10	1	0	0.930(2.4)	0.254	1	0
Ring 2	10	0.897(0.6)	0.524	0.873(1.8)	0.280	1	0
Ring 3	10	0.717(3.0)	0.440	1	0	1	0
Ring 4	10	1	0	1	0	1	0
ANOVA		$F_{(3,36)}$=1.883, P=0.150		$F_{(3,36)}$=1.220, P=0.317		$F_{(3,36)}$=2.768, P=0.056	
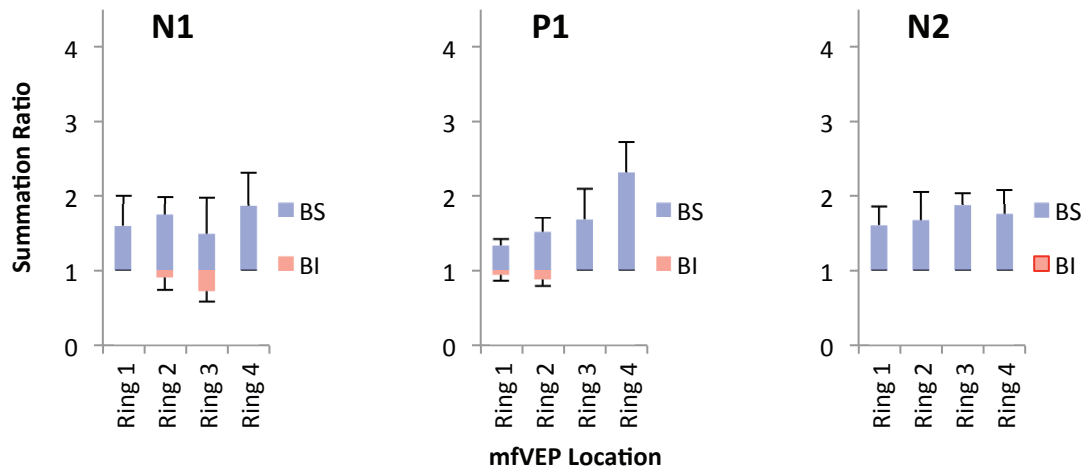
Figure 18. Effect of mfVEP stimulus location on maximal binocular interactions.

4.3.3 Area Under The Curve

ANOVA results show the average AUTC is not significant between mfVEP ring location for all three VEP components: mfVEP ring location does not influence average AUTC (BI). The P1 component produced the most AUTC, with central ring locations R1 and R2 showing similar amounts of AUTC (Figure 19).

Table 13. Effect of mfVEP stimulus location on AUTC.

Location	N	N1		P1		N2	
		AUTC	SD	AUTC	SD	AUTC	SD
Ring1	10	0	18.702	37.583	20.408	0	18.952
Ring2	10	9.376	20.819	35.052	30.563	0	28.744
Ring3	10	20.277	20.158	0	21.382	0	15.470
Ring4	10	0	33.074	0	23.434	0	20.702
ANOVA		$F_{(3,36)}=0.274$ $p=0.843$		$F_{(3,36)}=2.076$ $p=0.121$		$F_{(3,36)}=2.021$ $p=0.128$	
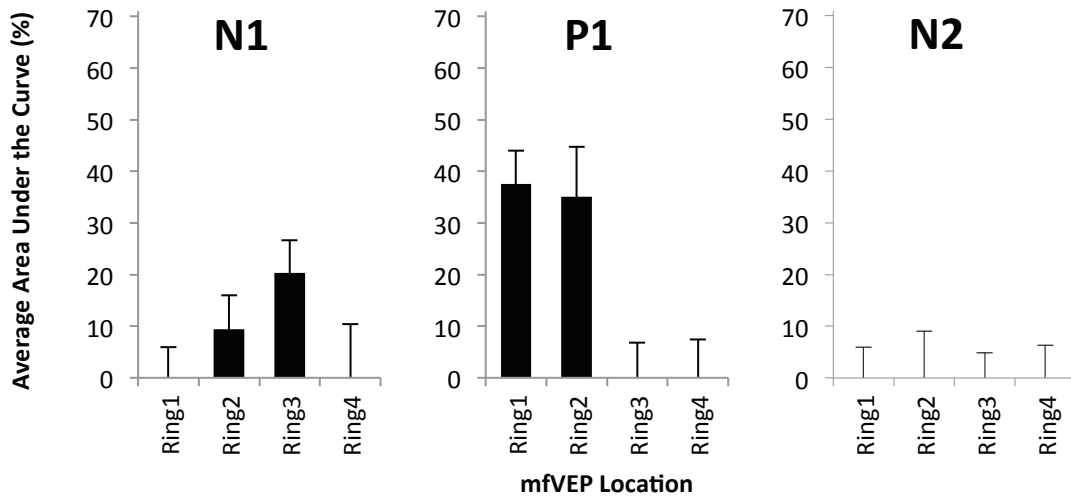
Figure 19. Effect of mfVEP stimulus location on AUTC.

4.4 Effect Of Ganzfeld Stimulus On Binocular Interactions

4.4.1 Between Filter Analysis

Data obtained on a group of 5 individuals (age 25-52 years) is summarized in Table 14 and Figure 20. The ANOVA for all 3 VEP components did not demonstrate significance between ND filters and their SR for Ganzfeld stimulation.

Table 14. Effect of Ganzfeld stimulus and NDF strength on SR of N1, P1, and N2.

NDF	N	N1		P1		N2	
		Ave	SD	Ave	SD	Ave	SD
Ganzfeld							
BINO	5	1.545	0.879	1.551*	0.459	1.583	0.329
0.3	5	1.721*	0.641	1.575**	0.286	1.024	0.592
0.6	5	1.606	0.625	1.440	0.3946	1.433	0.518
1.2	5	1.172	0.464	1.353	0.637	0.805	0.493
1.8	5	1.296	0.456	1.262	0.242	0.793	0.425
2.4	5	1.442	0.787	1.302	0.299	0.896	0.536
3.0	5	1.208	0.490	1.205	0.251	1.058	0.648
MONO	5	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,32)}=0.846$ p=0.558		$F_{(7,32)}=1.348$ p=0.261		$F_{(7,32)}=1.179$ p=0.126	
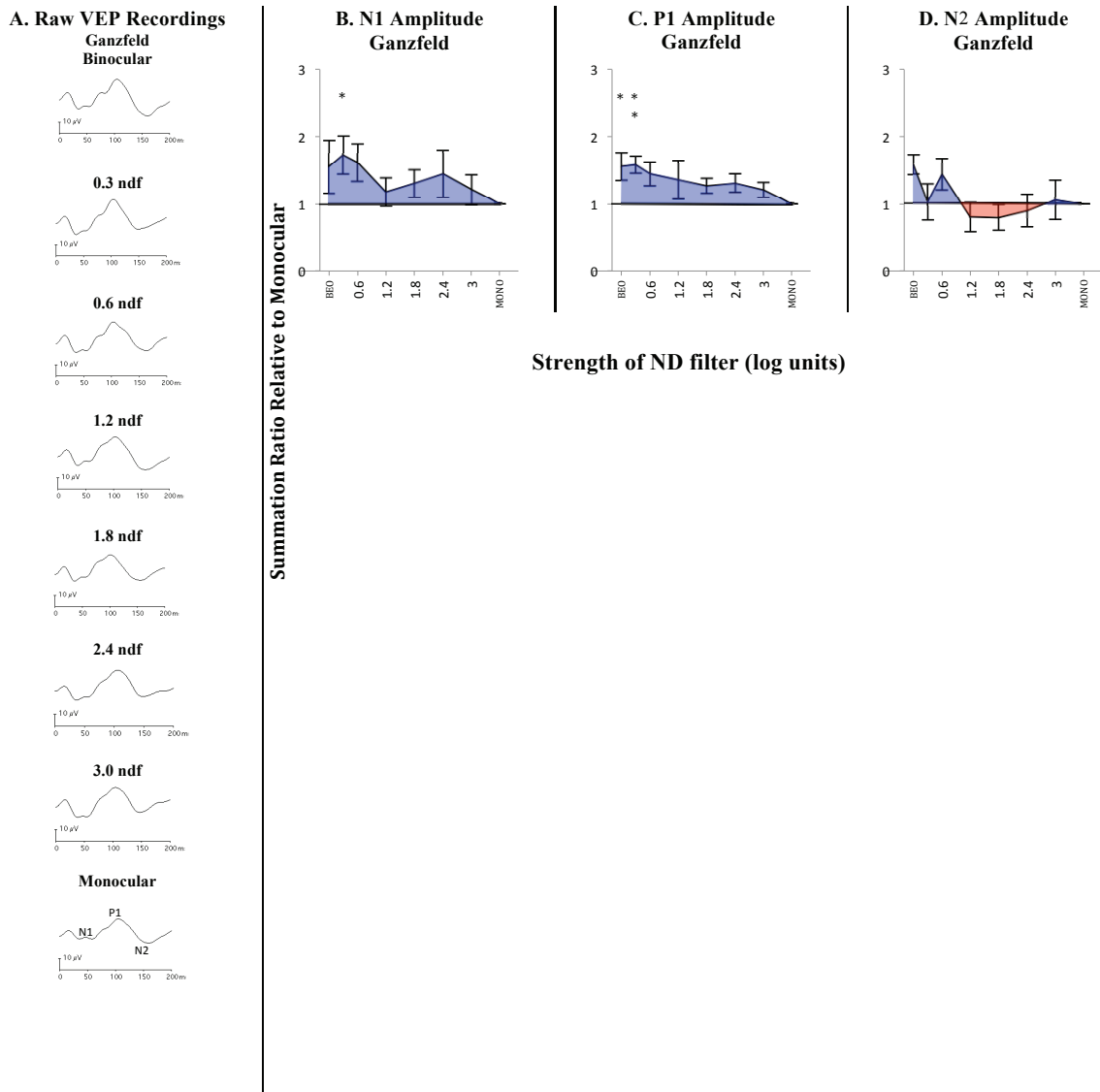
Figure 20. Effect of Ganzfeld stimulus and NDF strength on SR of N1, P1, and N2. Column A depicts raw VEP recordings. Under the monocular condition the N1, P1, and N2 components are identified. Column B, C, and D represent the average SR for N1, P1, and N2.

4.4.2 Maximal Binocular Interactions

A high level of BS was obtained under binocular conditions or with a mild ND, and very little BI was obtained for all 3 VEP components (Figure 21). The highest amount of BS for N1 was 1.721 with a 0.3 log unit ND filter, and no BI occurred. The highest amount of BS for P1 was 1.551 with a 0.3 log unit ND filter, and no BI occurred.

The highest amount of BS for N2 was 1.583 under binocular condition, and highest BI was 0.793 with a 1.8 log unit ND filter.

Table 15. Effect of Ganzfeld stimulus on maximum binocular interactions.

Ganzfeld	N	N1		P1		N2	
		Max	SD	Max	SD	Max	SD
BS	5	1.721*(0.3)	0.641	1.551**(0.3)	0.459	1.583(B)	0.329
BI	5	1	0	1	0	0.793(1.8)	0.425
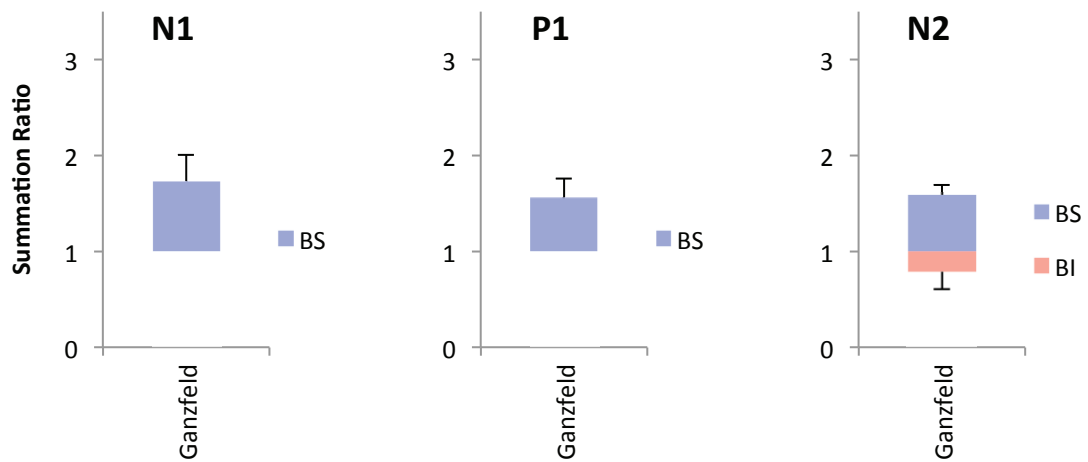
Figure 21. Effect of Ganzfeld stimulus on maximal binocular interactions.

4.4.3 Area Under The Curve

N2 was the only VEP component to show AUTC (BI).

Table 16. Effect of Ganzfeld stimulus on AUTC.

	N	N1		P1		N2	
		AUTC	SD	AUTC	SD	AUTC	SD
Ganzfeld	5	0	42.483	0	21.583	32.856	23.895
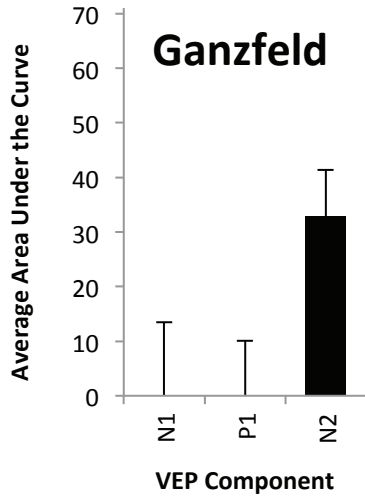
Figure 22. Effect of Ganzfeld stimulus on AUTC.

4.5 Effect Of Contrast On Binocular Interactions

4.5.1 Between Filter Analysis

Data obtained on a group of 6 individuals (age 19-52 years) is summarized in Table 17 and Figure 23. Results from an ANOVA show a significant difference between filters and their SR at the highest three contrast levels for the P1 component. The N1 and N2 component did not demonstrate a significant difference between filters and their SR.

Table 17. Effect of contrast and NDF strength on SR of N1, P1, and N2.

| NDF	N	N1		P1		N2	
		Ave	SD	Ave	SD	Ave	SD
100%							
BINO	6	1.888	1.021	1.428*	0.300	1.026	0.293
0.3	6	1.275	0.605	1.263	0.259	1.111	0.192
0.6	6	1.277	0.567	0.926	0.205	0.914	0.149
1.2	6	1.062	0.460	0.776*	0.156	0.778	0.267
1.8	6	0.859	0.239	0.746	0.261	0.796	0.226
2.4	6	1.265	0.957	0.833	0.242	0.964	0.151
3.0	6	1.104	0.492	0.906	0.173	0.999	0.204
MONO	6	1.000	0.000	1.000	0.000	1.000	0
ANOVA		$F_{(7,40)}=1.458$ p=0.210		$F_{(7,40)}=7.358$ p=0.000**		$F_{(7,40)}=1.888$ p=0.097	
70%							
BINO	6	1.645	0.651	1.196	0.290	1.039	0.409
0.3	6	1.415	0.451	1.059	0.224	0.987	0.391
0.6	6	1.315	0.823	0.821	0.173	0.926	0.159
1.2	6	1.133	0.609	0.707*	0.246	0.853	0.163
1.8	6	1.208	0.823	0.852	0.158	0.864	0.159
2.4	6	1.269	0.519	0.929	0.179	1.061	0.259
3.0	6	1.757	0.967	1.103	0.210	1.040	0.154
MONO	6	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,40)}=0.877$ p=0.533		$F_{(7,40)}=3.851$ p=0.003**		$F_{(7,40)}=0.642$ p=0.719	
40%							
BINO	6	1.236	0.863	1.210*	0.173	1.077	0.440
0.3	6	1.625	1.463	1.340*	0.239	1.215	0.257
0.6	6	1.796	1.406	1.175	0.183	1.001	0.209
1.2	6	1.317	0.647	0.726*	0.232	0.856	0.255
1.8	6	1.317	0.600	0.991	0.360	0.997	0.198
2.4	6	1.464	0.457	1.084	0.419	1.056	0.327
3.0	6	1.831*	0.728	1.096	0.254	1.110	0.298
MONO	6	1.000	0.000	1.00	0.000	1.000	0.000
ANOVA		$F_{(7,40)}=0.623$ p=0.734		$F_{(7,40)}=2.947$ p=0.014*		$F_{(7,40)}=0.861$ p=0.545	
15%							
BINO	6	1.304	1.108	1.155	0.316	1.229	0.576
0.3	6	1.380	0.687	0.872	0.233	1.060	0.580
0.6	6	1.606	1.258	0.745	0.288	0.975	0.500
1.2	6	1.0838	0.214	0.881	0.315	1.089	0.488
1.8	6	0.827	0.441	0.778	0.217	1.006	0.266
2.4	6	1.397	0.966	0.902	0.372	1.091	0.328
3.0	6	1.379	0.552	1.066	0.248	1.099	0.184
MONO	6	1.000	0.000	1.000	0.000	1.000	0.000
ANOVA		$F_{(7,40)}=0.654$ p=0.709		$F_{(7,40)}=0.617$ p=0.159		$F_{(7,40)}=0.225$ p=0.977	
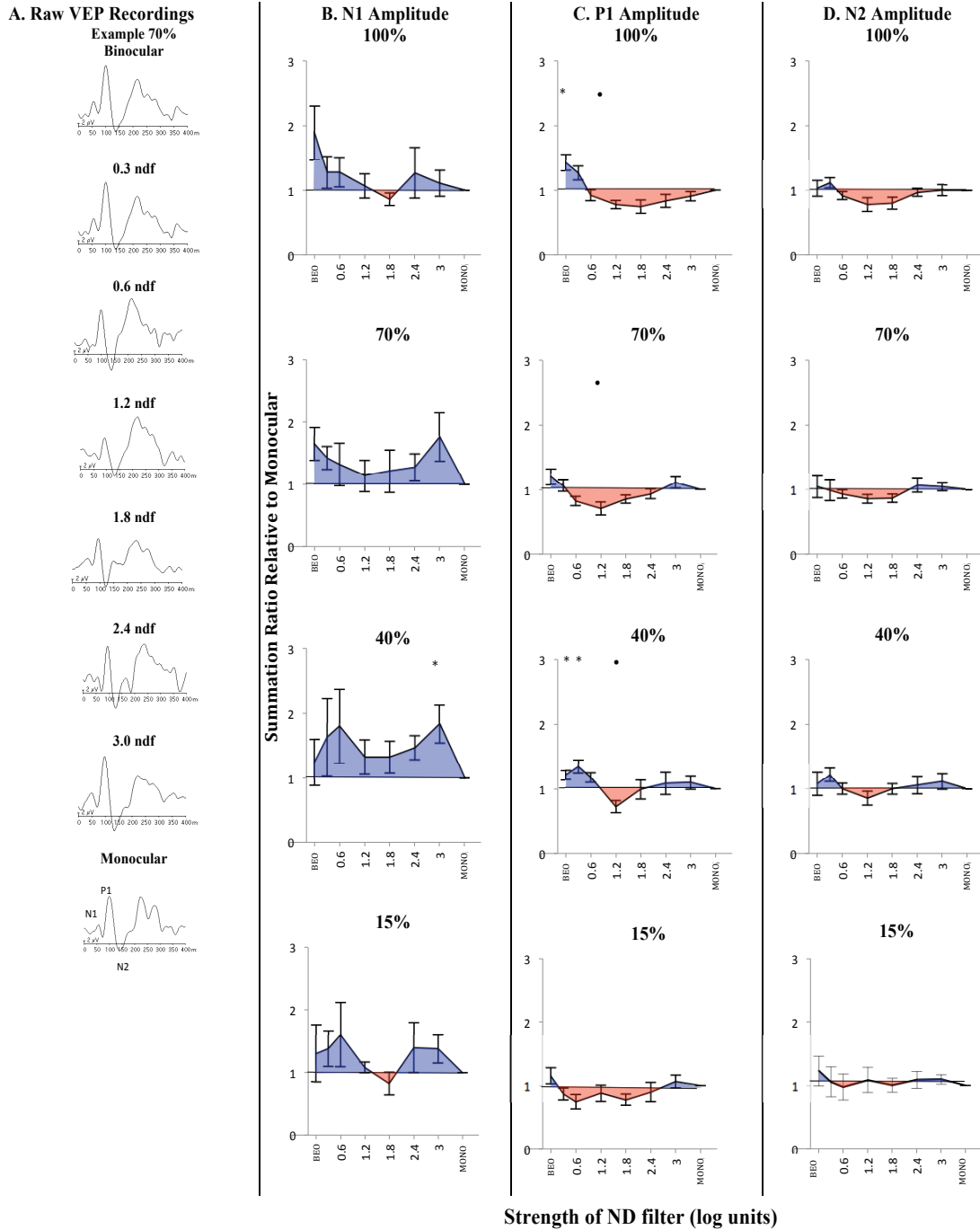
Figure 23. Effect of contrast and NDF strength on SR of N1, P1, and N2. Column A depicts raw VEP recordings. Under the monocular condition the N1, P1, and N2 components are identified. Column B, C, and D represent the average SR N1, P1, and P2 respectively for contrast 100%, 70%, 40%, and 15%.

61

4.5.2 Maximal Binocular Interactions

Results of an ANOVA to analyze the effect of contrast on maximal interocular interactions reveal contrast level does not have a significant effect on maximal BS and BI for all three VEP components. The amount of BS and BI seems fairly equal across all contrast levels (Figure 24). The highest amount of BS for N1 was 1.88 with 100% contrast under binocular condition, and highest BI was 0.827 at 15% contrast and 1.8 log unit ND filter. The highest amount of BS for P1 was 1.428 with 100% contrast under binocular condition, and highest BI was 0.707 with 70% contrast and 1.2 log unit ND filter. The highest amount of BS for N2 was 1.229 with 15% contrast under binocular condition, and highest BI was 0.778 with 100% contrast and 1.2 log unit ND filter.

Table 18. Effect of contrast on maximal binocular interactions.

Contrast	N	N1		P1		N2	
		Max	SD	Max	SD	Max	SD
BS							
100%	6	1.888(B)	1.021	1.428*(B)	0.300	1.111(0.3)	0.580
70%	6	1.645(B)	0.651	1.196(B)	0.290	1.061(2.4)	0.259
40%	6	1.831*(3.0)	0.728	1.340*(0.3)	0.239	1.215(0.3)	0.257
15%	6	1.606(0.6)	1.258	1.155(B)	0.316	1.229(B)	0.576
ANOVA		$F_{(3,20)}=0.381$, p=0.768		$F_{(3,20)}=1.167$, p=0.347		$F_{(3,20)}=0.423$, p=0.738	
BI							
100%	6	0.859(1.8)	0.239	0.746(1.8)	0.261	0.778(1.2)	0.488
70%	6	1	0	0.707*(1.2)	0.246	0.853(1.2)	0.163
40%	6	1	0	0.726*(1.2)	0.232	0.856(1.2)	0.255
15%	6	0.827(1.8)	0.441	0.745(1.8)	0.288	0.975(0.6)	0.500
ANOVA		$F_{(3,20)}=0.637$, p=0.600		$F_{(3,20)}=0.096$, p=0.961		$F_{(3,20)}=0.545$, p=0.657	
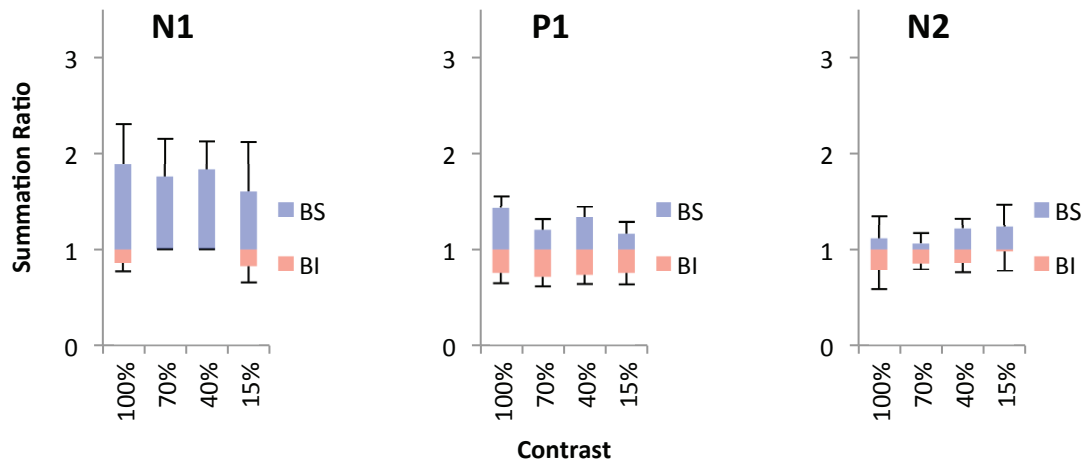
Figure 24. Effect of contrast on maximal binocular interactions.

4.5.3 Area Under The Curve

ANOVA results show the average AUTC is not significant between contrast levels for all three components (Table 19). The N1 component had very little AUTC at all contrast levels, while P1 and N2 show more AUTC with a general trend of higher contrast having more AUTC (Figure 25).

Table 19. Effect of Contrast on AUTC.

Contrast	N	N1		P1		N2	
		AUTC	SD	AUTC	SD	AUTC	SD
100%	6	9.845	28.137	60.852	19.337	67.561	17.588
70%	6	0	24.533	49.645	31.514	53.630	20.351
40%	6	0	25.577	22.521	17.779	25.339	25.901
15%	6	9.208	29.388	65.298	27.803	12.912	31.881
ANOVA		$F_{(3,20)}=0.431$ $p=0.733$		$F_{(3,20)}=0.615$ $p=0.613$		$F_{(3,20)}=0.553$ $p=0.652$	
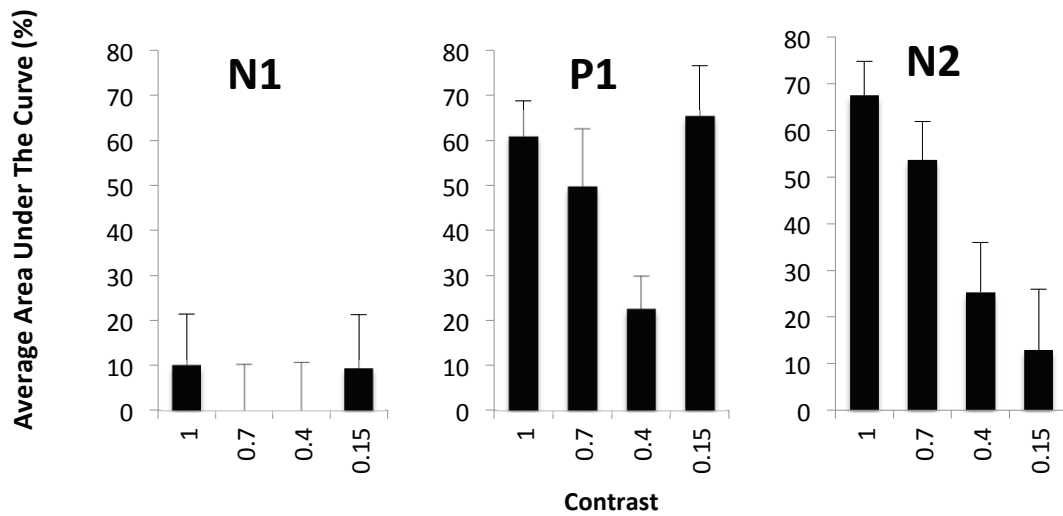
Figure 25. Effect of contrast on AUTC.

4.6 Pulfrich Effect

Results obtained from 12 individuals (age 19-52 years) with healthy eyes who completed Pulfrich computerized pendulum testing is summarized below (Figure 26). The individual data (A) and individual trend lines (B) show a positive slope, although starting points vary (2.62 to 11.91°, mean 5.43°). All but one subject has a slope varying between 1.33 and 4.24 °/log unit, with an average slope of 2.88 °/log unit. A linear regression analysis of the mean data gives a coefficient of determination of $R^2 = 0.95$ (C).

(A)
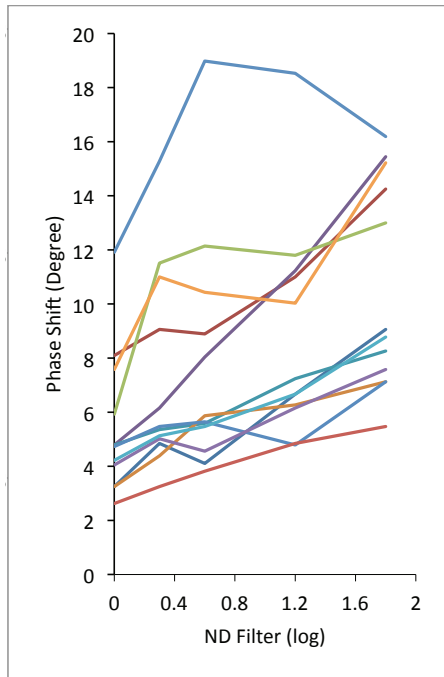
(B)
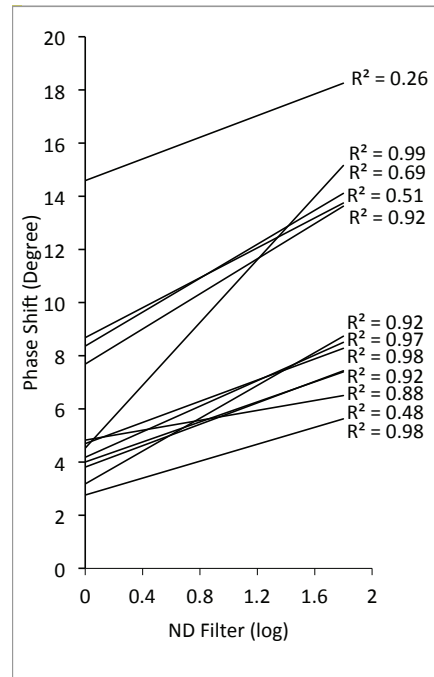
(C)
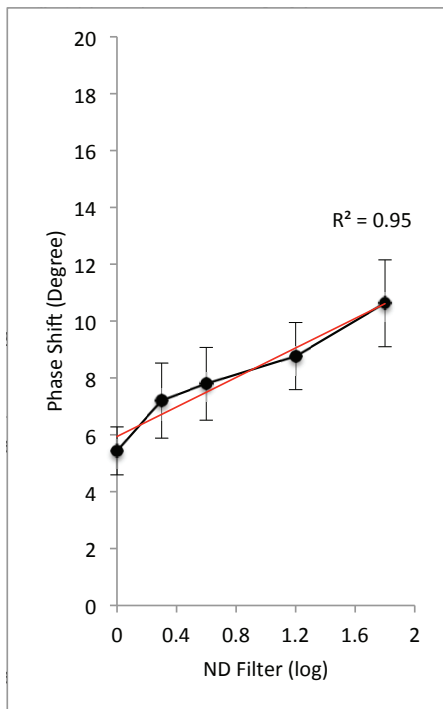
Figure 26. Phase shift reltitive to baseline as a function of ND filter strength.
A) Phase shift for each participants. B) Individual trend lines with their corresponding R^2
values. C) Mean phase shift with corresponding tend line, SE, and R^2 value.

CHAPTER 5: DISCUSSION

5.1. Components Of A VEP Waveform

Since P1 is the major component of the VEP waveform and is reliable between individuals and stable across a broad age, it will be the focus of future discussion. This will also allow for a more direct comparison of the results to previous studies.

5.2 Effect Of ND Filter On The SR

Irrelevant of stimulus parameters, the SR of the VEP response curve generally showed the same trend. Under binocular conditions (absence of ND filter) and when a mild ND filter was used (0.3 log unit), maximum amount of BS was obtained. This observation of BS when interocular luminosity difference was low agrees with reports by Spekreijse, van and Regan (1972), Spekreijse (1966), Ciganek (1970), Perry and Childers (1968), and more recently by Mitsuyu and Yanashima (1982), Gilchrist and Mciver (1985), and Pardhan and Gilchrist (1991). A possible explanation as to why a 0.3 log unit filter produced a high amount of BS, is that the filter was placed over the dominant eye, so a mild filter may make the sensitivity of the two eyes closer to equal resulting in higher summation.

The SR decreased with increasing ND filter strength (increasing interocular luminosity difference). When interocular luminosity difference exceeded 0.6 log unit, the SR was considerably reduced until equal to or smaller than the monocular VEP amplitude. With an interocular luminosity difference between 1.2 and 2.4 log unit, BI frequently occurred, with maximal BI typically obtained with a 1.8 log unit ND filter. This is similar to results observed by Trick, Dawson, & Compton (1981), where an interocular luminosity difference of more than 1.3 log unit ND filter produced a binocular VEP amplitude smaller than the monocular VEP. Katsumi et al. (1986a) reported an interocular luminosity difference of more than 0.8 log unit was enough to produced a binocular VEP amplitude smaller than the monocular VEP, and BI was maximal with a 2.0 log unit ND filter.

Similarly, Pardhan et al. (1990) observed the binocular VEP response amplitude decreased to monocular level with ND filter strength of 0.6 log unit, and BI was maximal with 2.0 log unit ND filter. Beyond an interocular difference of 2.4 log unit, our results

indicate suppression occurred and the binocular VEP amplitude was almost equal to the monocular amplitude. This was also observed by Katsumi et al. (1986a) beyond 2.5 log unit and Pardhan et al. (1990) beyond 2.7 log unit. Slight differences in the luminosity values can be explained by differing stimulus parameters such as contrast and check size (Katsumi et al: 30% and 25', and Pardhan: 96% and 41').

A three-phase explanation has been proposed by Katsumi et al. (1986a) to describe VEP amplitudes while increasing interocular luminosity difference: binocular summation, binocular inhibition, and suppression.

> **Phase I/Binocular Summation**-when interocular luminosity difference is low, the interocular system will compensate for the differences.
>
> **Phase II/ Binocular Inhibition**-when the interocular luminosity difference increases, the two eyes interact and as a result the binocular VEP amplitude response becomes smaller than the monocular response.
>
> **Phase III/Suppression**-when the interocular luminosity difference increases further, there is no binocular interaction due to the large difference in visual inputs, so as a result of suppression, the monocular and binocular response become almost equal.

Throughout our study, the ND filter was always placed over the dominant eye. A study by Heravain-Shandiz et al. (1991) compared the results of binocular VEP recordings and found it does not appear to be important whether the filter is before the dominant or non-dominant eye (no statistical difference). This also agrees with a similar study done by Spekreijse et al. (1972).

5.3 Effect Of Stimulus Parameters

Several studies have used flash and PR-VEPs to objectively evaluate binocular function. In early studies, the reported value of BS varied greatly, from 0% (Inoue, 1966) to more than 100% (Tsutsui & Fukai, 1980), with the average being about the square root of 2 (1.41 or 41%) (Cigánek, 1970; Perry & Childers, 1968; Spekreijse, 1966). The wide variation of the reported values can be partially explained by the differences of stimulus parameters. More recently, Katsumi et al. (1988) reported BS of 1.4, Pardhan (1996) also

found the average amount of BS to be 1.4, and Bourassa and Rule (1994) found the average BS to be 1.45.

It was one of the objectives of this study to explore these variations by examining the effects of stimulus check size, location, and contrast. Although many studies have investigated BS, studies reporting BI with the use of VEP are quite limited in comparison. If the effect of each stimulus parameter on VEPs were known, testing would become more reliable and could provide a more useful means of evaluating binocular function. The goal of this study was to shed light on the possible neural generators of BS and BI by determining if the structure and location of the stimulus is important to elicit these binocular interactions using VEPs. If both BS and BI are caused by the same neural generator, then stimulus conditions that generate BS would also be expected to generate BI. Alternatively, if separate neural generators are responsible, the stimulus conditions that produce BS would differ from conditions that produce BI.

5.3.1 Check Size

Our results show the amount of BS was highest when a small check size was used, and as the check size increased, the amount of BS decreased (Figure 12). Maximal BS of 1.9 was obtained with the smallest check 6'. This is in agreement with Katsumi et al. (1988) who reported the amount of BS was highest when the smallest check size was used (7.5'), Mitsuyu & Yanashima (1982) who found BS was highest when using 9.5', and di Summa et al. (1997) who found BS mainly occurred when using smaller check sizes (15' compared to 84'). Aparkin, Nakayma, and Tyler (1981) used the frequency sweep technique which scans spatial frequencies from 150 to 1.5', and found highest amount of BS with 7.5'. Conversely, Hara (1984) reported the value of BS did not show significant changes between spatial frequencies.

Our results show the amount of BI was highest with a large check size (115') and occurred when using a 1.8 log unit ND filter. This agrees with results of Heravain-Shandiz et al. (1991), who found larger check size produced more BI compared to smaller check size (50' compared to 5.5') when 1.0 log unit ND filter was placed in front of one eye.

It appears that BS is tuned for small check sizes, while BI is not significantly tuned for check size there is a trend of increasing BI with larger check size, suggesting BS and BI have different neural generators. Check size will impact the neuronal cell population that is generating the response. Based on the non-uniformity in the size of the receptive fields for ganglion cells across the retina, small checks will generate more of their response from the central retina, and larger checks will generate more of their response from the peripheral retina. Harter (1970) reported when the foveal area (central 2°) was stimulated, relatively small checks (15-30') evoked the greatest amplitude response. However, when progressively more peripheral areas of the retina were stimulated (7.5°), the larger check sizes (60') produced the greatest amplitude response. To further explore this, next we examined the importance of stimulus location in producing binocular interactions.

5.3.2 VEPs With Central And Peripheral Stimulation

It has been observed that greater amounts of BS occurs when grating patterns for fine elements are subtending 10-20° (Harter, Seiple, & Salmon, 1973; White, 1969). These findings have been confirmed in other studies using various VEP testing techniques (Apkarian et al., 1981; Heravain-Shandiz et al., 1991), however, the hypothesis used by various authors to explain the results have not been consistent. Previous studies have shown that the magnitude of the BS can vary between 20-60% with an average increase of about 41% (Apkarian et al., 1981) depending on the parameters of the stimulus (spatial frequency, temporal frequency, luminance, contrast, etc.) and the recording techniques used (McKerral et al., 1995).

Our results show significant BS occurs at both central and peripheral locations of the visual field with VEP stimulation, however the peripheral visual field showed the highest amount of BS (Figure 14). Similar to our results of higher BS in the periphery, Tsutsui and Fukai (1980) reported BS at the fovea of 1.29, at the macula 1.51, and at the periphery of 1.49, and suggested BS in the periphery could be attributed to the activity of the Y (transient) system. Although highest amounts of BS were found at the periphery, it is not significantly different from the amount of BS found with central stimulation, suggesting with our parameters, stimulus location to not affect BS.

Caution must be taken when comparing results between studies of stimulus location in regards to the size of field location. In our study, "central" refers to the central 10°, while periphery refers to >10°, and 29' check size of 100% contrast was used. Mitsuyu and Yanashima (1981) reported that BS was higher at 2° (with 9.5' check) stimulation than at 4° (with 19' check). These results are difficult to directly compare because the check size was not constant. In contrast, using 24' check size at 30% contrast, Katsumi et al. (1986b) reported the values of BS was highest at the central stimulus field of 4x4° and at larger sizes there were no significant changes in BS. Furthermore, the value of BS showed a significant reduction with a small central scotoma and the authors concluded that PR-VEP is very sensitive to a central scotoma and that binocular function is mediated through the central stimulus field. Discrepancies between these reports might be partially attributed to the difference of the stimulus field size, check size, and contrast used.

In our study, BI occurred with both central and peripheral stimulation, but the central visual field showed the highest amount of BI. Again, using our parameters, the amount of BI obtained was not significantly different between stimulus locations suggesting stimulus location does not effect BI. To my knowledge, previous studies investigating BI with peripheral stimulus >10° are nonexistent.

Retinal sensitivity to targets of a given size depends on the area of the retina of which the targets are presented. Sensitivity is controlled by the distribution of retinal receptor elements and their representation in the visual cortex (Kooijman, Looijestijn, Welling, & van der Wildt, 1994). A constant decrease in retinal sensitivity exists with increasing eccentricity. This is thought to arise from the decrease in density of receptive fields, and the increase in size of receptive field of ganglion cells across the retina check sizes in the periphery. Central saturation is likely to occur because the receptive fields within the central regions are relatively small (Wood, Collins, & Carkeet, 1992). Previous reports suggest checks of less than 30' are effective for foveal stimulation and are suitable for obtaining the best central response; larger checks are effective for parafoveal stimulation (di Summa et al., 1997). Due to this non-uniformity of the receptive fields for ganglion cells across the retina, mfVEP stimulation was used as

another stimulation technique to allow optimal check size to be used to stimulate specific
eccentricities.

5.3.3 mfVEP Ring Stimulation

mfVEP ring stimulation was used to further investigate the influence of location
on BS and BI. mfVEP testing has many advantages: 1) the size of the pattern element is
scaled with eccentricity (inversely to cortical magnification) to generate approximately
the same signal amplitudes across the stimulated field, 2) allows for independent
responses from multiple areas of the visual field to be simultaneously obtained, and 3)
allows for the possibility of doing analysis with various eccentricities.

Our results show BS occurred at all ring locations and was maximal with most
peripheral ring stimulation (25.1-41°). The standard deviation associated with the SR at
peripherally location rings are quite high, suggesting the data is spread out over a large
range and may be quite variable. Contrary to our results, Norihiro et al. (2004) also used
mfVEPs to study BS and found the central 10° ring produced the highest amount of BS
(1.38), while paracentral filed (10-25° annular) only produce BS of 1.17. Furthermore,
our results show BI only occurred at the central two ring location, though these values
were not significant. To my knowledge, no previous studies have been conducted using
mfVEP to explore BI.

BS and BI appear to have a non-uniform distribution in the visual field. With our
sampling size, the ANOVA looking at the effect of mfVEP stimulus location on BS did
not reach significance levels; however there is clear indication that would suggest larger
BS occurs with increasing eccentricity. Initial testing with PR-VEPs using only central
or peripheral field stimulus supported this, and additional testing with mfVEPs confirmed
these findings. Although these results are similar, the P1 component of VEPs may not
directly correspond with the P1 component of mfVEPs. To further explore peripheral
stimulation, Ganzfeld diffuse flash was used.

5.3.4 Ganzfeld Stimulation

A study by Bourassa and Rule (1994) revealed Ganzfeld viewing conditions
produce a high degree of BS and Fechner's paradox was greatly reduced or absent in

theses conditions; our results are consistent with these findings. A brightness matching study by Leibowitz and Walker (1956) showed similar results, and they suggested that homogenous areas tend to produce binocular brightness summation, and that boundary contours inhibit the summation process. Our results agree with previous reports and suggest the neural dynamic of BS and BI differ, and there is a trade off between BS and BI under Ganzfeld stimulus conditions. Since the Ganzfeld stimulus is non-structured, it mainly generates VEP responses from the peripheral retina, which also correspond with our previous VEP and mfVEP findings.

5.3.5 Contrast

Our results show BS occurred at all contrast levels tested, and the amount of BS was maximal with the highest contrast level tested. Our results agree in part with Apkarian et al. (1981) who reported BS occurred with high stimulus contrast and being maximal with higher contrast stimulus (60-70%). Differing from these results, Srebro (1978) found maximum BS (1.25) at 3-10% stimulus contrast. Katsumi et al. (1985) evaluated binocular function with PR-VEPs and stimulus contrast levels from 20-95% and results showed BS was highest at 20-30% contrast and decreased with increasing contrast. At 40-50% contrast, BS was usually smaller than 1.40, and at high contrast (80-95%) BS was ~1.1 to 1.2.

VEP amplitudes have been found to saturate as stimulus contrast increases. In general, the VEP amplitude increases as contrast increases up to a certain level, but a further increase in contrast does not significantly effect the amplitude (Spafford & Cotnam, 1989). Katsumi et al. (1985) found that the binocular VEP amplitude reaches saturation at 20% contrast stimulus, while the monocular VEP amplitude reaches saturation at higher contrast stimulus, around 60%. Similar results were found using flash stimulation by Spekreiji (1966) and using PR-VEP stimulation by Mitsuyu and Yanasima (1982). The lower saturation level of the binocular VEP compared to the monocular VEP can be attributed to BS (Katsumi et al. 1995).

Our results show BI occurred at all contrast levels tested, and the amount of BI was maximal at 70% contrast, however the amount of BI was very similar at all contrast levels and not significant between contrast levels. This is similar to the findings of

Spafford and Cotnam (1989) who observed measurable BI for all contrast levels tested (4-65%), however they did not indicate which contrast level shows the most BI.

BS and BI do not seem to be modulated by stimulus contrast, suggesting these binocular interactions do not have a selective implication for the M and P pathways. This could be further investigated if lower contrast levels were used to tune for the M pathway, however a reliable VEP waveform still needs to be obtained. Furthermore, we could have varied the check size used with different contrast levels, large check size with low contrast to stimulate the M pathway, and small check size with high contrast to stimulate the P pathway. Analysis of the studies reviewed reveal significant differences in the stimulus and recording conditions, such as electrode placement, and temporal and spatial frequency, which likely account for a portion of the discrepancies.

Since the check size (29') was constant with all contrast levels, we can compare the 100% contrast data to the check size data of 29', where the contrast (100%) was constant, as both have the same stimulus condition preformed on different individuals. Both VEP response curves have similar form, with a significant ANOVA, significant BS and significant BI.

5.3.6 Summary

Table 20 below summarizes the effect each stimulation parameter has on binocular interactions. It appears that to produce maximal amount of BS, a peripheral stimulus of small check size and high contrast should be used. Alternatively, it appears a central stimulus of large check size and high contrast should be used to produce maximal amounts of BI. Since BS and BI are produced with differing stimulus parameters, our results suggest separate neural generators are responsible for BS and BI.

Table 20. Summary of effects of stimulus parameters on binocular interactions.

Stimulation Parameter	Maximal BS	Maximal BI
Check size	Small	Large
VEP Center/Periphery	Peripheral	Center
Location-mfVEP ring	Peripheral	Center
Ganzfeld	Yes	No
Contrast	High	High

5.4 VEP Model

The following VEP model was produced using data obtained from participant ks016 with 100% contrast and 29' check size PR-VEP. The VEP response obtained under monocular conditions was added to the VEP response obtained under monocular conditions with a ND filter over the eye. The sum of these responses (hypothetical binocular response) was compared to the actual response obtained under binocular conditions with a ND filter over one eye (Figure 27).

Under monocular viewing conditions with a ND filter over the eye, the VEP P1 amplitude response is maximal with no filter and decreases as the strength of the filter increases (column B). Furthermore, the IT increases linearly as the strength of the ND filter increases. When these responses are mathematically added to the monocular response (column A), the amplitude of the resultant hypothetical binocular response (column C) has the same trend as the monocular response, but at higher values. The actual binocular response amplitude (column D) shows a different tend, the initial binocular amplitude is high and decreases with increasing filter strength, then increased again to the monocular level. Furthermore, with the 1.2 and 1.8 log unit ND filter, the actual binocular response is much smaller than the hypothetical response, as well it is smaller than the monocular response, indicating BI has occurred.

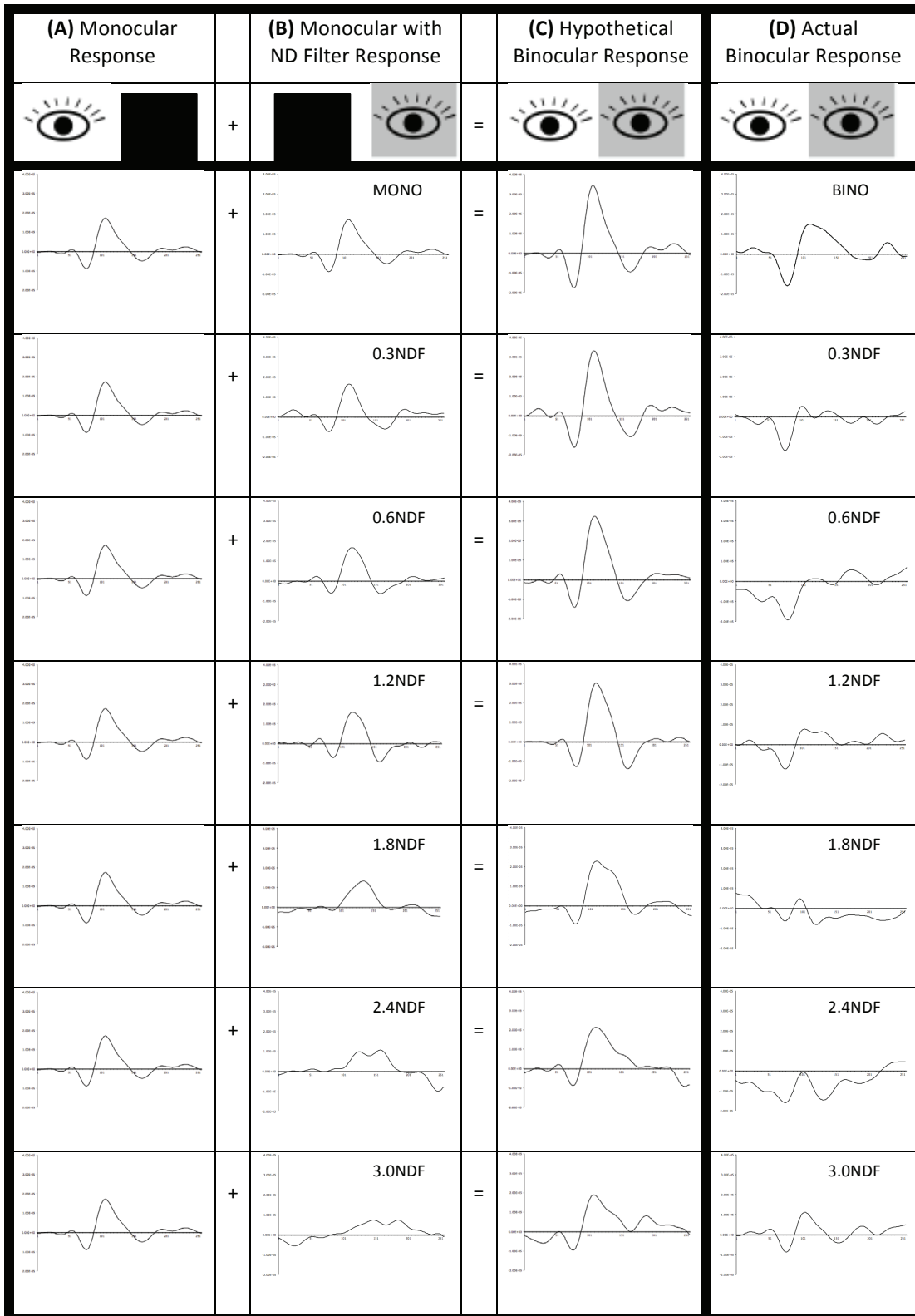*Figure 27. VEP Model"* Open eye indicates the eye is viewing the stimulus, the black square indicated the eye is occluded and not viewing the stimulus, and the grey box around the eye indicates the eye is viewing the stimulus through a ND filter.

In addition to exploring the amplitude of the VEP response with this model, we also explored the IT. The contribution of each monocular pathway to the timing of the binocular VEP was explored by McKerral et al. (1995). Results show that in binocular viewing conditions with a monocular blur, the artificially delayed input from the blurred eye is suppressed and does not seem to contribute to the making of the binocular response. This is similar to the results of Heravian-Shandiz et al. (1991) that showed when an interocular timing difference was induced using a ND filter in front of one eye, the peak time of the binocular VEP was similar to that of the unfiltered eye. Our results of the above VEP model are supported by these studies. Our VEP model shows with increasing ND filter strength, the monocular and hypothetical binocular IT increases, while the actual binocular IT does not show much of an increase.

To further investigate the effects IT on binocular interaction, we also looked at the Pulfrich effect.

5.5 The Pulfrich Effect

5.5.1 Computerized Pendulum Test

Using computerized pendulum tests with a ND filter over the RE, we determined the phase shift needed to change the PE to a CW direction is proportional to the strength of the ND filter used: increasing ND filter strength required an increase phase shift that can be adequately represented with a linear fit. A linear regression analysis of the mean gives a coefficient of determination of $R^2 = 0.95$, suggesting a strong positive linear relationship. Results show the average minimum phase shift needed to change the PE in a CW direction under binocular conditions was 2.26°, maximum phases shift needed was 11.9°, with a mean of 5.43°.

Testing for PE is the only way to clinically determine if motion stereopsis is normal (Stadelmann et al., 2009). Until recently, no simple method to quantify the PE has been available. Traditional bedside testing of PE involves the swinging pen test to determine if a spontaneous PE is present and can only estimate the size. Additionally, a mechanical pendulum can be used for a more accurate estimate, but few eye clinics have such a device. Our computerized Pulfrich testing was based off a design by Stadelmann et al. (2009), who provided promising results with a computer based method for

quantifying the PE using an interocular image phase shift to measure delays. Although the authors did use ND filters to compare the computerized pendulum to the mechanical pendulum, they did not provide any data on the correlation of individual data. The few subjects they did analyze did show individual slopes were quite variable, between 0.8 and 1.2, while in our study, individual slopes were more stable (except one individual).

Similar to our results, Stadelmann et al. (2009) observed that the filter strength influenced the size of the illusion. Variations between individuals such as starting point to neutralize the effect under binocular conditions and different slope values are difficult to explain. It appears that age, sex, and visual acuity do not influence these values. Individual reaction times may account for some differences. Beyond ND filter strength of 1.8 log unit the PE could not be perceived, which coincides with Stadelmann et al. (2009) results of 1.7 log unit.

5.5.2 Comparing PE To VEPs And Clinical Applications

VEPs measure the transmission times in each visual pathway independently, whereas the computerized pendulum test is designed to measure interocular latency differences. Both are able to detect an abnormal delay in the visual pathway when the vision of the two eyes is unequal, however it is difficult to directly compare the two measurements, as the visual pathways for PE and VEPs might be different (Mojon et al. 1998).

Several studies have attempted to compare interocular delays measured from the PE and to VEP latency recordings. Rushton (1975) and Delplace and Guillaumat (1982) investigated cases of optic neuritis and found similar results of no correlation between the two measurements. Contrary to these results, Wist et al. (1978) found a good correlation between the interocular delay for the PE and VEP measurements. More recently when Heron, McCulloch and Dutton (2002) compared visual latency using VEPs to the spontaneous PE in individuals with secondary traumatic optic neuropathy, results showed interocular latency from the PE and from VEPs correlate significantly, however interocular delays measured from VEPs was much larger than those calculated from the spontaneous PE. Additionally, this study showed interocular latency from the PE and

from VEPs correlate when normal subjects were tested with a ND filters in front of one eye.

Our results also suggest a correlation between the Fechner's paradox and the PE. It takes the pendulum 780ms to complete a full cycle of sin0° to sin90° (0 to 1.57 rad), by design the pendulum has a lag of -11.4° (0.199 rad), which should take 99ms to account for the induced phase lag. However under binocular conditions, the delay measured to notice the pendulums change to CW direction is 5.34° (0.095 rad), thus is delayed by 47ms. The 47ms value now becomes the relative zero that subsequent measurements will be compared to in order to determine the IT delay caused by the ND filter. Furthermore, these calculated latency delays can be compared to the IT measured with VEPs under monocular conditions and with a ND filter in front of the eye (Figure 28).
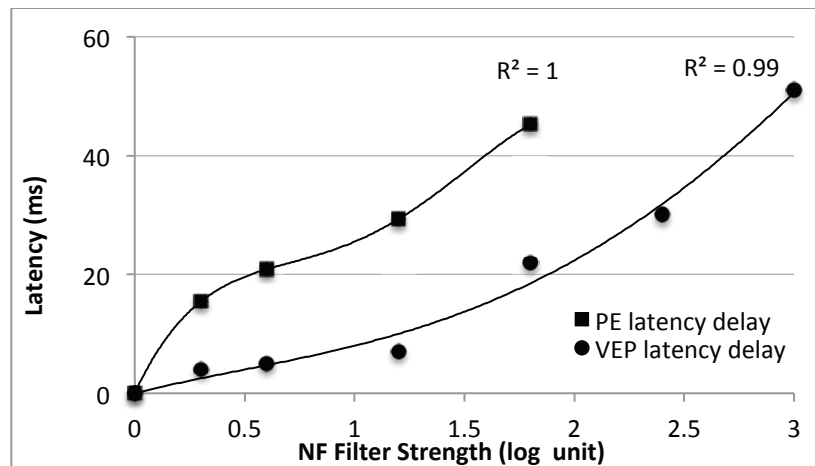
Figure 28. Comparison of the IT induced by various ND filter strengths as measured by VEPs and calculated by the PE.

It appears that the IT measured with VEPs and calculated with the PE correlate as both increase with increasing ND filter strength, however the delays measured by the PE are larger than those of the measured VEPs. This is likely due to the nature of PE having a low sensitivity to subtle change in conjunction with the end point being beyond neutralization so that pendulums reversed. For this reason, measuring latency delays with VEPs is more appropriate for clinical application.

78

Both visual phenomena can occur spontaneously in every day life and can also be induced experimentally with the use of ND filters. Under experimental conditions, both are produced with high contrast stimuli. Of interest however, is that the nature of the PE (linear) differs from what is observed with VEP amplitude and Fecher's paradox (non-linear). At ND filter strength 1.8 log unit, maximum BI is observed with VEPs, while the PE is maximum at 1.8 log unit, and is diminished and not possible with a stronger filter.

It has been reported that compared to the unaffected eye, the amblyopic eye has a significantly lower VEP amplitude (Spekreijse at al., 1972), however other reports have also found no significant difference between the amplitude of the two eyes (Halfeld Furtado et al., 2013). Furthermore, BI of the VEP amplitude has been reported (Apkarian et al., 1981; Fiorentini, Maffei, Prichio and Spinelli, 1978), but no significant BI of VEP IT in amblyopes has been observed (McKerral, 1995). Atilllisa et al. (2006) reported that ON VEP latency values were significantly longer in the affected eye compared to the unaffected eye, and a latency delay of 107ms can be accepted as a sign of a defect in optic nerve transmission. In regards to binocular latency, BS (shorter peak time) can be found if the monocular latency difference is small between the two eyes, and BI (longer peak time) is present ON cases with larger latency differences in peak latency between the two eyes. Hoeppner (1980) examined the binocular VEPs in patients with delayed latency of one eye due to demyelination and reported that when the interocular latency difference was smaller than 34ms BS was present, but when interocular latency difference was larger and 34ms BI was present.

Also of interest are results of a study by Plainis et al. (2013) who determined a small-aperture monovision opaque contact lens worn in the non dominant eye resulted in marked interocular differences in visual latencies and also induced the PE.

5.6 Other Forms Of Binocular Interactions

Binocular rivalry is another visual phenomenon that occurs in individuals with normal binocular vision, in which perception alters between dissimilar images presented to each eye. When different images are present to each eye, instead of the two images being superimposed, one image is seen for a few moments then the other. At the transition point, a brief unstable composite of the two images may be seen. Rivalry can

be demonstrated most dramatically by presenting parallel lines to each eye separated 90°. This study did not explore binocular rivalry.

It has been psychophysically established that a dark-adapted eye exerts a measure of tonic interocular suppression upon spatial vision that is mediated by the contralateral eye. The results of this study may support the suggestion that, rather than binocular physiological summation, the removal of tonic interocular suppression accounts for the superiority of binocular over monocular sensitivity, and consequently for the changes in VEP amplitude (di Summa et al. 1997).

Nuzzi and Franchi (1985) used VEPs and stereo tests (Titmus and TNO) to compare binocular responses, and found there was no clear relationship found between the degree of stereo and the amplitude of binocular VER. Similar results were also found by Shea, Aslin, and McCulloch (1987) who studied binocular VEP summation in infants and adults with abnormal binocular histories, and concluded that binocular VEP summation is not correlated with the presence or level of stereopsis in infants, stereonormal adults, and stereodeficient adults.

5.7 Limitations And Future Studies

Further testing on individuals with normal vision may have included using a combination of the stimulus parameters that produced maximal binocular interactions. For example we could use larger then optimal check sizes to further investigate peripheral stimulus location for BS, and smaller then optimal check sizes to further investigate central location for BI. We did not examine individuals with asymmetric visual function (amblyopia, optic neuritis, unilateral cataract, anisocoria etc.). However we did investigate two individuals with visual dysfunctions (optic neuritis and amblyopia) and preliminary results suggest results differ from normal, though this is only anecdotal and needs to be further investigated. By our means of testing, all individuals had normal vision and a disparity between the two eyes was induced by a ND filter. Additionally we did not examine individuals with spontaneous PE, therefore we cannot exclude the possibility that patients might behave differently than normal subjects with an induced PE.

5.8 Conclusion

      The results of this study suggest binocular interaction of BS and BI are more complex then the addition of the two monocular inputs. With the use of VEPs to evaluate binocular interactions, it appears separate neural generators are responsible for BS and BI. BS is tuned for stimulus check size, potentially for location, but not for contrast. Stimulus parameters that tend to produce higher amounts of BS are of small check size, high contrast and peripherally located. BI is not clearly tuned for stimulus size or location, however stimulus parameters that tend to produce higher amounts of BI are of large check size, high contrast, and centrally located. With computerized pendulum experiments, the phase shift required to neutralize the PE is proportional to the strength of the ND filter used, and also correlates with the IT measured using VEPs, however due to the variability of psychophysical experiments, VEPs appears to be a more accurate test to measure timing difference between the two eyes.

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Information and Consent Form

Research Title
How the Use of the Two Eyes is Changed When One Eye Has Lower Vision;
Characterization of Inhibitory Binocular Interactions and Clinical Significance

Researchers
Principal Investigator (Graduate Student)
Kari Smith
Masters of Clinical Vision Science Student
Dalhousie University

Co-Principal Investigator (Supervisor)
Dr. Francois Tremblay
Professor in the Departments of Ophthalmology and Visual Science, Physiology and
Biophysics, Faculty of Medicine, and the Clinical Vision Science Program, Health
Professions
Dalhousie University
Director of the Visual Electrodiagnostic Laboratory and electrophysiologist, Visual
Electrodiagnostic Labrator, Eye Care Team
IWK Health Centre

Co-Princial Investigator (Co-supervisor)
Joan Parkinson
Assistant Professor, Clinical Vision Science Program, Faculty of Health Professions
Dalhousie University
Certified Orthoptist and Certified Ophthalmic Medical Technologist
IWK Health Centre

Introduction
You are being invited to take part in the research study named above. This form provides
information about the study. Before you decide if you want to take part, it is important
that you understand the purpose of the study, the risks and benefits and what you will be
asked to do. You do not have to take part in this study. Taking part is entirely voluntary
(your choice). Informed consent starts with the initial contact about the study and
continues until the end of the study. A staff member of the research team will be
available to answer any questions you have.   You may decide not to take part or you may
withdraw from the study at any time. This will not affect the care you or your family
members will receive from the IWK Health Centre in any way.

Why are the researchers doing the study?
Vision loss is a major health threat that can affect people of all ages. Some people have
low vision because of a lazy eye (amblyopia), or because a part of their eye is damaged.
Parts that might be damages can be the optic nerve which carries information from the
eyes to the brain (optic neuropathy), or the macula which is a spot at the back of the eye
(maculopathy).

How the Use of the Two Eyes is Changed When One Eye Has Lower Vision;
Characterization of Inhibitory Binocular Interactions and Clinical Significance

Visual Evoked Potential (VEP) is a simple test used that tells us how information travels from the eyes to the brain. To do a VEP test, small metal discs are placed on the head while the person looks at a computer screen with a checkerboard pattern. This test does not hurt.

It is easy to think that you see better with both eyes open, as compared to only having one eye open, but this is not always true. When vision is worse with both eyes open and better when only having one eye open, it is called Inhibitory Binocular Interaction (IBI). IBI is normal and usually does not change how someone with normal vision sees. People who have lower vision in one eye have more IBI, so vision may be better when using only one eye as compared to using both eyes.

With the use of VEPs, we want to find how to get the most IBI possible. We want to find if 1) a certain size and brightness of the checkerboard 2) if a certain spot of the eye is more sensitive to IBI, and 3) if IBI will be found in conditions that make vision lower in only one eye. The conditions affecting only one which we are interested in are amblyopia, optic neuropathies, and maculopathies.

If we are able to find how to get the most IBI in normal eyes, we may be able to use this as a test for early detection of conditions lowering vision in one eye in people of all ages.

How will the researchers do the study?
This will be a prospective non randomized comparative cohort study. The prospective aspect of this study means that it is designed to observe events, and it is non-randomized because the subjects are assigned to be in a certain group. The results from each group will be compared to each other.

All of the research will be done at the IWK Health Centre. We are looking for a total of 65 participants: 20 participants with normal vision, 15 participants with lazy eye (amblyopia), 15 participants with optic neuropathy, and 15 patients with maculopathy.

What will I be asked to do?
If you are interested in taking part in the study, we will first go over the information and consent form; you will get a copy of this form to keep. If you decide to take part in the study and are eligible, you can either perform the testing at the end of your current eye exam, or another appointment can be scheduled for testing.

When you arrive for testing, one of the researchers will review this information and consent form with you and answer any questions. You will be asked a few questions about the study to ensure your understanding, and then asked to sign the consent form. All testing will be for research purpose only. Testing will take place during a single visit to the IWK Health Centre and is expected to take about 90 minutes.

The testing will start with a short eye exam: visual acuity (reading letters), depth perception (seeing in 3D), eye alignment, fixation behavior (looking into your eye with a light). These are all tests that are preformed in a normal eye exam. There is no need to touch your eye or have eye drops. The VEP testing will follow. A small area of your

forehead, back of the head, and earlobe will be gently cleaned with an alcohol swab, and then rubbed with a slightly rough gel for the skin. A small metal disc will be placed on the skin at each spot using a small amount of cream.

You will first sit in front of large bowl shaped piece of equipment called a Ganzfeld bowl, which will show bight flashes of light. This will be done with both eyes open, then with each eye covered with a piece of tape, then with both eyes open and a filter held over the better seeing eye. The strength of the filter will be changed throughout testing. You will then sit in front of a computer monitor that will show a checkerboard pattern. This will be done with both eyes open, then with each eye covered with a piece of tape, then with both eyes open and a filter held over the better seeing eye. The strength of the filter will be changed throughout testing. The activity in the part of your brain that deals with vision will be recorded while you are looking at the light flashes and the checkerboard on the screen. You will not feel anything during this process.

None of the equipment or procedures used pose any risk to your well being. VEP testing is used clinically when needed, however in your situation, the VEP testing will be used for research purposes only and is an additional test that is not normally done as a standard of care.

If previously unidentified abnormal results are found during testing which suggest pathology may exist, the participant will be referred to the ophthalmology fellow in the IWK Eye Care Clinic. The ophthalmology fellow will review the testing results and decide how to proceed with patient care.

What are the burdens, harms, and potential harms?
There are few anticipated risks to you during testing. None of these tests are considered invasive and do not require touching of the eye or the use of medications. You may become tired from having to look at a computer screen or light for a long period of time. A slight skin irritation may develop at the sites where metal discs were placed, but this is extremely rare and has not been a source of complaints. In very rare cases, some skin irritation may occur from the sticky patch used to cover one eye.

Your personal information will be kept confidential.

What are the possible benefits?
Taking part in this study may be of no help to you personally. It is hoped that what is learned will be of future benefit to others suffering from vision loss of one eye (amblyopia, optic neuropathy, maculopathy). Our results may prove to be better way to find condition with vision loss of one eye, and help doctors in the detection of vision loss.

What alternatives to participation do I have?
You do not have to take part in the study. Taking part is completely optional (your choice). If you decide not to take part, your decision will not affect the care you or other family members receive at the IWK Health Centre.

Can I withdraw from the study?
You can withdraw from the study at any time. Withdrawing from the study at any time will not affect the care you or other family members receive at the IWK Health Centre. If you choose to withdraw, personal or study data compiled up until that point will not be withdrawn from the study. At any time, you can verbally indicate to any of the researches that you would like to withdraw from the study.

Will the study cost me anything and, if so, how will I be reimbursed?
The study will not cost you anything to participate and you will not be paid for joining the study. To make up for your time and travel expenses (i.e. parking, gas), a onetime honorarium of $15.00 cash will be given. If you withdraw before the end of the study, the onetime honorarium of $15.00 cash will still be given.

Are there any conflicts of interest?
There are no conflicts of interest on the part of the researchers or the IWK Health Centre.

What about possible profit from commercialization of the study results?
The researchers will not receive any profit from commercialization of the study results and neither will any participants.

How will my privacy be protected?
All personal information collected from you will be kept private. The only people who will have access to your information will be those who are involved in doing the research and the IWK Health Centre research office. Exceptions to this may include the IWK Research Ethics Audit Committee, which reviews research to make sure it is being done properly. Paper records will be held in a locked area and electronic data will be password protected. These records will be kept for five years after publication of the results, as required by the IWK Research Ethics Board. If the results are published in the medical literature, no information that could identify you will be included.

What if I have study questions or problems?
If you have any additional questions about this study, you may contact the principal investigator (Kari Smith) by e-mail at ksmith@dal.ca or the Eye Care Team Research Associate (Steve van Iderstine) at (902) 470-2741 or by email at steve.van-iderstine@iwk.nshealth.ca, Monday to Friday between 8:30am and 4:30 pm.

What are my Research Rights?
Your signature on the form indicates that you have understood to your satisfaction the information regarding participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. If you become ill or injured as a direct result of participating in this study, necessary medical treatment will be available at no additional cost to you. You are free to withdraw from the study at any time without jeopardizing the health care you are entitled to receive.

If you have any questions at any time during or after the study about research in general you may contact the Research Office of the IWK Health Centre at (902) 470-8765,

How the Use of the Two Eyes is Changed When One Eye Has Lower Vision;
Characterization of Inhibitory Binocular Interactions and Clinical Significance

Monday to Friday between 9a.m. and 5p.m.

Future contact/future research/other use.
May we contact you about participating in future studies similar to this one?
Yes _____ No_____

May we keep the information/ samples gathered during this study for other research?
Yes _____ No _____

May we use the information/samples gathered at some time in the future for purposes
other than research (e.g. teaching)?
 Yes _____ No _____

How will I be informed of study results?
Due to the exploratory nature of this research and because it is does not have clinical
usage at this time, individual testing results will not be offered to the participants.

The study results will be available to you once the research is complete. Please indicate
below whether you would like to receive a summary of the study results.

Would you like to receive a summary of the study results? Yes _____ No _____

If you checked 'yes", please indicate if you would like results sent by mail or e-mail and
provide appropriate address (mailing or e-mail):

_____

_____

How the Use of the Two Eyes is Changed When One Eye Has Lower Vision;
Characterization of Inhibitory Binocular Interactions and Clinical Significance

Consent Form

Study title: Characterization of Inhibitory Binocular Interactions and Clinical
Significance.

Participant ID:_____
Participant INITIALS:_____

Participant Consent
I have read or had read to me this Information and Consent Form and have had the
chance to ask questions which have been answered to my satisfaction before signing my
name. I understand the nature of the study and I understand the potential risks. I
understand that I have the right to withdraw from the study at any time without affecting
my care in any way. I have received a copy of the Information and Consent Form for
future reference. I freely agree to participate in this research study.

Name of Participant: (Print) _____

Participant Signature: _____

Date (dd-mmm-yyyy): _____ Time: _____

STATEMENT BY PERSON PROVIDING INFORMATION ON STUDY
I have explained the nature and demands of the research study and judge that the
participant named above understands the nature and demands of the study.

Name: (Print)_____

Signature: _____ Position: _____

Date (dd-mmm-yyyy): _____ Time:_____

STATEMENT BY PERSON OBTAINING CONSENT
I have explained the nature of the consent process to the participant and judge that they
understand that participation is voluntary and that they may withdraw at any time from
participating

Name: (Print)_____

Signature: _____ Position: _____

Date (dd-mmm-yyyy): _____ Time:_____

Volunteers
Needed For Vision

The IWK Health Centre and Dalhousie University are conducting a study on how the brain responds to different patterns of visual stimulation. We are currently looking for people **between 10 and 65 years of age to take part in the study.**

You or your child may take part in the study if:

➢ You have normal vision in both eyes (with glasses or contact lenses if needed).

OR

➢ You have a condition known as amblyopia ("lazy eye") usually treated by patching one eye in childhood.

OR

➢ You have a condition known as optic neuropathy (frequently associated with multiple sclerosis, diabetes, rheumatoid arthritis)

OR

➢ You have a condition affecting the retina known as maculopathy (frequently associated with diabetes and ageing)

AND

➢ You **do not** have cataracts, reduced co-operation, or nystagmus (shaky eyes)

The study will take place at the IWK Health Centre and take about 90 minutes of your time. If you are interested in participating in this research study, or would like more information please contact:
Kari Smith at ksmith@dal.ca or 902-293-3865

Volunteer Poster   Page 1 of 1   Version 2-05 July 2010