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Low-Level Neural Processing of Photoreceptor Neuron Signals

by

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MASTERTHESIS

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Abstract

Purpose:

Novel myopia control spectacle lenses induce peripheral contrast reduction via optical diffusion. It is suggested, that the contrast reduction alters retinal processes in the low-level neural circuity, leading to an inhibition of eye growth. The purpose of this thesis is to evaluate the influence of full-field contrast reduction on low-level neural processing of the retina, described by the edge contrast sensitivity.

Methods:

In order to measure the contrast sensitivity thresholds for edge detection, a two-alternative forced-choice psychophysical test was developed. Edge contrast sensitivity thresholds for different spatial frequencies (3, 6, 12, 18 and 24 cpd) were tested using a two-sided achromatic stimulus embedded in Gaussian noise. Edge contrast sensitivity was evaluated under three conditions: one clear control lens, as well as two Bangerter foils with0.4 and 0.8 density. Each condition was repeated three times for n=5 study participants. The influence of foil density and spatial frequency on edge contrast sensitivity was analyzed using repeated measures ANOVA.

Results:

The edge contrast sensitivity with the Bangerter foils differed significantly to the control condition ($p<0.001$ The influence on the mid spatial frequencies (12 and 18 cpd) was highest (0.4 foil $p<0.001$; 0.8 foil $p<0.001$), followed by 24 cpd (0.4 foil $p=0.011$;0.8 foil $p=0.008$) and 3 cpd (0.4 foil $p=0.007$;0.8 foil $p<0.001$). The 6 cpd stimulus with the 0.4 foil did not show significance, the other test condition showed significance (0.4 foil $p>0.05$; 0.8 foil $p=0.033$). The expected difference in Bangerter foil densities could not be verified in the current study ($p>0.05$). Qualitative comparison of two subjects revealed influence of refractive error on edge CS, suggesting lower edge CS with myopia.

Conclusion:

The study provided evidence that contrast reduction via induced diffusion has an impact on edge contrast sensitivity, especially in the mid spatial frequency range. Therefore, changes in low-level neural processing of the retina could figure as possible working mechanism for novel myopia control strategies.

Keywords:

Myopia Control, Diffusion, Edge Detection, Contrast Reduction, Receptive Field, Bangerter Foil

Abstract (German)

Zweck:

Ein neuartiges Brillenglas zur Myopiekontrolle erwirkt eine Kontrastreduktion durch optische Diffusion. Der zugrundeliegende Mechanismus und Hypothese legen nahe, dass durch optische Diffusion die neuro-retinalen Prozesse verändert werden und somit das Augenwachstum gehemmt wird. Der Zweck dieser Arbeit ist es, den Einfluss von induzierter Kontrastreduzierung auf die neuronalen Prozesse der Netzhaut zu zeigen, welche durch die Kantenkontrastempfindlichkeit beschrieben werden.

Methodik:

Zur Schwellenwertbestimmung der Kantenkontrastempfindlichkeit wurde ein psychophysikalischer Test mit einem 2AFC-Paradigma entwickelt. Unter Verwendung eines bipolaren achromatischen Stimulus, eingebettet in Gauss'schem Rauschen wurden Schwellenwerte für verschiedene Ortsfrequenzen (3, 6, 12, 18 und 24 cpd) gemessen. Die Kantenkontrastempfindlichkeit wurde unter drei Bedingungen evaluiert: einer klaren Kontrolllinse, sowie zwei Bangerter-Folien mit unterschiedlichen optischen Dichten (0,4 und 0,8). Jede Testbedingung wurde dreimal für n=5 Studienteilnehmer wiederholt. De Einfluss der Foliendichte und der Ortsfrequenz auf die resultierende Kantenkontrastempfindlichkeit wurde über eine zwei-faktorielle ANOVA mit wiederholten Messungen statistisch ausgewertet.

Ergebnisse:

Die Sensitivität der Kantenkontrastempfindlichkeit der beiden Folienbedingungen Unterschied sich signifikant von der Kontrollbedingung (p-wert < 0,001). Obwohl die meisten getesteten Ortsfrequenzen signifikant durch Diffusion beeinflusst wurden war die höchste (24 cpd: 0,4 Folie p-Wert = 0,011; 0,4 Folie p-Wert = 0,008) und die niedrigsten (3 cpd: 0,4 Folie p-Wert =0,007; 0,8 Folie p-Wert < 0,001) am wenigsten verändert. Der Einfluss auf die mittleren Ortsfrequenzen (12 und 18 cpd: 0,4 Folie p-Wert < 0,001; 0,8 Folie p-Wert < 0,001) war am größten. Lediglich der 6 cpd Stimulus durch die 0,4 Folie zeigte keine Signifikanz, die andere Testbedingung zeigte Signifikanz (0,4 Folie p-Wert > 0,05; 0,8 Folie p-Wert = 0,033). Der erwartete Einfluss der Dichte der Bangerter Folien konnte in der aktuellen Studie nicht gezeigt werden (p > 0,05).

Fazit:

Die Studie liefert Beweise dafür, dass induzierte Diffusion einen Einfluss auf die Kantenkontrastempfindlichkeit hat, insbesondere im mittleren Ortsfrequenzbereich. Daher könnten durch Diffusion bedingte Änderungen der neuronalen Verarbeitung der Netzhaut, auf niedriger Ebene, als möglicher Mechanismus für neuartige Stategien zur Myopiekontrolle gelten.

Schlagwörter:

Myopie Kontrolle, Diffusion, Kantendetektion, Kontrastreduzierung, Rezeptives Feld, Bangerter Folie

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List of Abbreviations

2AFC	Two-alternative forced-choice
4AFC	Four-alternative forced-choice
CoR	Coefficient of repeatability
CS	Contrast sensitivity
Cpd	Cycles per degree
D	Diopter
DIMS	Defocus Incorporated Multiple Segments
edge CS	Edge contrast sensitivity
F.A.C.T	Functional Acuity Contrast Test
FrACT	Freiburg Acuity and Contrast Test
IQR	Interquartile range
MAR	Minimum angle of resulution
MET	Melbourne Edge Test
qCSF	quick CSF
SF	Spatial frequency
SER	Spherical equivalent refraction
TueCST	Tuebingen Contrast Sensitivity Test
VA	Visual acuity

1 Introduction

The following chapter will provide introductory information about myopia, retinal neural processing and contrast vision.

1.1 Myopia onset, progression and control

Myopia is one of three basic refractive errors besides hyperopia and astigmatism, also known as short- or near-sightedness. In a myopic eye, the far point is located in front of the retina, the magnitude of myopia is defined by the distance between the par point and the central retina. Accommodation cannot compensate for myopic refractive errors. Refractive errors of -0.50 diopters (D) or more are referred to as myopia (1). 80% of myopia occurs due to axial elongation of the eye, the other 20% are due to corneal curvature and the lens (2). Therefore, incoming rays of light focus in front of the retina in a myopic eye with relaxed accommodation, as depicted in Figure 1. Consequently, myopia is corrected with concave optics to achieve focused retinal images.

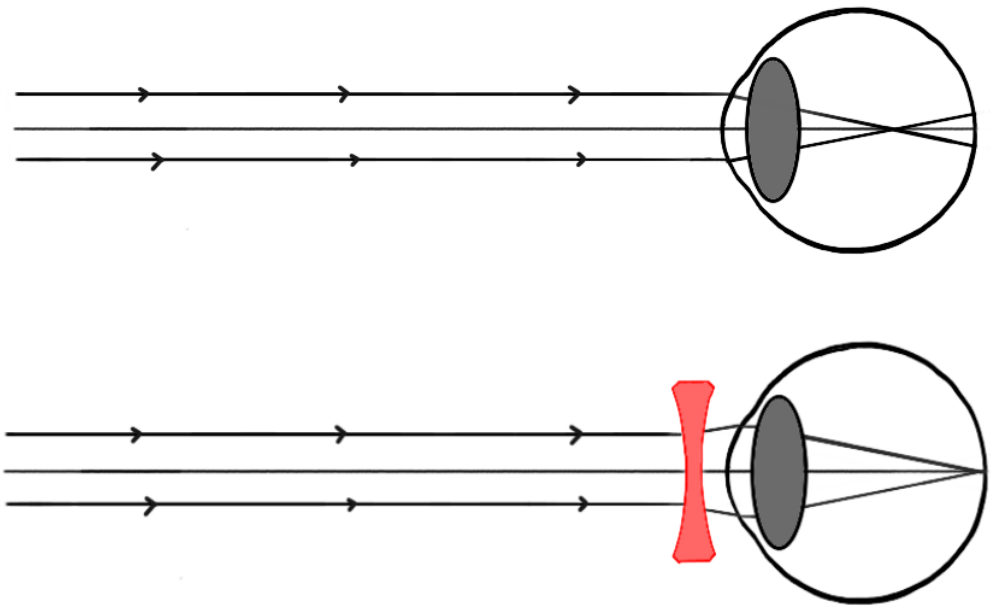

Figure 1: Myopic eyes with relaxed accommodation, without and with correction. The focal point without correction is projected in front of the retina, instead of directly on the retina.

The world-wide prevalence of myopia has been increasing and is expected to affect half of the global population by 2050. Simultaneously, the number of high myopes will rise up to 10% world-wide (3). High myopia is commonly defined as a refractive error of -6.00 D or more (1). However, perceived blur is not the only inconvenience associated with myopia and especially high myopia. The risk for several medical and potentially blinding ocular pathologies increases with the amount of myopic refractive error (4–6).The amount of myopic refraction dictates the odds to suffer from retinal detachments, -3.00 D, -6.00 D and -9.00 D result in 3-fold, 9-fold, 22-fold higher odds ratio (7,8). Myopes suffer up to 350 times more often of macular degeneration (7). Earlier onset of myopia leads to higher risk of getting ocular pathologies earlier in life, having to undergo treatments for longer periods of time. Moreover, visual impairment occurs earlier in life (3). Therefore, the socio-economic and public health burdens will arise with higher prevalence rates of myopia (7).

1.1.1 Onset and progression of myopia

On the one hand, myopia onset is defined as the point of time at which myopia is first clinically measurable. Myopia onset can be classified into four sub categories: congenital myopia, youth onset, as well as early and late adult-onset myopia (9). On the other hand, myopia progression describes the amount of increase of refractive error and axial length within a set time interval. Moreover, myopia progression and myopia onset are related: Chua et al. (10) showed that there is a higher risk for developing high myopia, if there is an earlier onset of myopia. However, myopia is further considered as a multifactorial condition, meaning that its onset and progression are influenced by multiple other genetic, environmental and behavioral aspects and their interactions.

One major factor is the genetic predisposition from parental myopia. Children with two myopic patients are at six-fold greater risk of developing myopia and have greater odds of developing high myopia (11). Furthermore, ethnicity might play a role in progression of myopia, since Asian populations show a faster progression of myopia (12).

Moreover, environmental factors play an important role in myopia development. For example, in urban regions of norther China the prevalence of myopia in adults is higher compared to rural areas (13). Furthermore, myopia is also associated with a higher level of education (6):

On the one hand, near work activities, like reading or smart phone use, seem to increase the possibility for myopia progression (14,15). On the other hand, other studies suggest that there is no correlation between near work and myopia (16,17). Nevertheless, it is still recommended to decrease the time spent on near tasks (14). The hypothesis behind the near work theory is, that a high lag off accommodation causes a hyperopic defocus on the retina. Research has not shown a correlation between onset or progression of myopia and the lag of accommodation (18,19).

Literature proposes a correlation between time spend outdoors and risk of myopia onset and progression (20,21). Several mechanisms could act together when time is spent outdoors in the prevention and inhibition of myopia. One hypothesis is that children that spend more time outdoors do not spend as much time on near tasks, however, there is no correlation between amount of near task and time spend outdoors (22). It is hypothesized, that light exposure is linked to slower axial growth (23). Further, the light intensity is a factor that has to be taken in consideration, since children that spend time outdoors during the middle of the day show better uncorrected visual acuity (VA) (15). Other indoors-induced factors that have a negative influence on myopia are the disruption of cardiac rhythms, lack of Vitamin D and dopamine, lower spatial frequency (SF) input and more peripheral retinal defocus due limited distances (22).

The SF spectrum and peripheral retinal defocus are major visual processing and perceptual aspects on which various hypotheses on myopia progression and myopia control are based.

In experiments with chicks it was shown that high SFs are needed for emmetropization and exposure to only low SFs results in form-deprivation myopia (24). Indoor scenes consist of fewer high and mid SFs, as compared to outdoor scenes (25). Translated to humans, spending more time outdoors during childhood increases the exposure to high and mid SFs, thus enhances emmetropization and reduces the likelihood of myopia development.

As aforementioned retinal defocus is suspected to promote the axial elongation, thus creating myopia progression. Defocus means that the image plane and retinal plane do not coincide. Hyperopic defocus is present if the light focuses behind the retina, myopic defocus if the light focuses in front of the retina. It can be distinguished between peripheral and central defocus on the retina. Hyperopic defocus, leads to excessive compensatory eye growth to the required focal plane and results in to lens-induced myopia (26,27).

Peripheral defocus acts on the peripheral areas of the retina only, while the central retina is optimally corrected for its refractive error. Single vision lenses with negative power produce a clear image on the central retina, but create relative hyperopic defocus in the periphery, due to off-axis optical properties (28,29). Hyperopic peripheral defocus is commonly associated with myopia progression. The hyperopic peripheral defocus profile is further enhanced in myopes, caused by the relatively prolonged and prolate eye shape compared to hyperopes or emmetropes.(30).

1.1.2 Myopia control

In order to counteract the current and future myopia "pandemic", several myopia control methods were developed (31,32). These aim at avoiding or postponing the onset of myopia, as well as trying to slow down or stop the progression of myopia. Even though some control mechanisms have not been fully understood yet, many already are applied in clinical practice. Not all aspects of myopia control will be covered in detail in this chapter, as it is emphasized on the optical strategies.

1.1.2.1 Behavioral control strategies

As mentioned previously, behavioral aspects, such as near activities and periods spend in outdoor environments, influence emmetropization and the progression of myopia. Therefore, it is recommended to increase the time spend in outdoor environments, especially during the mid of the day, as well as reducing and taking breaks from near activities (14,15,22). Increasing time outdoors can reduce the progression of myopia by up to 0.13 D a year (20).

1.1.2.2 Pharmacological control strategies

The most common pharmacological treatment used for myopia control is Atropine as cholinergic antagonist. However, several ocular and systemic side effects arise with the use of Atropine, like pupil dilation, photophobia, allergic reactions and limited accommodative

function. These unwanted side effects can be reduced by a lower concentration. Instead of using a 1% concentration, both 0.1% and 0.01% concentrations show more tolerable side effects and still maintain a protective effect on myopia, by reducing myopia progression to about 0.1 D/year (31,33,34). Another benefit of lower dosages is a smaller rebound effect (35).

1.1.2.3 Optical control strategies

Table 1 provides overview of the optical control strategies against the progression of myopia compared to control groups.

Control Method	Axial Elongation	Dioptric change	Reference
Orthokeratology	-0.27mm/ 2 years	†	(36)
Concentric Ring Contact Lenses	-0.12 mm/ year	0.31 D/ year	(37)
Peripheral Addition Contact Lenses	-0.10 mm/ year	0.22 D/ year	(37)
Progressive Addition Lenses	-0.11 mm/ 3 years	0.20 D/ 3 years	(38)
Defocus Incorporated Multiple Segments (DIMS)-Lenses	-0.34 mm/ 2 years	0.44 D/ 2 years	(39)
Optical diffusion spectacle lenses	-50%*/ year	-74%*/ year	(40)

*Table 1: Overview of optical myopia control strategies compared to control groups. Eg Concentric Ring Contact Lenses 0.12 mm less axial elongation and 0.31 D less dioptric progression occurred. *no absolute numbers were available. †no dioptric change numbers available for orthokeratology.*

In the following, the beforehand mentioned optical control strategies are illustrated in more detail. There are two types of optical control methods: contact lenses and spectacle lenses. In both cases, different optical designs are used, depending on the underlying

control hypothesis, such as reducing the lag of accommodation vs. inducing peripheral myopic defocus on the retina.

Soft contact lenses are used to achieve a myopic peripheral defocus by using either of two lens designs. Concentric rings with alternating distance correction are one of those designs. Secondly, peripheral additive gradient contact lenses are used for myopia control (37,41). In a three year trial, a concentric ring design showed 59% less change in refractive error compared to a single vision contact lens (42). Meta-Analysis of the two different designs presents 0.22 D less myopia progression for peripheral addition contact lenses and 0.3 D less myopia for concentric ring designs in a 12 month period (37).

Orthokeratology lenses represent a type of rigid gas permeable contact lenses. These are worn overnight and correct refractive error by reshaping the corneal epithelium (43). and have proven to reduce the speed of axial elongation by 43% (36). This effect is suggested to result from induced peripheral myopic defocus by the reshaped corneal epithelium (41).

Spectacle lens designs for myopia control vary over a wide range of optical designs. Under correction of near-sightedness has created contradictory results. Most studies show no beneficial impact on myopia progression, or even promoted increasing myopia (44–46). Bifocal and progressive addition lenses aim to reduce the lag of accommodation via the additive power in the near zone. Progressive addition lenses showed statistically, but not clinically significant lower myopia progression rates (-0.2 D in 3 years) (38). In children with near esophoria and large lag of accommodation progressive lenses were most effective (47). Bifocal lenses seem to have similar effects like progressive lenses (41). If bifocal lenses are combined with base in prisms in the near vision segment, the lenses become more effective in preventing myopia progression, also in patients with low baseline lags of accommodation (48).

Lens designs like the DIMS spectacle lens suggests high control efficacy. A 2-year clinical trial showed 62% less axial elongation with DIMS lenses, compared to single vision lenses. Centrally, the lens consists of a clear optical zone correcting the refractive error, surrounded by small circular segments. The peripheral segments incorporate positive addition, therefore reducing peripheral hyperopic defocus (39). Another approach are radial refractive gradient lenses with radially oriented positive defocus to achieve less

hyperopic peripheral defocus. Those lenses reduced myopia progression by up to 30% in children 6 to 12 years with myopic parents (49).

A novel approach in myopia control spectacle lenses is recently undergoing clinical trials. These lenses are similar in structure compared to the DIMS lenses, but with diffusing instead of defocusing segments. Due to the diffusion purposes of those lenses they are further referred to as optical diffusion spectacle lenses. The induced diffusion aims at decreasing contrast and leading to a more diffused retinal image in the periphery (50,51). This type of blur, created by diffusion but not defocusing of light, reduces the excitation of ON-bipolar cells in the retina, as described later. It is suggested that high retinal contrast is an additional cause for myopia progression and that the previously listed myopia control interventions reduce retinal contrast as well (40,52). This is a new approach in the management of myopia progression and is completely independent of the accommodative lag hypothesis and somewhat connected to the defocus hypothesis (40,50). A recent study demonstrates promising results with up to 74% less refractive error progression and up to 50% less axial elongation in a 12-month trial (40).

1.2 Neural processes in the retina

The retina as a direct extension of the brain is a complex structure and to this day, its functions have still not been fully understood. This chapter discusses necessary retinal knowledge on which the conducted experiment is based.

1.2.1 Structure of the retina

The retina absorbs light and converts it to an electric signal, which travels the optic nerve to the visual cortex. However, the first steps of visual processing occur already in the retina (53). The neural retina comprises ten layers, of which each contains specific cells. The most posterior structure is the retinal pigment epithelium, followed by the photoreceptor layer where the outer segments of rods and cones are found. After the outer limiting membrane, the outer nuclear layer is located with the cell bodies of the photoreceptors. The outer plexiform layer contains synapses between rods and cones and the amacrine, bipolar and

horizontal cells from the inner nuclear layer. The following layer is the inner plexiform layer with synapses between bipolar and ganglion cells. Retinal ganglion cell bodies are found in ganglion cell layer. The most anterior layers are the nerve fiber layer, containing ganglion cell axons and the inner limiting membrane as the basement membrane and innermost layer of the retina (54,55). These neuronal connections can be described as low-level neural processing of visual signals.

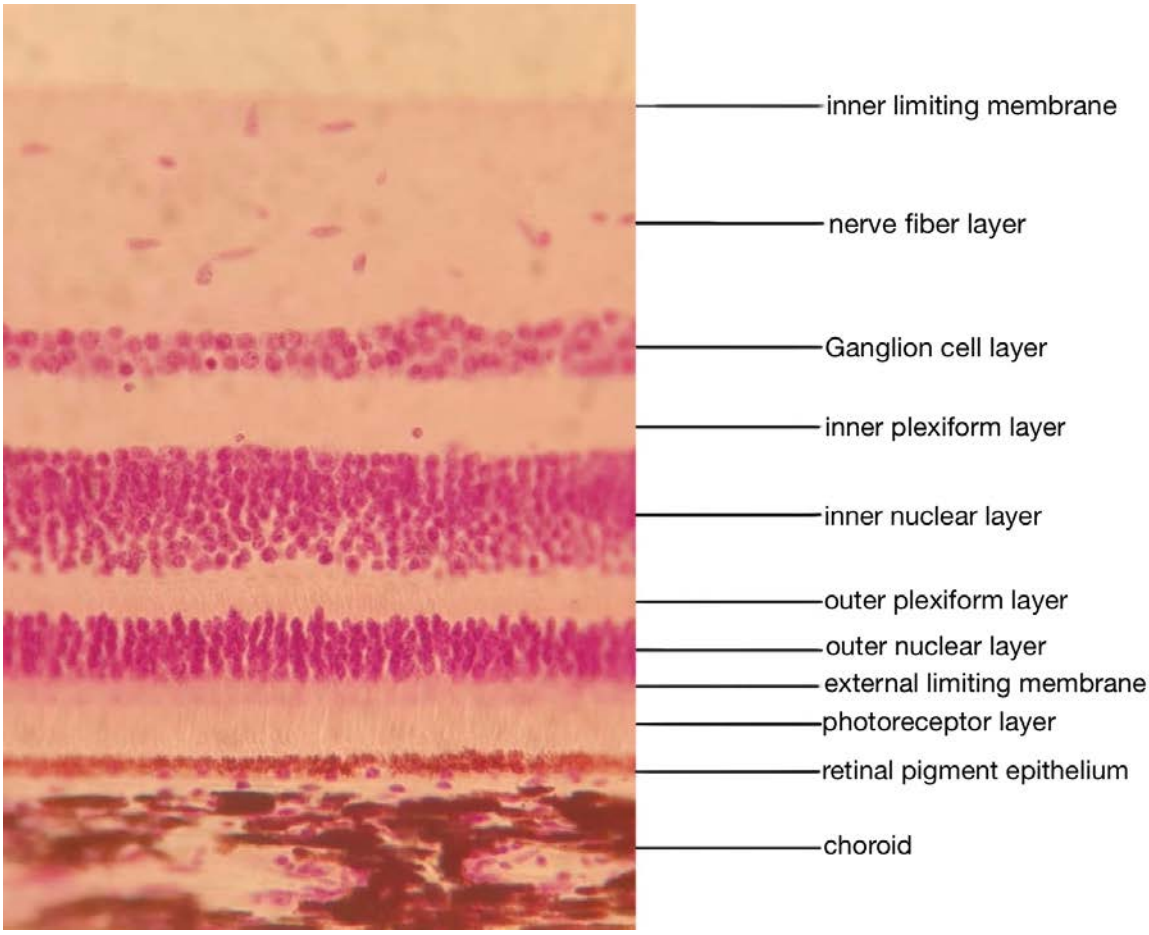

Figure 2: Retina under the microscope with accordingly labeled retinal layers.

Light enters the eye, gets transmitted through all layers and is first processed at the photoreceptor level where a signal is conducted. This signal then travels back along the layers of the retina and gets further processed before reaching the optic nerve. From there the visual information is moving along the chiasm and the optical tracts to the visual cortex, to higher levels of neural processing, where information is finally interpreted (55).

1.2.2 Receptive fields and ON/OFF-pathways

The signal of about 125 million photoreceptors has to be converged to only about one million ganglion cells, which process the signal further to the brain. The retinal area with all receptors that are connected to one ganglion cell, via synapses of bipolar, horizontal or amacrine cells, form a receptive field. (53,56).

There are two types of receptive fields, ON- and OFF-center. ON-center receptive fields give an excitatory reaction when the center is illuminated and inhibitory if no light is present. The periphery shows opposite signs and therefore an opposite reaction to present or not present light. The contrary appears in OFF-center receptive fields (57). The bipolar cell circuits enhance function in changing light conditions, in constant luminance conditions they are highly non responsive. Therefore, diffuse low contrast settings with minimal luminance changes inhibit excitatory reactions. Receptive fields can also be found in higher levels of neural processing (58). Figure 3 illustrates the schematic structure of a ON-center receptive field and the connected independent pathways.

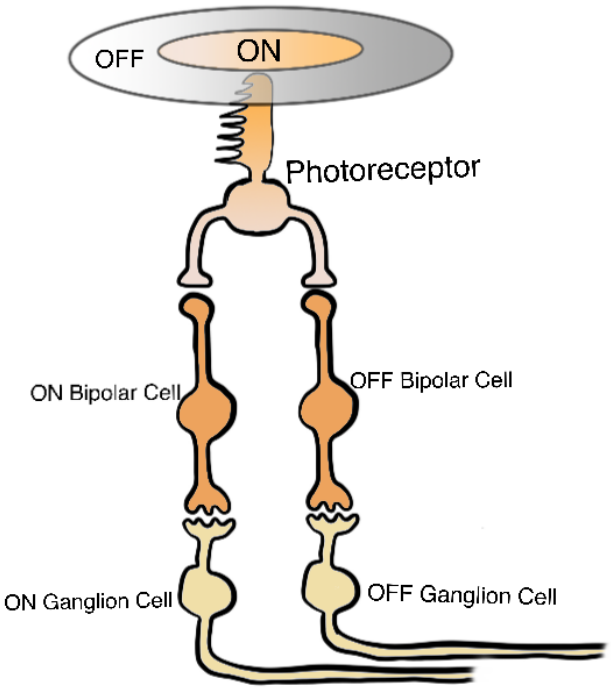

Figure 3: Schematic of an ON-center/OFF-surround receptive field of a photoreceptor with connected ON and OFF channels, the retinal bipolar and ganglion cells

The ON and OFF center receptive fields have separate neural pathways, originating from the bipolar cells. Pharmacological inhibition of the ON-channel synapses has proven that pathways remain largely independent of each other throughout higher levels of neurological processing (59,60). Moreover, Pan (61) demonstrated alterations of ON- and OFF-retinal ganglion cell responses by inducing defocus on mice retina, highlighting that plus and minus defocus produced different responses in subtypes of OFF cells compared to ON cells.

Despite these findings, the exact mechanisms of selective ON/ OFF pathway interactions on emmetropization remain unclear due to controversial study results. In experiments with monkeys, an impairment of contrast sensitivity (CS) was present after ON-pathway inhibition (59). By blocking the ON system pharmacologically in kitten, Smith et al. (62) found that the axial elongation process is dependent on the ON-channel activities. Decreasing axial length, and therefore hyperopia resulted from ON-channel inhibition. An experiment with chicken showed similar outcomes (63).

Electroretinogram experiments with mice retina demonstrated a reduction of negative lens induced myopia, after ON response elimination. Respectively, blockage of OFF responses lead to reduction of positive lens induced hyperopia (64). Mice with a mutation, preventing ON-channel development show a higher susceptibility for high and rapid processing deprivation myopia (65). The dynamic visual stimulation of ON-channels by increasing light stimuli leads to a thickening of the choroid, both in animal models and experiments with humans and vice versa for OFF-stimuli (66). Overstimulation of ON pathways in humans, by reading white on black text, thins the choroid about 16 µm within one hour (67). Choroidal interactions are suggested to have a direct link to myopia progress, a thickening of the choroid leads to less myopia. Whereas, a choroidal thinning is increasing myopia progression (68).

The underlying hypotheses of the novel diffusion spectacle lenses, proposes that myopia progression can be reduced by decreasing the ON-channel stimulation with optical diffusion. High myopia occurs due to abnormally high retinal contrast signaling, therefore a reduction of contrast is beneficial for myopia control (40). With diffusion lenses, less sharp edges are projected on the retina, the diffuse retinal images down-modulate the stimulation of receptive fields.

1.3 Contrast and edge sensitivity testing in vision and its relation to refractive error

This chapter illustrates the relations of CS, detection of edges and refractive error.

1.3.1 Contrast sensitivity

Contrast is described as the measure of the brightness or darkness of a field compared to its background. CS is the reciprocal of the contrast threshold required for the detection of a given SF. Contrast thresholds can be measured for different SFs. Plotting the CS against the SFs leads to the human CS function (69).

In humans, the peak of the CS function is between 3 to 6 cycles per degree (cpd) (70). Human resolution is limited by density of photoreceptors, hence a maximum SF of about 60 cpd can be resolved, which equals a VA of -0.30 log(minimum angle of resolution (MAR)) (70).

In a research setting, CS is typically measured with sinusoidal gratings called “Gabor patches” (71) or square wave gratings. Figure 4 illustrates the structure of a sinusoidal grating covered with a Gaussian envelope, a so called Gabor patch.

Figure 4: High contrast Gabor patch in 45° direction with Gaussian envelope.

Contrast in gratings is calculated using the Michelson contrast (Equation 1). Where L_{max} describes the maximum luminance, L_{min} the minimum luminance of the stimulus and C the resulting contrast value.

$$C = \frac{L_{max} - L_{min}}{L_{max} + L_{min}}$$

Equation 1: Michelson Contrast Equation, where L_{max}= maximum stimulus luminance, L_{min}= minimum stimulus luminance.

Computer based adaptive staircase tests are frequently applied, as found with the Freiburg Acuity and Contrast Test (FrACT) or the Tuebingen Contrast Sensitivity Test (TueCST) (69,72,73).

In a clinical setting, however, contrast charts are often used for CS testing, due to convenience and time factors (74). For example, Pelli-Robson optotype charts with decreasing contrast (75). Another chart based test is the Vistech test, where five SFs (1.5, 3, 6, 12, 18 cpd) are displayed with decreasing contrast values. The subject has to indicate the direction of the grating or if no grating is visible at all, so in total four choices (76).

1.3.2 Edge detection

In vision, edges are needed in the process of perception for the discrimination of shapes and structures. Hubel and Wiesel (58) found receptive fields in the cat's visual cortex which were specifically responsive to sharp luminance edges. Also in computer vision edges are crucial for image recognition by artificial intelligence (77).

In the detection of edges, a sharp luminance difference is needed. In classical CS testing no sharp distinction between luminance values is present, rather sinusoidal patterns with smooth transition in luminance are used. Campbell and Robson (78) investigated different grating patterns, such as sine and square patterns over a range of SFs. They could find a correlation between classic CS testing and the detection of edges. Shapley and Tolhurst (79) researched edge detectors in human vision psychophysically by measuring contrast

thresholds. Subthreshold addition was used for different stimulus patters, including sharp edges. Moreover, they could show a peak of CS for edges at about 3 cpd.

The Melbourne Edge Test (MET) is a screening test to measured edge contrast sensitivity (edge CS) at the peak of 3 cpd by indicating the directionality (0°, 45°,90°, 135°) of a presented edge (80). The average log (edge CS) for a 3 cpd stimulus is about 1.97 (81). Elder and Sachs (82) used a similar test to evaluate models for edge detection in human perception utilizing elongated and round bipolar stimuli. Suggesting that the peak SF tuning of receptive fields mediates edge detection, lies between 0.8 and 1.8 cpd.

1.3.3 Psychophysical test procedures for (edge) contrast threshold determination

Psychophysics researches the relationship between stimuli and perception. Psychophysical experiments can be distinguished into performance based and appearance based procedures, contrast detection tasks are considered performance procedures.

Several methods for the determination of thresholds are offered, like the method of constant stimuli, the method of limits, and the method of adjustment (56). By determining the threshold of a stimulus the psychometric function can be created. A stimulus that is detectable at 50% of all times is considered the threshold.

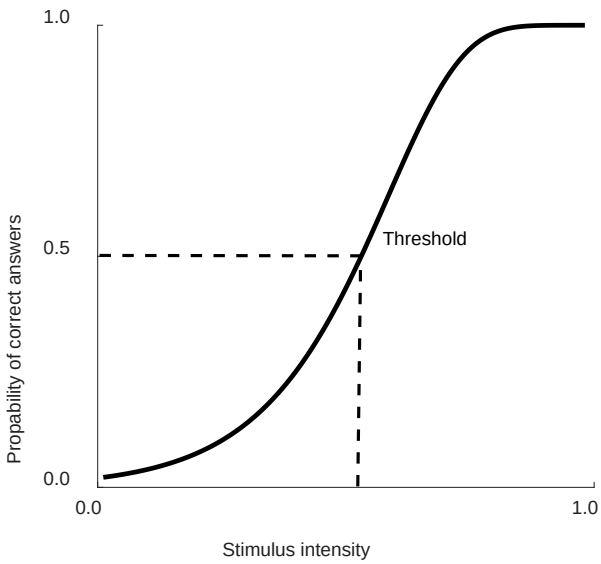

Figure 5: Psychometric function of a fictional experiment, threshold is indicated with dotted lines, abscissa: stimulus level, ordinate: subject performance.

In contrast testing, psychometric functions for different SFs are gained. The reciprocals of the thresholds for the individual SFs form the CS function.

Forced-choice tests are frequently used in psychophysical testing. If a subject is unsure about the correct answer, they are still asked to randomly guess an answer. Therefore, guessing rates occur. In a two-alternative forced choice test (2AFC) to probability to give a correct answer is 50%, in a four-alternative forced-choice test (4AFC) guessing rate is at 25%. Because of guessing rates, adjustments of the threshold need to be made: in a 2AFC test the threshold is at 75% of correct answers, for 4AFC test at 62.5% (83).

Computer based contrast tests are able to incorporate algorithms for time efficient and accurate threshold determination (84). The so called adaptive staircase procedures adjust stimulus step size to circle in thresholds (56). Figure 6 demonstrates the staircase of stimuli for a fictional 2AFC test. The used staircase method is the psi-method (85).

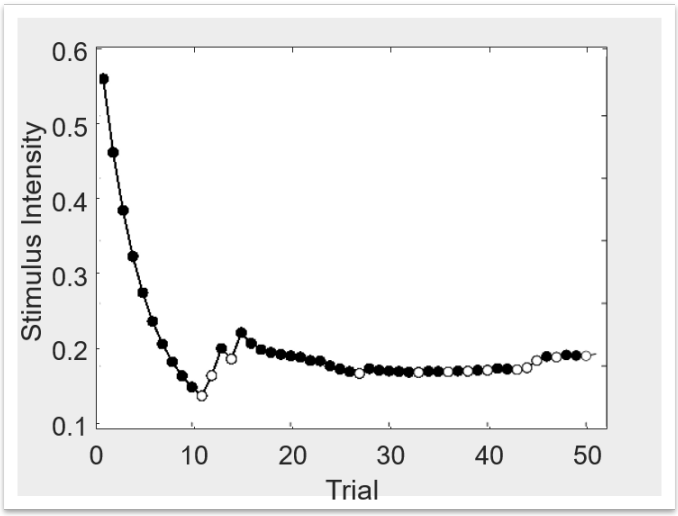

Figure 6: Example of stimulus presentations with an adaptive staircase procedure for a 2AFC test, black dots represent correct answers and white dots incorrect answers.

The next predicted stimulus intensity level after the predefined number of trials in considered the threshold.

1.3.4 Influence of blur, optical diffusion and myopia on (edge) contrast sensitivity

Since contrast and the detection edges are crucial visual functions, it is necessary to understand to which degree they can be influenced. Uncorrected refractive error and ocular media opacification are examples for internally induced blur and image diffusion.

Defocus-induced blur causes a decrease in CS. In non-myopic patients, CS reduction occurs systematic with increasing level of defocus, similar for positive and negative defocus values. The CS loss in myopes is significantly higher with positive lenses compared to negative defocus. Comparable, to the reduction of VA with defocus lenses (86,87). The higher the degree of defocus, the stronger the decrease of CS, with more impact on higher SFs.

Jansonius and Kooijman (81) investigated the influence of blur on the detection of edges and found a decline of edge CS with defocus amounts as small as ±0.5 D. Furthermore, they showed a reduction of CS of about 50% per each D of defocus. Compared to sine gratings, low SFs are more sensitive to blur than higher frequencies. At 3 cpd, effects of blur on sinusoidal stimuli and edges are equal.

Optical diffusion can be achieved by the induction of optical occlusion foils, so called Bangerter foils. The foils act as filters, reducing contrast and VA through a microbubble structure on the surface of the foils. The degradation of contrast is more pronounced in higher SFs (88,89). The density of the foil is indicated by a number, describing the VA that is still reachable with diffusion in place. During optical testing the filters did not show a match of image degradation and indicated density (89). Measured with optotype contrast charts, CS decreases significantly with a Bangerter foil in place. Thus, no significant difference between the single foils could be found (except the 0.1 foil) (88).

Stoimenova et al. (90) investigated the influence of refractive error on contrast thresholds and found higher threshold levels in myopes, despite optical correction. The study also proofed a negative correlation of CS and the amount of myopia. In another study, only high myopia influenced contrast thresholds (91).

On the other hand, Thorn et al. (92) cloud not validate an impact of high myopia on CS. Moreover, no impact of refractive error cloud be shown on the contrast thresholds of chromatic Gabor patches (93). Still, circular stimuli reveal a diminished sensitivity to low SFs.

An important factor influencing contrast thresholds over time is adaptation. In order to compensate for changes of visual contrast input, retinal cells enhance or decrease their sensitivity to contrast. High contrast inputs lead to reduced CS after an adaptation period and vice versa. In experiments with chicks, enhancement of CS could be achieved via optical

diffusion or defocus (94). Selectivity for SFs could be shown by Blakemore and Campbell (95). After short adaption periods, induced positive defocus increases CS responses also in humans (87). This asymmetry of reduction was also shown by Ohlendorf and Schaeffel (96). It is suggested that adaptation processes differ in emmetropes vs myopes. Myopic subjects have higher adaptation to high-contrast stimuli. Retinal contrast adaptation is suggested to be a possible signal for emmetropization processes (96).

2 Purpose of the study

The novel myopia control strategy induces peripheral contrast reduction via optical diffusion. the hypothesis of the underlying working mechanism suggests that retinal processes are altered by the contrast reduction. Especially, the inhibition of ON-channels mediated by receptive fields is expected to have a beneficial impact on myopia progression. The modified processes take place in the lower levels of neural circuity, which mainly influence signal processing towards the higher levels of visual processing in the brain. This study evaluates the influence of different levels of contrast reduction on the mechanisms of low-level neural circuity. The chosen unit to express the function of these low-level neural processes in the visual system is the edge CS for different SFs. Therefore, the aim of the study is to perform a psychophysical investigation of neural working mechanisms of the novel myopia control strategy.

3 Material and methods

In this chapter, the structure of the experiment, as well as the procedure of study are elucidated.

3.1 Study design, inclusion and exclusion criteria

This prospective, monocentric, randomized single-blind study was carried out at the University of Tübingen. The study protocol was approved by the ethics committee of the university and the protocol followed the Declaration of Helsinki 1975 and amends. Informed consent was obtained prior to measurements from each participant. To follow data protection regulations, a pseudo-anonymized ID was assigned to each subject.

In order to fulfill the inclusion criteria, participants had to be between 18 and 35 years of age with a distance visual acuity (VA) of 0.0 logMAR or better. Subjects with self-reported eye diseases and spherical equivalent refraction (SER) of greater than ±6.0 D and a cylindrical refraction greater than ±0.5 D were excluded. Subjects had no history of ocular surgery, did not use any optical myopia control strategies and did not wear contact lenses on the examination day.

3.2 Apparatus

The pre-measurements to check the inclusion and exclusion criteria. These included objective refraction (ZEISS i.Profiler plus, Carl Zeiss Vision GmbH, Germany) as well as subjective refraction (VISUPHOR 500, Carl Zeiss Meditec AG, Germany and VISUSCREEN 500, Carl Zeiss Vision GmbH, Germany). Biometry (IOLMaster 700, Carl Zeiss Meditec AG, Germany) was performed to measure axial length. OCT imaging (PlexElite, Carl Zeiss Meditec AG, Germany) was used in order to rule out retinal structural pathologies. During the experiment a trial frame (Universal Trial Frame UB 4, OCULUS Optikgeräte GmbH, Germany) is used to correct for patients' refractive error and to hold the lenses with Bangerter foils (Bangerter Occlusion Foils, Ryser Ophthalmologie, Switzerland).

Stimuli were generated on a DELL-Laptop with an Intel HD 4600 Graphic card (Intel, Santa Clara, CA, USA), operating on Windows 7 (Microsoft Inc., USA). Furthermore, MatLab (Matlab R2019b, MathWorks Inc., USA),the Psychtoolbox (97–99), as well as the Palamedes (100) Toolboxes were used. The stimulus was presented on a 9.7-inch retina display (Adafruit Industries, LLC, USA) with a 2048 x 1536 resolution and 256 grey levels. The mean display luminance was set to 146 cd/m2 using a candelameter (LS-100, Minolta, Germany).

A magnified view on the Bangerter foils was achieved with a 10x magnification microscope (CBS Beck, Kassel, Germany).

3.3 Stimulus

The experiment consisted of a psychophysical testing procedure with a two-sided stimulus achromatic stimulus. Subjects had to state the polarity of the stimulus via key press under different contrast and SF settings. Model for this test were the Melbourne Edge Test (80) and a similar noise layered test by Elder and Sachs 2004 (82). Noise in this experiment's stimuli consisted of zero-mean Gaussian noise with a variance of 0.01.

Figure 7 presents two examples of stimuli, the top right stimulus describes a high contrast and low SF, whereas the right stimulus is lower in contrast, but higher in SF.

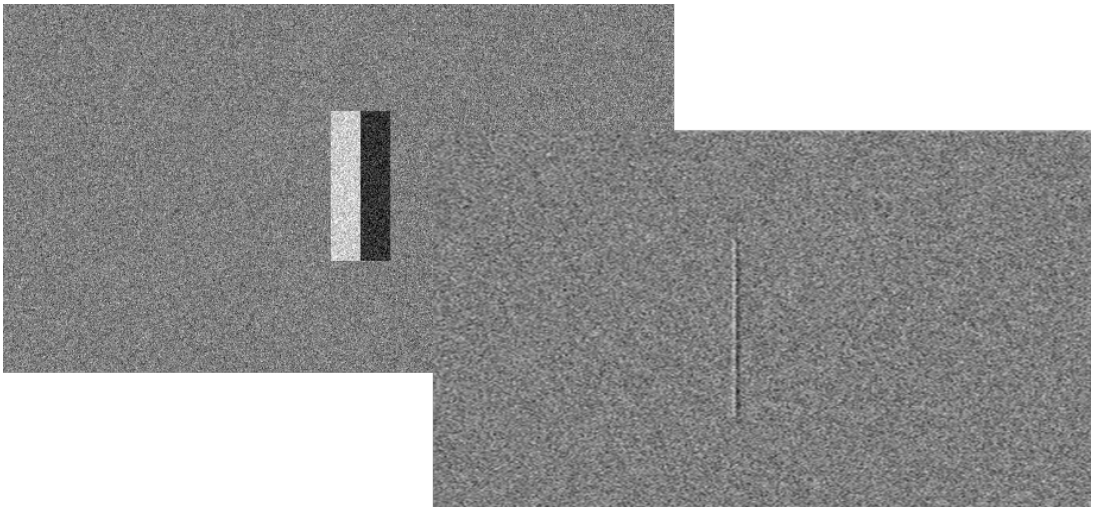

Figure 7: Example of two different stimulus widths and contrast settings embedded in Gaussian noise, top left: high contrast and lower SF, bottom right: low contrast and high SF.

The stimulus subtended one degree of visual angle in height, with varying width depending on the presented SF. The width of the stimulus was aligned to match SFs of 3, 6, 12, 18 and 24 cpd, respectively, as obtained via Equation 2. The SFs appeared in a randomized order.

$$w = \mathrm{d} \times \tan\frac{1}{SF}$$

Equation 2: Calculation of total stimulus width.

The distance between the eye and the stimulus (d) and the wanted spatial frequency (SF) were used to calculate the width (w) of the total stimulus, thus the two parts of the stimulus each exceed to half of the stimulus width. In this setup the distance to the stimulus was set to 1 m.

In order to compensate for effects of optical image magnification, the stimulus size was altered depending on the lenses that were in place for the correction of ametropia and near compensation. The thickness of the lens (d), refractive index (n), vertex distance (e), distance between cornea and first principal point of the eye (e') all influence the total magnification (N_G), described in Equation 3 .

$$N_G = \frac{1}{(1 - \frac{d}{n} - D)} \times \frac{1}{(1 - (e + e')S')}$$

Equation 3: Total Magnification factor of an optical system (101).

In this experiment lenses with n = 1.52 were used, negative lenses show a thickness of d = 0.5 mm and positive lenses of d = 1.0 mm. The distance from the lenses to the eyes was e = 8 mm and e' = 1.348 mm.

3.4 Study procedure

The experiment consisted of a psychophysical 2AFC performance test. Prior to the main experiment, a practice trial was performed to make sure the subject understood the task.

Only right eyes were measured, while left eyes were occluded. The test was executed in a dim room with an illuminance level of 15 lux. Test distance was set to 1 m. Therefore, a lens for accommodation compensation of +1.00 D was used. Constant distance to the monitor was guaranteed by the use of a headrest. Edge CS was tested for three conditions (Control, Bangerter foil 0.4 and Bangerter foil 0.8). The control condition used a clear plano lens and no Bangerter foil was in place.

The order of the test conditions was randomized and five minutes for adaption and washout time were given at the beginning and between the sessions. During these times the study participants were advised to look into distance.

The contrast of the stimulus changed depending on the answer by using the psi-method as an adaptive staircase method (85). After the adaptation, the experiment started, for each SF the contrast threshold was measured with 30 stimulus presentations. In each trial, three sub trials were performed, to test repeatability within the subjects. A complete session, including pre measurements, took about two and a half hours.

Study participants could start the trials by pressing the space bar on a keyboard, after audio signaling during the start screen occurred. Each stimulus presentation lasted 153 ms. After the stimulus, a grey response screen occurred with a fixation dot. Here, the participant had to state the polarity of the stimulus: Key “1” for the brighter part of the stimulus being located on the left side and “2” for being located on the right side. Figure 8 illustrates the different screens during the experiment.

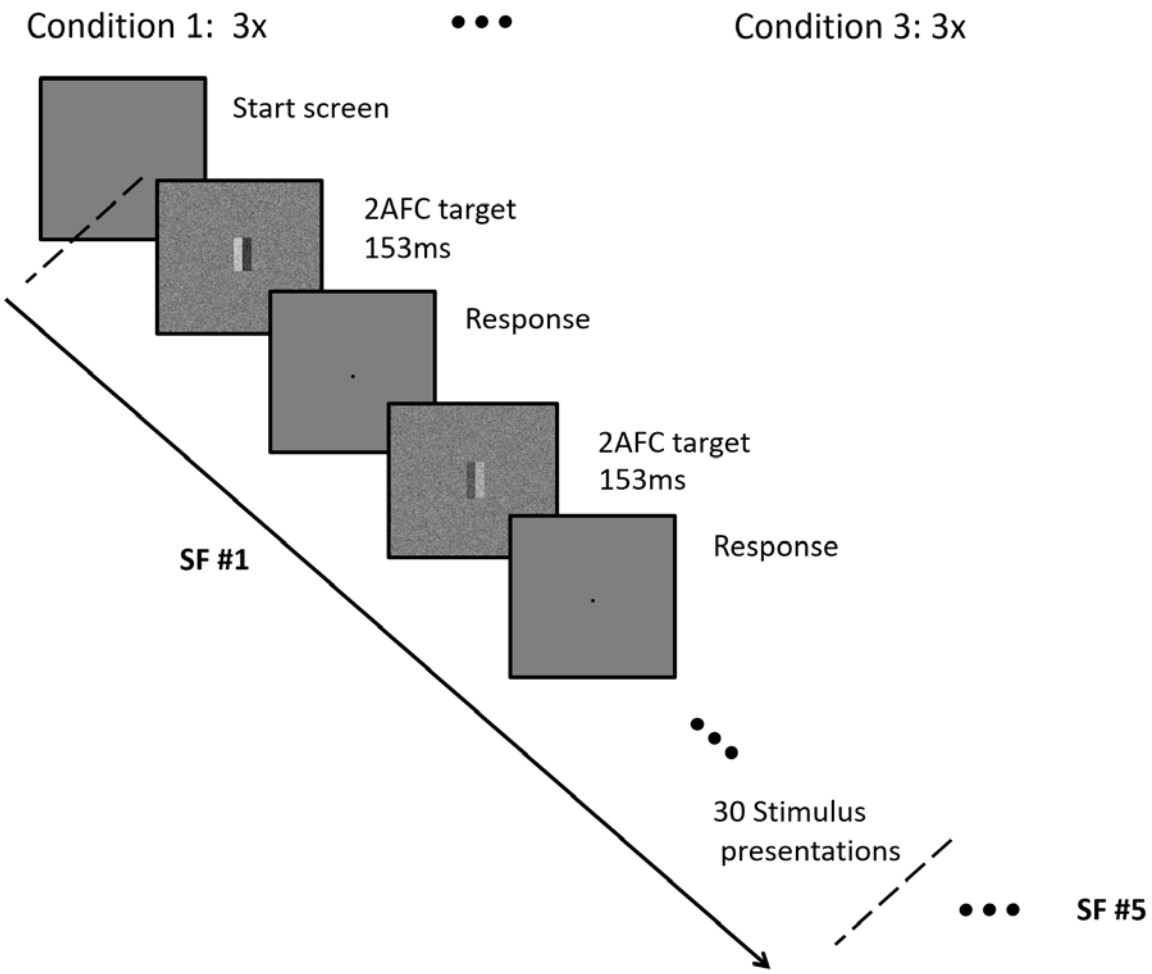

Figure 8: Detailed study procedure displaying two stimulus presentations of different contrast for SF #1 in the first condition.

3.5 Data analysis

Data collection and analysis both were performed using the MatLab software (Matlab R2019b, MathWorks Inc., Natick, USA). Repeatability of the testing procedure was analyzed via the coefficient of repeatability (CoR) separately for SFs and foil conditions using the within-subject standard deviation from a one-way ANOVA (102,103). Although data was not normally distributed as tested with Lillietest, a two-way repeated measures ANOVA was used for statistical analysis of results. Despite of the fact that ANOVA is created for normal distributions, Vasey and Thayer (1987) stated a robustness of repeated measures ANOVA for not normally distributed values (104).

The ANOVA consisted of two within-subject factors: SF and Bangerter foil density. No between-subject factor was existent for analysis. The dependent variable was the logarithmic reciprocal of the measured threshold, the log(edge CS), which was averaged across the three separate trials per subject and SF. The alpha-level was set to 0.05 and p-values lower than 0.05 were considered as significant.

4 Results

This study investigated the influence of Bangerter foil density on the edge contrast. Results of this experiment are given in the following paragraphs.

4.1 Study subject data

The total number of participating subjects was n = 5, consisting of four females and one male. The mean age was 24.60 ± 1.67 years. Axial lengths of the right eyes ranged from 21.67 to 24.70 mm, with a mean of 23.04 ± 1.18 mm. The averaged SER of the right eyes was -1.08 ± 2.53 D, with a range from +1.50 D to -5.25 D.

4.2 Repeatability

The CoR was calculated for each SF in each condition. Values are displayed in Table 2.

	CoR (log(edge CS))		
	Condition		
SF (cpd)	**Control**	**Bangerter foil 0.4**	**Bangerter foil 0.8**
3	0.23	0.21	0.12
6	0.30	0.31	0.45
12	0.31	0.45	0.19
18	0.25	0.25	0.15
24	0.30	0.01	0.02

Table 2: CoR (log(edge CS) for the three test conditions for the five measured SFs.

The CoR ranged between 0.01 and 0.45 log(edge CS). Lowest values were obtained with the Bangerter foils in the high frequencies. The mean CoR for the control group is 0.28 log(edge CS) and respectively 0.25 and 0.19 log(edge CS) for the 0.4 and 0.8 Bangerter foil conditions.

4.3 Effect of Bangerter foil density on edge CS

Median log(edge CS) values decrease with increasing SF. Bangerter foils induce a reduction in all SFs. Median log(edge CS) ± interquartile range (IQR) for 3, 6, 12, 18 and 24 cpd for all three test conditions are displayed in Table 3, as well as in Figure 1 showing the edge CS curve for the three test conditions.

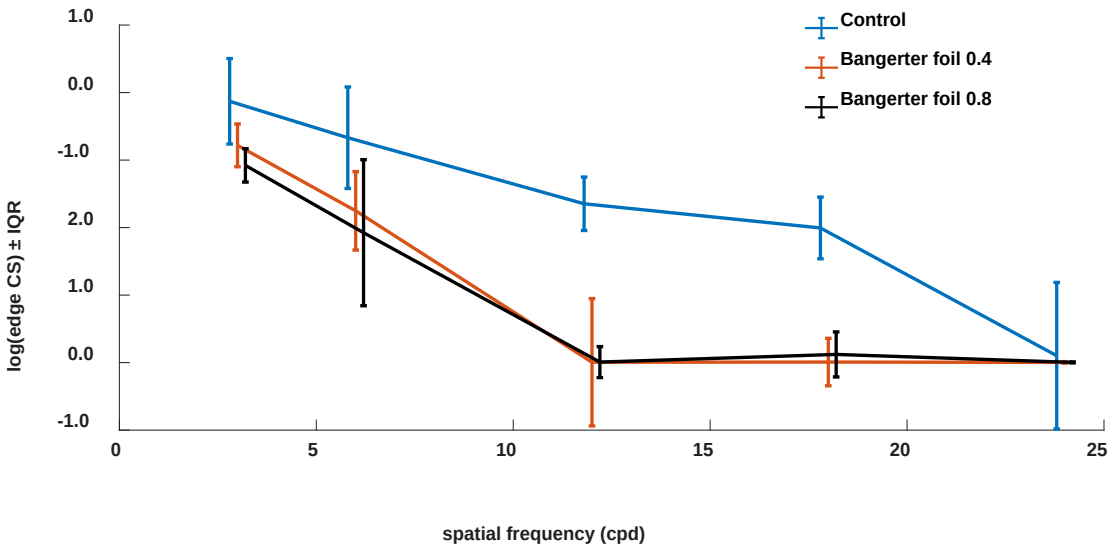

Figure 9: Median log(edge CS) ± IQR for the three test conditions (Control, Bangerter foil 0.4, Bangerter foil 0.8) for all tested SFs (3, 6, 12, 18 and 24 cpd).

	Median log(edge CS) ± IQR		
SF	**Control**	**Bangerter foil 0.4**	**Bangerter foil 0.8**
3 cpd	1.93 ± 0.32	1.61 ± 0.16	1.46 ± 0.12
6 cpd	1.67 ± 0.38	1.12 ± 0.29	0.96 ± 0.54
12 cpd	1.18 ± 0.20	0.00 ± 0.47	0.00 ± 0.11
18 cpd	0.99 ± 0.23	0.00 ± 0.18	0.06 ± 0.17
24 cpd	0.05 ± 0.54	0.00 ± 0.01	0.00 ± 0.00

Table 3: Median log(edge CS) ± IQR for the three test conditions (Control, Bangerter foil 0.4, Bangerter foil 0.8) for all tested SFs (3, 6, 12, 18 and 24 cpd).

Repeated measures 2-way ANOVA showed significant reduction of edge CS with optical diffusion in place ($p < 0.001$ in both cases), where in between the two test foils no significant difference ($p > 0.05$) was present, as seen in Figure 10. The foil with 0.8 density results in lower edge CS in the low frequency range, compared to the 0.4 foil. For frequencies of 12 cpd or higher the edge CS equalizes more for both diffusion foil conditions.

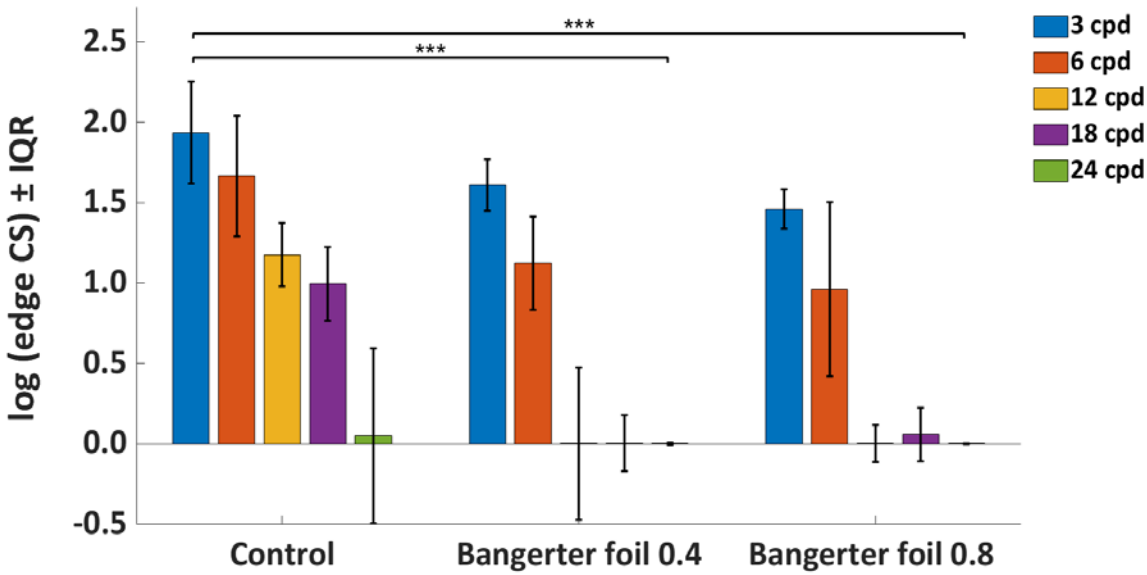

Figure 10: Comparison of median log(edge CS) ± IQR for the three test conditions with indicated significance levels between the conditions.

The reduction of edge CS is highest in the mid SFs. The differences between the control and the Bangerter Foil 0.4 all show significance, except for the 6 cpd ($p > 0.05$). The 24 cpd shows the least change ($p = 0.011$) followed by 3 cpd ($p = 0.007$), the remaining frequencies (12 and 18 cpd) show the greatest reduction of threshold values and also highest significance ($p < 0.001$).

In the case of the 0.8 Bangerter foil the reduction of log(edge CS) is lowest for 24 cpd ($p = 0.008$), followed by 3 cpd ($p < 0.001$). The reduction of mid SFs is highest (6 cpd $p = 0.033$; 1 cpd $p < 0.001$ and 18 cpd $p < 0.001$).

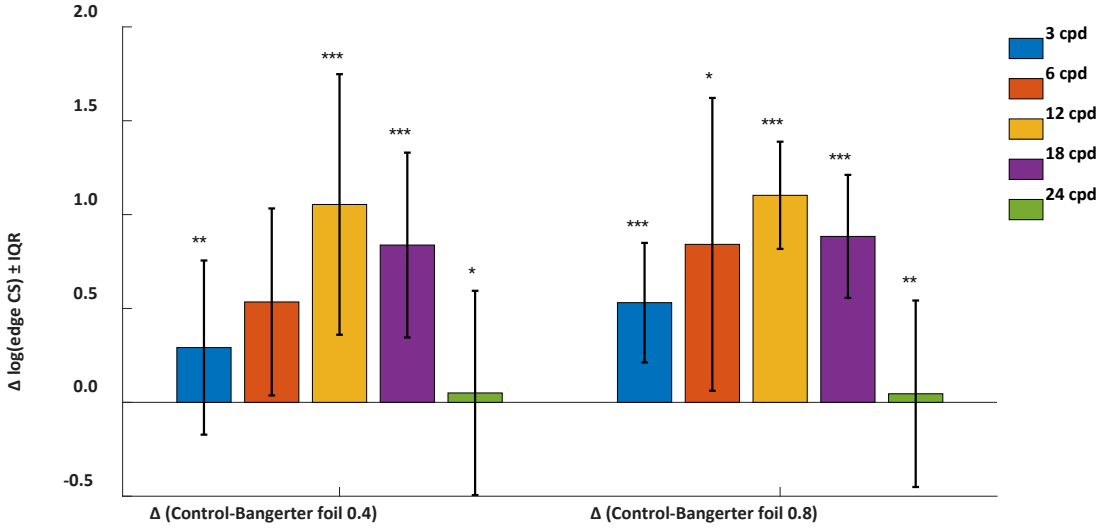

Figure 11: Differences of log(edge CS) of the control condition minus the foil conditions ± IQR with indicated significance levels.

4.4 Influence of axial length

The comparison of the most hyperopic and most myopic subject show lower baseline edge CS in the myopic subject. Edge CS for all measured SFs and conditions for the two subjects is displayed in Figure 12.

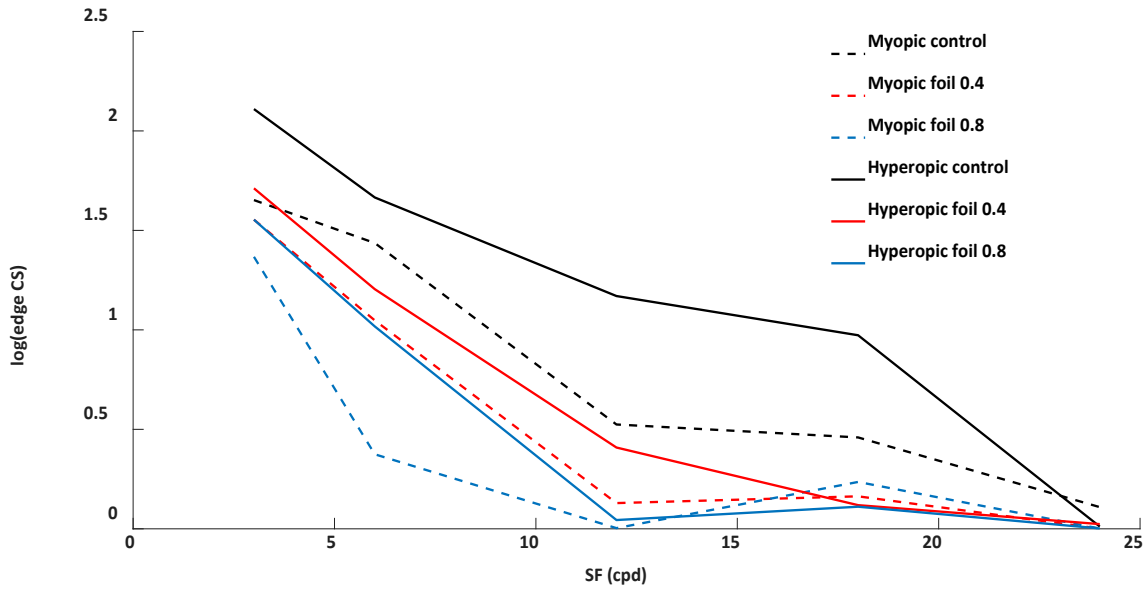

Figure 12: log(edge CS) of the most myopic (Subject 2) and most hyperopic (Subject 5) subjects for each test condition.

5 Discussion

The study analyzed the effect of contrast reduction via optical diffusion on edge CS thresholds, to investigate the low-level neural circuity of the retinal connections as a reflection of receptive field functions.

A significant reduction of edge CS could be found for both Bangerter foils compared to the control condition, but no difference between the two foils. The highest reductions could be found in the mid SF range. Repeatability of the edge CS test was in the range of other computer based CS testing and typically lower than found effect sizes.

5.1 Comparison of edge CS testing to classic contrast sensitivity tests

The question arises whether the used edge CS test is comparable to classic CS testing in research and what value the testing of edges adds to the already available procedures. Campbell and Robson (78) revealed a strong relation of sine wave (e.g. Gabor patches) and square wave gratings, as used in the current study. Moreover, both edge CS and CS peak at about 3 cpd a similar log CS or log(edge CS) is expected (70,81). Therefore, the testing of edges - also of single luminance edges - and sine gratings is comparable. Schilling et al. (72) compared CS for four different computer based contrast tests, namely the TueCST, FrACT, Functional Acuity Contrast Test (F.A.C.T) and quick CSF (qCSF). It is of interest to compare the results from the TueCST and the FrACT with the results from the current study, as shown in Table 3. All three tests exhibit the peak of sensitivity at 3 cpd. However, with egde CS being lower of almost 0.1 log(edge CS) than the other two tests at 6 and 12 cpd.

		SF			
		3 cpd	**6 cpd**	**12 cpd**	**18 cpd**
log CS/ log(edge CS)	**Edge CS**	1.93	1.67	1.18	0.99
	TueCST	1.91	1.74	1.29	0.93
	FrACT	1.96	1.78	1.36	1.02

Table 4: Comparison of edge CS testing to TueCST and FrACT . For the edge CS test median values of the five subjects are displayed, for TuCST and FrACT mean values from Schilling et al. are used (72).

The mentioned differences could possibly derive from the different testing procedures among the tests: The TueCST, as well as the FrACT use Gabor patches and circular grating patches with different directionalities in a 4AFC manner, respectively (72,73). However, all tests utilize an adaptive staircase procedure for threshold determination. It is important to mention, that the edge CS test only had 30 stimulus presentations for time efficiency reasons instead of 50, as used for the TueCST and the FrACT.

Repeatability of the edge CS test was calculated and showed best results in the filter conditions with 24 cpd. This is probably because the edge CS was reduced to a minimal value. Variability of repeatability throughout the different SFs might be because of adaptation processes. CoR in the control group compared to effect sizes is smaller for 3, 6 and 24 cpd. Therefore, valid results for these SFs can be considered. For the remaining SFs effect sizes exceed the repeatability values and log(edge CS) measurements are not as reliable. Looking at the foil conditions effect sizes and repeatability measures are very close.

Considering the repeatability of the edge CS test compared to the TueCST and FrACT, stimulus presentation time in the edge CS test was approximately halved. Furthermore, three test runs instead of two were present in this study. It is also important to mention, that twelve instead of five subjects were measured in the experiments by Schilling et al. (72). If assumed both repeatability units are directly comparable the edge CS test scores worse in the control condition. Schilling et al. calculated coefficients of repeatability for 3, 6, 12 and 18 cpd for the FrACT (0.20, 0.26, 0.33 and 0.48 log CS) and the TueCST (0.18, 0.15,

0.23 and 0.38 log CS). The control condition of the edge CS test provides similar or slightly better repeatability than the FrACT, but worse than the TueCST. Overall the edge CS test as a more uniform repeatability over all SFs and does not provide more reliable outcomes for certain SFs, like the TueCST.

5.2 Detection of edges

The detection of edges is a crucial visual function for object and shape recognition. The correlation of CS and edge detection was shown by Campbell and Robson (78).

This experiment was created as a measure of edge CS with strong guidance of the test used by Edler and Sachs (82), who utilized their setup to valuate a number of models for the psychophysical detection of edges. They further suggested stimulus noise as a useful tool to minimize pooling mechanisms. Therefore, the stimulus in this experiment was also covered in Gaussian noise. The overlying noise might have given higher thresholds for the detection of edges compared to a stimulus without noise, since the luminance edge was more difficult to distinguish. On the other hand, the noise reduces the impact of the edges that are created by the background.

Another approach to reduce the background-stimulus interaction would have been the use of a Gaussian envelope over the stimulus. Stimuli like this are also described to investigate the function of edge detectors and Gaussian envelopes are used in classic CS testing (72,79). Higher threshold levels could be expected with this type of stimulus setup; hence the luminance edge might be easier to distinguish.

Measurements with edge CS charts renounce any background interaction reduction means (80). Due to the fact, that the MET is a simple screening test only measuring at the peak SF of 3 cpd, there is no need for the test to control background interactions, especially in a clinical setting. Still, average log(edge CS) of the MET (1.97) and the test in this experiment (1.93 ± 0.32 at 3 cpd) are comparable. Furthermore, the descending edge CS values with increasing SFs proof the functionality of the test. Therefore, it can be assumed that the test used in this study is a useful experiment for the assessment of edge CS.

5.3 Impact of contrast reduction by optical diffusion on the detection of edges

This experiment showed that optical diffusion has an impact on the edge CS, although no impact of the density of image diffusion could be found. Optical occlusion filters (Bangerter foils) use optical diffusion to reduce contrast and VA, the number indicates to which VA the reduction occurs.

Bangerter foils of the densities 0.4 and 0.8 were used. Pérez et al. mentioned the inhomogeneity of the supposed filter density and the physical structure and optical properties of the foils (89).

Effects of optical diffusion on edges are not yet investigated by literature, however influence on CS was examined by the following studies: Odell et al. also measured the reduction of CS with different Bangerter foil densities using Pelli-Robson optotype charts. They showed higher changes with the 0.4 foil compared to the 0.8 foil (88).

Hence the results of this experiment seem surprising, where the 0.4 foil showed slightly less reduction of edge CS than the 0.8 density, however without statistical significance. Main differences between this experiment and the one used by Odell et al. (88) are the different testing mechanisms (Pelli-Robson chart vs. computerized edge CS test) and the measured test variable (CS vs. edge CS). Other probable reasons for this outcome might be manufacturing errors of the foils or, as already mentioned, the inconsistency of the physical structure and the optical properties.

In order to judge the used foils, microscopy was performed with the foils. A visible difference of dot density could be observed. Figure 13 depicts the microscopic view on the optical diffusion foils, where a higher number of dots can be counted on the 0.4 foil in comparison to the 0.8 foil. Same magnification and image size were used for the pictures.

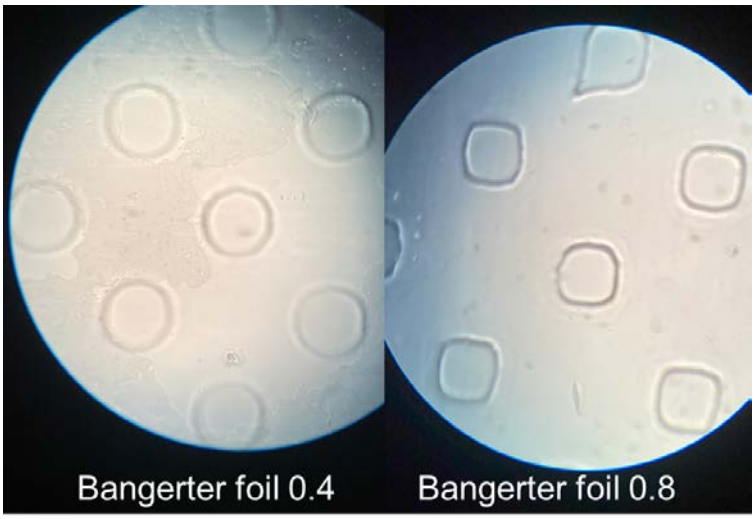

Figure 13: Microscopic view of the used Bangerter foils, left: Bangerter foil with 0.4 density, right: Bangerter foil with 0.8 density

The view through the three test conditions on a optotype chart shows a reduction of contrast and VA with the two used foils, as displayed in Figure 14. This leads to the conclusion, that the foils do not differ enough for significant distinction.

Figure 14: Demonstrated view through the control condition, Bangerter foil 0.4 and Bangerter foil 0.8 on optotypes

Still a significant degradation of edge CS occurred with the foils in place, especially in the mid and high frequency range. This outcome correlates with the results presented by Pérez et al. (89), who simulated retinal images with Bangerter foils and defocus. The denser the filter, the more SFs are influenced, starting high to low.

5.4 Edge CS and myopia

The comparison of the most myopic subject and the most hyperopic study participant (Figure 12) shows an overall lower edge CS for the myopic subject. Since the edge CS test is comparable to classic CS testing, the reduced edge CS for myopes correlates with findings of Stoimenova (90).

Contrary results are presented by Taylor et al. (93), not finding any significant correlation between refractive error and CS for gratings. In a study, where myopic patients were separated into groups, based on the amount of refractive error. Only in subjects with more -6.0 D of myopia showed significant decrease of CS (91).

Vera-Diaz et al. (105) could show an expansion of receptive fields in the periphery in myopes, whereas there was no difference between myopes and emmetropesfor foveal viewing conditions. This suggests, that receptive field interactions, and therefore the detection of edges, is altered more in peripheral regions of the retina. Therefore, receptive field functions in the periphery should be subject of further investigation.

This experiment revealed that optical diffusion interacts with low-level neural processes of the retinal circuity, by reducing edge CS. The question arises whether a lens design like the optical diffusion spectacle lenses can work for the control of myopia progression. The experiment simulated those lensess with Bangerter foils, inducing optical diffusion. In contrast to real spectacle lenses, the simulation did not have a clear aperture for clear foveal vision (50).

It is suggested that the optical diffusion minimizes the activation of ON-channels, by reducing visual edge stimuli. Pharmacological experiments proofed that inhibition of ON-pathways reduces axial elongation.

Fast increasing luminance stimuli, trigger ON-pathway interaction and showed choroidal thickening, both in animal and human studies. Therefore, it is questionable if the reduced contrast induces by optical diffusion lenses really causes less myopia progression. The preliminary results indicate that myopia progression can be decelerated with diffusion lenses (40).

Hence, a reduction of edge CS is more pronounced for mid and high SFs the same can be expected for real optical diffusion spectacle lenses. If myopia control via optical diffusion works, the SFs not affected by the optical diffusion have to be the ones needed for emmetropization processes.

Therefore, the question arises which SFs are essential for emmetropization. Visual feedback is the key guideline for emmetropization. It is known that occlusion causes excessive eye growth, deprivation myopia. Smith and Hung (106) could show a direct relationship of the degree of image and contrast degradation, and the amount of form-deprivation myopia. Suggesting, that also small alterations of image contrast can cause form-deprivation. In experiments with guinea pigs deprivation myopia occurred even when SFs (up to 12 cpd) above their maximum resolution (about 6 cpd) were cut off (107,108). An experiment with chicken demonstrated, that chicken exposed to mid SFs experience less form-deprivation, compared to low and high frequencies (109). Nevertheless, it is suggested that emmetropization and form-deprivation are not mediated by the same processes (110,111). As mentioned beforehand, spending more time in outdoor environments decreases risks for myopia onset and progression (20,21). Therefore, it is important to understand composition of SFs in different environments. Flitcroft et al. (25) analyzed 191 images of outdoor and indoor scenes. Outdoor scenes show in this comparison more mid and high SFs, relative to lower SFs. This might explain the myogenic differences of urban and rural populations of Chinese adults (13).

If the proposed hypotheses of diffusion lenses is true, there is still controversy about the mechanisms of action. Wang et al. (66) demonstrated that the visual stimulation of ON-pathways causes less myopia. The usage of proposed mechanism would inhibit ON-pathway stimulation. If optical diffusion acts more like pharmacological ON-channel blockage on receptive field processes, less myopia can be expected (59,59,62). The nature of optical diffusion presumes that the acting mechanism that resembles most is visual suppression of ON-pathway interactions. The promising results, of up to 74% less myopia progression within one year compared to a control group, show that the optical diffusion spectacle lenses are a working for myopia control. Nevertheless, further research on working mechanisms and long term results are needed.

5.5 Limitations of the study

This experiment limited the adaptive staircase to 30 stimulus presentations per SF for reasons of time efficiency. Test runs during programming leveled out, that the threshold at about 25 stimulus presentations is already representative for the threshold obtained after 50 presentations. Still, it is suggested that less than 30 trials are needed to achieve a 23% precision (85). Therefore, accuracy might be more limited in the current study compared to an experimental procedure with more staircase trials.

A factor that probably influenced the outcomes of this study is the small number of participants (n=5). Therefore, the findings are representative only for this group of healthy, young adults with various refractive errors.

The influence of axial length on edge CS was assessed only qualitatively in two subjects. As controversial results on myopia and CS are published, it would be interesting to gain knowledge about myopia and edge detection.

Time course of adaptation to full field optical diffusion was not measured, as mentioned beforehand, adaption to SFs has impact on threshold values. Long term effects of adaption to optical diffusion are of interest, since real optical diffusion lenses are designed to be worn fulltime.

Hence, simulated optical diffusion lenses were used in this experiment, there is limited common features for direct comparison. The Bangerter foils were administered without a clear aperture in the central visual field, because the goal was to gain basic understanding of processes. Therefore, the low-level neural process changes with a clear aperture are unknown and need further investigation.

6 Conclusion and outlook

This study provides evidence that central contrast reduction, induced by optical diffusion from Bangerter foils, has an impact on the edge CS. Mainly, edge CS in the mid SF range is reduced by optical diffusion. No impact of optical diffusion density could be proven. It can be thus concluded, that central contrast reduction via optical diffusion leads to changes in the low-level neural processing in the retina. Therefore, alterations of receptive field interactions could figure as a possible working mechanism for novel myopia control strategies.

In the future, the experiment should be continued with a larger population and the influence of axial length should be taken in the analyzation. Moreover, more Bangerter foil densities could be evaluated, as well as the influence of optical diffusion on peripheral edge CS. It would also be interesting to investigate the influence of contrast adaptation with optical diffusion foils in place. When real optical diffusion spectacle lenses are going to be available a comparison between the simulated and real ones has to be conducted. Hence, the real optical diffusion spectacle lenses have a clear aperture the influence of the size of this clear zone on edge CS centrally and peripherally should be investigated. Furthermore, the resulting edge CS with other myopia control methods should be subject of future scientific research.

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Declaration

I declare that this thesis, which I submit to Aalen University for examination in consideration of the award of a higher degree M.Sc. Vision Science and Business (Optometry) is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research program this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own. I have not already obtained a degree at Aalen University or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and acknowledged within the text.

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